ABSTRACTS

accp

American College of Clinical Pharmacy
2005 Annual Meeting
October 23–26 • 2005
San Francisco • California

ACCP Annual Meeting

October 23–26, 2005
San Francisco, CA

ORIGINAL RESEARCH

These papers describe original research in therapeutics, pharmacokinetics, pharmacodynamics, pharmacoeconomics, pharmacoepidemiology, and pharmacogenomics.

ADR/Drug Interactions

1. Adverse drug reactions in medicare patients: clinical and economic outcomes of pharmacist provided ADR management programs. *CA Bond, Pharm.D.*, Cynthia L. Raehl; Texas Tech University Health Sciences Center School of Pharmacy, Amarillo, TX.

PURPOSE: This study examines adverse drug reactions (ADR) in 8,208,960 hospitalized Medicare patients in 1998. An analysis of the impact of having an ADR, and the presence of pharmacist provided ADR management on clinical and economic healthcare outcomes is provided. A database was constructed from the 1998 MedPAR database and the 1998 National Clinical Pharmacy Services survey.
METHODS: The study population was composed of 141,398 Medicare patients who experienced an ADRs (incidence 1.73%). The most common classes of medications associated with ADRs were cardiotonic glycosides, adrenal corticosteroids, antineoplastic agents, anticoagulants, and analgesics. The most common diagnoses associated with ADRs were hypertension, congestive heart failure, atrial fibrillation, volume depletion disorders, and atherosclerotic heart disease. In patients developing an ADR, death rates were 19.18% higher (odds ratio = 1.208, 95%CI (1.184,1.234), length of stay was 8.98% higher (t = 23.695, p<0.0001), total Medicare charges were 19.86% higher (t = 39.398, p<0.0001), drug charges were 9.15% higher (t = 12.374, p<0.0001, and laboratory charges were 2.82% higher (t = 5.888, p<0.0001).
Pharmacist provided ADR management was evaluated in 1,945,296 patients from 572 hospitals. In hospitals that did not have pharmacist provided ADR management, the mean number of ADRs/100 admissions was 34.90% higher (odds ratio = 1.360, 95%CI (1.328, 1.392), death rates were 53.64% higher (odds ratio = 1.574, 95%CI (1.421,1.744), length of stay was 13.64% higher (t = 2.349, p=0.019), total Medicare charges were 6.88% higher (t = 2.462, p=0.015), and drug charges were 8.16% higher (t = 3.127, p=0.002). This is the first study to evaluate the incidence of ADRs in hospitalized Medicare patients.

2E. Rate of early-onset hypoglycemia associated with gatifloxacin in elderly patients. *Mark C. Decerbo, Pharm.D., BCPS*[1], Jingyang Fan, Pharm.D., BCPS[1], Alan L. Greenberg, MD[2]; (1)University of Southern Nevada College of Pharmacy, Henderson, NV; (2)University of Nevada School of Medicine, Las Vegas, NV.

PURPOSE: Sporadic case reports have linked fluoroquinolone antibiotics (FQAs), in particular gatifloxacin, with early-onset hypoglycemia. Most reports were in diabetic patients ≥ 65 years old who also received sulfonylurea therapy. We conducted a prospective cohort study to examine the rate of hypoglycemia associated with gatifloxacin in elderly patients.
METHODS: Patients ≥ 65 years old admitted to an urban, tertiary-care teaching hospital and initiated on antibiotic therapy were screened for eligibility. Patients were excluded if they were admitted to the ICU, received any antibiotics within the preceding 48 hours or received FQAs other than gatifloxacin. Eligibile patients receiving gatifloxacin were enrolled in the FQA cohort, while those receiving non-FQAs served as the control cohort. The primary outcome was the rate of hypoglycemia defined as a blood glucose level ≤ 60 mg/dl within 48 h after the first dose of antibiotic.
RESULTS: Of the patients in the FQA cohort, 22 of 77 (29%) were diabetic, compared with 41 of 119 (34%) in the control cohort (p=0.48). Hypoglycemia occurred in 10 of 77 (13%) patients receiving gatifloxacin as compared to 1 of 119 (0.8%) patients receiving non-FQAs (p=0.001). In the FQA cohort, hypoglycemia developed in 7 of 22 (32%) diabetic patients compared with 3 of 55 non-diabetics (5%), yielding a relative risk of 5.8 (95% CI 1.7–20.5, p=0.006). Of the 11 total patients who developed hypoglycemia, 8 were diabetic with 5 receiving sulfonylurea therapy.
CONCLUSION: This small, prospective cohort study supports the relationship between gatifloxacin therapy and the development of hypoglycemia within 48 h of the initial dose in patients ≥ 65 years old, especially if they have diabetes. Concomitant administration of oral hypoglycemic therapy is not required to experience this event. Clinicians should consider this association when selecting antibiotic therapy for elderly diabetic patients.
Presented at the 43rd Annual Meeting of the Infectious Diseases Society of America, San Francisco, CA, October 6–9, 2005.

3E. A 12-hour dosing interval reduces the pharmacokinetic interaction between simvastatin and telithromycin. *G. Montay, PhD*[1], P. Chevalier, PhD[1], C. Guimart, PhD[1], M. Guillaume, MD[2], V. Bhargava, PhD[3]; (1)sanofi-aventis, 13 Quai Jules Guesde, 94400 Vitry sur Seine, France; (2)Aster-Cephac, Paris, France; (3)sanofi-aventis, Bridgewater, NJ.

PURPOSE: Pharmacokinetic (PK) interactions have been reported between simvastatin (SIM) and drugs that inhibit cytochrome P450 3A4, including macrolide and ketolide antibiotics. This open, randomized, crossover study evaluated the extent of interaction following concomitant dosing of the ketolide telithromycin (TEL) and SIM vs dosing separated by a 12-hour interval (made possible as TEL can be administered once daily).
METHODS: Healthy adult males (n=14) received a single dose of SIM 40 mg (Day 1), followed by TEL 800 mg once daily (Days 2–6). A further 40 mg dose of SIM was coadministered with TEL on Day 5, or administered 12 hours before the final TEL dose on Day 6. Plasma concentrations of SIM and its active metabolite SIM acid were measured for 24 hours after each dose.
RESULTS: Compared with SIM alone, coadministration of TEL with SIM significantly (p<0.0001) increased peak plasma concentration (C_{max}) and area under the concentration–time curve ($AUC_{(0–z)}$) of both SIM (7.7- and 8.5-fold, respectively) and SIM acid (10.0- and 9.4-fold, respectively). Dosing of TEL 12 hours after SIM decreased the magnitude of this effect by >50%: C_{max} for SIM/SIM acid by 3.4- and 3.2-fold and $AUC_{(0–z)}$ for SIM/SIM acid by 4.0- and 4.3-fold, respectively. Study treatments were well tolerated.
CONCLUSIONS: Coadministration of TEL with SIM significantly increases plasma levels of SIM/SIM acid. A 12-hour interval between SIM and TEL administration reduces the magnitude of this interaction by >50%. This represents an advantage of TEL over macrolides, which are dosed 2–4 times daily.
Presented at the 43rd Annual Interscience Conference on Antimicrobial Agents and Chemotherapy, Chicago, IL, September 14-17, 2003.

4E. Multidrug resistance-associated protein 2 inhibition by ritonavir increases tenofovir-associated cytotoxicity. *Jerika T. Lam, Pharm.D.*, Michael N. Neely, M.D., Paul Beringer, Pharm.D., Stan G. Louie, Pharm.D.; University of Southern California (USC), Los Angeles, CA.

PURPOSE: This study evaluated the intracellular drug interaction between tenofovir (TFV) and ritonavir (RTV) and the role of multidrug resistance-associated protein 2 (MRP2) in renal cytotoxicity so to 1) compare the findings to documented clinical case reports of TFV in renal dysfunction, with the majority of cases in patients receiving both TFV and RTV-containing regimens, and 2) explore the intracellular mechanism(s) for the drug interaction.
METHODS: Madin-Darby Canine Kidney (MDCK) epithelial cell line and its overexpressing MRP2 (MDCK-MRP2) variants were exposed to TFV, RTV, or lopinavir (LPV) alone at concentrations ranging from 10 µg/ml to 1000 µg/ml. In addition, TFV 10 µg/mL was combined with increasing concentrations of RTV and other MRP2 inhibitors such as LPV, cyclosporine (CSA), and MK571. MDCK and MDCK-MRP2 variants were grown in the presence of these drugs, and their viability measured using MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide] assay. IC50 values for each drug combination were estimated by fitting the data to a Hill equation using the University of Southern California Laboratory of Applied Pharmacokinetics USC*PACK software.
RESULTS: The IC50 values after 24 hours of exposure to TFV, RTV, LPV, alone were ~1000, 130, and 130 µg/ml, respectively. When TFV 10 µg/ml was combined with either RTV or LPV, the estimated IC50 values were both approximately 100 µg/ml. However, when TFV was combined with MK571 and CSA, IC50 values could not be estimated. Similarly, when MDCK-MRP2 was treated with combinations of TFV plus MRP2 inhibitors, IC50 values could not be estimated after 24 hours of treatment exposure.
CONCLUSION: In the presence of TFV, inhibition of MRP2 inversely correlates with MDCK proliferation. However, MDCK-MRP2 cells are resistant to TFV plus MRP2 inhibitors even at the highest concentrations, suggesting overexpression of MRP2 may reduce TFV accumulation. This study suggests the role of MRP2 inhibition in TFV-associated renal dysfunction.
Presented at the 6th International Workshop on Clinical Pharmacology of HIV Therapy, Quebec, Canada, April 28-30, 2005.

5. Retrospective analysis of adverse drug reactions in pediatrics over a 10-year period. Jennifer Le, Pharm.D.[1], *Thuy Nguyen, Pharm.D.*[1], Anandi V. Law, Ph.D.[1], Jane Hodding, Pharm.D.[2]; (1)Western University of Health Sciences, Pomona, CA; (2)Miller Children's Hospital, Long Beach, CA.

PURPOSE: Considering the impact of adverse drug reactions (ADR) on morbidity and mortality, and the vulnerability of children to experience ADR, this study was designed to evaluate: 1) the incidence and common types of ADR with respect to severity level in hospitalized children, 2) frequency of ADR reporting by health-care providers and 3) follow-up processes resulting from the ADR.
METHODS: ADR report forms completed at Miller Children's Hospital between January 1995 and December 2004 were reviewed. A standardized form was used to collect data which included: patient demographics, ADR description and health outcome.
RESULTS: A total of 1,087 ADR were reported. The mean age was 7.0 (± 6.2) years and length of stay was 26.5 (± 36.4) days. The overall ADR incidence was 1.7%. Antibiotics (33%), narcotic analgesics (12%), anticonvulsants (11%) and anxiolytics (10%) were most commonly associated with ADR. The most common organ systems involved were: dermatologic (37%), cardiovascular (23%), and neurologic (16%). The severity of most ADR was low (89% level 1-3 vs 11% high level 4-6). There were no significant differences between ADR with low severity and high severity in terms of age and length of stay. Anticonvulsants and antineoplastic agents were more common with ADR rated high in severity. In addition, ADR occurring during surgery or before hospital admission were more commonly associated with a high severity. ADR were reported by pharmacists (89%), nurses (10%) and physicians (<1%). Although documentation of physician notification occurred in 93% ADR, only 29% were documented in patient's medical chart, 13% included follow-up education for individuals involved, and 10% were updated in the electronic allergy profile.
CONCLUSION: Measures to improve reporting and documenting of ADR by all health-care professionals should be undertaken to increase awareness and better understand the impact of ADR in pediatrics.

6. Intraparenchymal hemorrhage associated with sildenafil. *Paul L. Price, PharmD*[1], Christopher J. Holewinski, PharmD[2], Nancy L. Fagan, PharmD[1], Ronald W. Anderson, MD[2], Mark A. Malesker, PharmD[3]; (1)Creighton University Medical Center/Alegent Health Immanuel Medical Center, Omaha, NE; (2)Alegent Health Immanuel Medical Center, Omaha, NE; (3)Creighton University Medical Center, Omaha, NE.

PURPOSE: Sildenafil is approved for the treatment of male erectile dysfunction. It may cause serious central nervous system problems including stroke, subarachnoid, and intraparenchymal hemorrhages as reported in this case.
METHODS: A case of a left basal ganglia intraparenchymal hemorrhage occurring in a 58 year old white male is discussed. He was admitted on warfarin and PRN sildenafil. The patient developed slight numbness in the right hand, leg and foot without weakness after using sildenafil 25 mg. He proceeded to take an aspirin and went to bed. Upon awakening the same symptoms persisted so he went to the emergency room. A CT of his head showed a hemorrhage in the left frontal region. Upon discharge he was to follow up with primary care for future anticoagulation management, and instructed to have a MRI in four to five weeks.
RESULTS: Previous case reports describe sildenafil to cause central nervous system problems. Morgan reported a 50 year old man developed a transient ischaemic attack, after taking 50 mg tablet. Savizt and Caplan reported a 51-year-old man who suffered from 12 hour episode of transient global amnesia, and Monastero et al. reported a case of a 67 year old that developed a large left temporal subcortical hemorrhage. Finally Buxton et al. reported a case of a 44 year old man who took an unknown dose of sildenafil and developed a spontaneous intracerebral haemorrhage, which ultimately lead to his death. No history of strokes or intracerebral hemorrhage was noted in any patient.
CONCLUSION: Combining the inhibition of platelet activation with a probable increase in blood pressure during sexual activity may place patients at risk for hemorrhage. Physicians should use caution when prescribing sildenafil in patients with a history of strokes or risk factors for a stroke.

7E. Effects of clarithromycin on the pharmacokinetics of simvastatin. *G. Montay, MD*[1], P. Chevalier, PhD[1], C. Guimart, PhD[1], M. Guillaume, PhD[2], V. Bhargava, PhD[3]; (1)sanofi-aventis, 13 Quai Jules Guesde, 94400 Vitry sur Seine, France; (2)Aster-Cephac, Paris, France; (3)sanofi-aventis, Bridgewater, NJ.

PURPOSE: Concomitant administration of simvastatin (SIM) and erythromycin (ERY) has been shown to increase bioavailability of SIM 6-fold (Kantola T, et al. Clin Pharmacol Ther 1998;64:177–182). This open, non-randomized, repeated-dose study evaluated the magnitude of the pharmacokinetic (PK) interaction between standard doses of SIM and clarithromycin (CLA).
METHODS: Twelve healthy adult males received a single dose of SIM 40 mg on Day 1, followed by CLA 500 mg twice daily (morning and evening, 12-hour intervals) on Days 2–8. A further dose of SIM was administered concomitantly with the morning dose of CLA on Day 8 (evening dose of CLA administered 12 hours later). Plasma samples were collected for up to 24 hours post-dosing (Days 1 and 8) for assay of SIM and its active metabolite SIM acid.
RESULTS: Compared with SIM alone, coadministration of CLA and SIM significantly increased both peak plasma concentration and area under the concentration–time curve for SIM by approximately 8-fold ($p<0.0001$). Levels of SIM acid were also significantly (approximately 14-fold) higher during CLA treatment compared with SIM alone ($p<0.0001$). CLA had no significant effect on elimination of SIM or SIM acid. Both study treatments were well tolerated.
CONCLUSIONS: A standard dosing regimen of CLA significantly increases the plasma levels of SIM and SIM acid. The magnitude of interaction is considerably higher than that published for ERY; however, the lesser frequency of dosing with CLA (twice-daily dosing vs three-or four-times daily for ERY) may represent an advantage for CLA over ERY.
Presented at the 43rd Annual Interscience Conference on Antimicrobial Agents and Chemotherapy, Chicago, IL, September 14-17, 2003.

8. Case series: bosentan and warfarin interaction. *Kathleen B. Haynes, Pharm.D., BCPS*; Butler University, Indianapolis, IN.

PURPOSE: To report a case series of decreased international normalized ratios (INRs), and subsequent dose increase of warfarin, in patients receiving bosentan and warfarin.
METHODS: Patients in a pharmacist-managed anticoagulation clinic were directly observed for potential drug interactions at each clinic visit. Three clinic patients were initiated on bosentan while already taking warfarin. Along with other clinically significant information, new drug therapy and dose changes of all medications were documented in the patient's chart. This information suggested a drug interaction that may require dosage adjustments of warfarin.
RESULTS: Patient #1 was stable on warfarin for approximately 6 months with a 30 mg weekly dose. After initiation of bosentan, it was difficult to stabilize the warfarin dose. The most common weekly warfarin dose did increase by 40% to 42 mg weekly. Patient #2 was relatively stable on 47.5 to 50 mg weekly of warfarin, when bosentan was initiated. As with the previous patient, it took multiple dose adjustments of warfarin before finding a recommended new dose. This patient eventually became quite stable on warfarin 65 mg weekly, a 23-27% increase in dose. Patient #3 was discharged from the hospital after initiating warfarin with an INR of 1.95 and on a dose of 28 mg weekly. Bosentan was started upon discharge and the bosentan dose was subsequently increased in four weeks. This patent required an initial increased warfarin dose of 32 mg weekly, which increased to 36 mg weekly with the bosentan dose increase. This is a final increase of 22% in the weekly warfarin dose.
CONCLUSION: Based on evidence from the case series, it suggests a potential clinically significant drug interaction between bosentan and warfarin. Bosentan is known to induce the CYP2C9, CYP3A4, and possibly the CYP2C19 enzymes, which all play a role in warfarin metabolism.

Analgesia

9E. Evaluation of functional outcomes: duloxetine in the treatment of diabetic peripheral neuropathic pain. Amy Chappell, MD[1], Kar Wong, PhD[1], James Russell, MD[1], Misha Backonja, MD[2], *Jeff Hille, MS*[3], Deborah D'Souza, PhD[1], Trong Le, MS[1]; (1)Eli Lilly and Company, Indianapolis, IN; (2)University of Wisconsin Medical School, Madison, WI; (3)Eli Lilly and Company, San Francisco, CA.

OBJECTIVE: Determine the impact of duloxetine compared with placebo on patient-reported health outcomes over a 12-week period, in the treatment of diabetic peripheral neuropathic pain (DPNP).
METHODS: The results were pooled from three 12-week (acute treatment period) multicenter, double-blind studies. In study 1 (N=457) patients with DPNP were randomly assigned to treatment with duloxetine 20 mg QD, 60 mg QD, 60 mg BID, or placebo. In studies 2 (N=334) and 3 (N=348), patients with DPNP were randomly assigned to treatment with duloxetine 60 mg QD, 60 mg BID, or placebo. Patient-reported functional outcomes were measured by the interference portion of the Brief Pain Inventory (BPI), Short Form 36 (SF-36), and European Quality of Life Instrument 5D version (EQ-5D). The reported results were all the functional outcomes from the completer (patients who remained at the end of the study) data of patients treated with duloxetine 60 mg QD and 60 mg BID (patients treated with duloxetine 20 mg QD were excluded from the analyses).
RESULTS: In the SF-36 health survey, duloxetine 60 mg QD and 60 mg BID were significantly superior to placebo in the subscale of general health, bodily pain, vitality, SF12 physical score, physical functioning, and role physical ($p\leq.014$). In the BPI interference scales, duloxetine 60 mg QD and 60 mg BID were significantly superior in the scales of general activity, walking ability, normal work, and sleep ($p\leq.003$). In the analysis of the EQ-5D, duloxetine 60 mg QD ($p=.004$) and 60 mg BID ($p<.001$) were both significantly better than placebo.

CONCLUSION: Treatment with duloxetine was associated with significant improvement in functional outcomes. The results highlight the functional improvement associated with duloxetine in the treatment of DPNP.
Presented at the 65the Scientific Session of the American Diabetes Association, San Diego, CA, June 10-14, 2005.

10E. Developing a study protocol to compare topical tetracaine to placebo before the administration of botulinum toxin for axillary hyperhidrosis. *Caitriona M. Gowing, BSc, (Pharm), MSc, (Hosp, Pharm)*, James M O Riordan, MB, Sean Tierney, MCh; AMNCH, Dublin, Ireland.

INTRODUCTION: Botulinum toxin injection is an effective treatment for axillary hyperhydrosis but many patients find the injections quite painful.
PURPOSE: (1) To develop and extemporaneously compound a placebo that would facilitate blinding of the study. (2) To design a study protocol. (3) To determine the effectiveness of a topical anaesthetic cream in reducing the pain and discomfort associated with botulinum toxin injections for axillary hyperhydrosis.
METHODS: A number of topical preparations were compounded and their physical characteristics (colour, texture, texture on refrigeration) compared to tetracaine gel (Ametop Gel™). A study protocol was designed to allow randomization and blinding of the study. Fifteen patients having botulinum toxin injection (Dysport™) were randomized. Tetracaine gel (Ametop Gel™) was applied to one axilla and the chosen placebo (surgilube and aqueous cream) to the other axilla 45 minutes prior to the procedure. Ten 100 µl (250 unit/axilla) intradermal injections of Dysport were then administered in each axilla. After injection, each patient completed a questionnaire and marked their subjective impression of the pain associated with the injections in each axilla on visual analogue scales (0-10) and stated which side they found more painful.
RESULTS: All patients completed the study and all fifteen found that the injections in the treated side were less painful than the placebo side. The mean pain score (± standard deviation) associated with the tetracaine use was 1.5 (±1.1) versus 4.7 (±1.9) for the placebo side (p=0.001, Wilcoxon). There were no adverse effects associated with either the placebo or the tetracaine gel.
CONCLUSIONS: Topical tetracaine gel is a safe and effective method of reducing patient discomfort associated with botulinum A toxin injections for axillary hyperhydrosis.
Presented at the Annual Educational Conference of the Hospital Pharmacists Association of Ireland, Dublin, Ireland, April 22-24, 2005.

11E. Duloxetine in the treatment of diabetic peripheral neuropathic pain: results from three clinical trials. Joel Raskin, MD[1], Yili Pritchett, PhD[2], Amy Chappell, MD[2], *Wahiba Estergard, PharmD*[3], Deborah D'Souza, PhD[2], Shuyi Shen, PhD[2], Joachim Wernicke, MD[2]; (1)Eli Lilly Canada, Scarborough, ON, Canada; (2)Eli Lilly and Company, Indianapolis, IN; (3)Eli Lilly and Company, Phoenix, AZ.

PURPOSE:The efficacy and safety of duloxetine, a dual reuptake inhibitor of serotonin and norepinephrine, on the treatment of diabetic peripheral neuropathic pain (DPNP) was assessed in 3 studies.
METHODS:Patients with DPNP of at least 6 months duration, and without depression as diagnosed by DSM-IV were enrolled in the 12-week acute therapy studies. Study 1 (N=457) had treatment groups of duloxetine 20-mg once daily (QD), 60-mg QD, 60-mg twice daily (BID), and placebo; Studies 2 (N=334) and 3 (N=348) compared duloxetine 60-mg QD and 60-mg BID with placebo. The primary outcome measure was the weekly mean score for 24-hour average pain severity based on an 11-point Likert scale.
RESULTS: Across all three studies, duloxetine 60-mg QD and duloxetine 60-mg BID demonstrated significant treatment effect on DPNP and showed rapid onset of action, with separation from placebo occurring at week one on the 24-hour average pain severity score (p<.001). This finding was confirmed in most secondary measures for pain. Duloxetine 60-mg QD and 60-mg BID achieved similar efficacy results on most measures, with duloxetine 60-mg BID showing significantly more improvement on some McGill pain descriptors. The evaluation of Clinical Global Impression of Severity and Patient Global Impression of Improvement also demonstrated superiority of duloxetine 60-mg QD and 60-mg BID over placebo. A significant treatment effect for duloxetine was observed for most health outcome measures. Duloxetine showed no adverse effects on diabetic control or complications, and was safely administered and well tolerated.
CONCLUSION: In these clinical trials, duloxetine (only FDA-approved drug for DPNP) was an efficacious and safe treatment for patients suffering from DPNP.
Presented at the Annual Meeting of the American Psychiatric Association, Atlanta, GA, May 2005.

12E. Randomized, multi-center study of oral once-a-day AVINZA® (morphine sulfate extended-release capsules) vs. twice daily OxyContin® (oxycodone hydrochloride controlled-release) for the treatment of chronic moderate to severe low back pain. *Richard L. Rauck, MD*[1], Stephen A. Bookbinder, MD[2], Timothy R. Bunker, MD[3], Christopher D. Alftine, MD[4], E. De Jong, MD[5], Steven L. Gershon, MD[6]; (1)The Center for Clinical Research, Winston-Salem, NC; (2)Ocala Rheumatology Research Center, Ocala, FL; (3)The Birmingham Pain Center, Birmingham, AL; (4)Medford Medical Clinic, Medford, OR; (5)Organon Pharmaceuticals USA, Inc., Roseland, NJ; (6)Advanced Pain Management & Rehabilitation, PC, Virginia Beach, VA.

OBJECTIVE: To evaluate the efficacy of oral once daily AVINZA vs. twice daily OxyContin in patients 30-70 years old requiring opioid therapy for chronic moderate to severe low back pain.
METHODS: Randomized, parallel-group, multi-center study. Patients were randomized to receive either AVINZA once-a-day or OxyContin twice-a-day. Ibuprofen (200 mg tablets) was given for rescue medication. After randomization, patients underwent a three- to six-week titration period before entering the eight-week study period. Evaluation criteria included daily pain assessment (through the Brief Pain Inventory), sleep parameters (PSQI), rescue medication requirements and daily doses of study medication.
RESULTS: This abstract presents the initial data from the first group of 329 patients enrolled in the study. The demographics for both groups of patients were similar. Patients in the AVINZA group (n=105) reported greater decreases in their mean absolute BPI pain scores throughout the 8 weeks of the trial than patients using OxyContin (n = 107). These decreases were statistically significant at both 9 (P = 0.03) and 12 hours (P < 0.01) post-dose. Patients taking AVINZA also reported a statistically better quality of sleep as measured by their PSQI scores (P< 0.01) along with a statistically significant reduction in the number of rescue medication doses (total number of rescue doses: AVINZA = 2092 vs. OxyContin = 2493; P< 0.01). AVINZA-treated patients also used a lower total daily opioid requirement than OxyContin-treated patients when calculated as median morphine equivalents (58 vs. 82.5 mg). The mean incidence rate of elicited opioid side effects was similar between the treatment groups.
CONCLUSIONS: In this cohort of patients with chronic low back pain, those using once-daily AVINZA experienced better pain relief, quality of sleep and fewer rescue medication doses than patients using twice-daily OxyContin. Final study data will be presented.
Published in J Pain 2005;6(3 Suppl 1):S45.

13E. Topical Xibrom™ (bromfenac ophthalmic solution) 0.09%, an investigational NSAID, significantly and rapidly decreased post-cataract surgery inflammation and reduced ocular pain. *Lisa R. Grillone, PhD*[1], Eric D. Donnenfeld, MD[2], Edward J. Holland, MD[3], Robert Stewart, MD[4]; (1)ISTA Pharmaceuticals, Inc., Irvine, CA; (2)Ophthalmic Consultants of Long Island, Rockville Center, NY; (3)Cincinnati Eye Institute, Cincinnati, OH; (4)Houston Eye Associates, Houston, TX.

PURPOSE: To evaluate the efficacy and safety of Xibrom (bromfenac ophthalmic solution) 0.09%, compared with placebo (vehicle) dosed b.i.d. for 14 days following cataract surgery with a 14 day follow-up for safety, in two Phase III randomized, placebo controlled studies conducted under a common protocol.
METHODS: Subjects with Summed (cell + flare) Ocular Inflammation Score (SOIS)greater than or equal to 3 following cataract surgery, in the absence of any anti-inflammatory medication, were randomly assigned to bromfenac or placebo (2:1). Treatment was initiated 16-32 hours following surgery. Efficacy assessments: days 3, 8, 15, 22 and 29. Key secondary efficacy endpoints included mean change from baseline for SOIS prior to receipt of any rescue medication and time to resolution of ocular pain. Ocular and systemic safety was assessed throughout the study.
RESULTS: Eligible subjects (527) with mean baseline SOIS=3.7, were treated with bromfenac 0.09% (356) or placebo (171). Mean change in SOIS from baseline was statistically significant on days 3, 8 and 15 following initiation of treatment. Day 3 mean change was 1.4 (bromfenac) vs. placebo 0.9 (p<0.0002); day 8 mean change was 2.4 (bromfenac) vs. placebo 1.1 (p<0.0001), and at day 15, mean change was 2.9 (bromfenac) vs. placebo 1.5 (p<0.0001). The mean number of days to resolution of ocular pain for bromfenac was 1.9 vs. placebo 5.9 (p<0.0001). Placebo treated patients had more ocular adverse events.
CONCLUSION: Bromfenac ophthalmic solution 0.09%, a b.i.d. NSAID was effective in reducing post-cataract surgery inflammation as early as the first post-treatment visit. Bromfenac was effective for treating ocular inflammation (mean change from SOIS baseline) and decreasing the days for resolution of ocular pain. Bromfenac was well tolerated with fewer ocular adverse events reported compared with placebo.
Presented at the Annual Meeting of the Association for Research in Vision and Opthalmology, Fort Lauderdale, FL, May 1-5, 2005.

Cardiovascular

14E. Effects of clopidogrel versus cilostazol in coronary artery stenting. *In S. Song, M.S.*[1], Jung Mi Oh, Pharm.D.[2], Seung K. Choi, Ph.D[3]; (1)Dept. of

pharmacy, Bundang CHA General Hospital, Kyeonggi-do, South Korea; (2)Graduate School of Clinical Pharmacy, Sookmyung Women's University, Seoul, South Korea; (3)Department of Pharmocology, College of medicine, Pochon University, Kyeonggio-do, South Korea.

PURPOSE: To evaluate the efficacy and safety of clopidogrel plus aspirin compared with cilostazol plus aspirin in coronary stenting and to evaluate the efficacy of clopidogrel loading dose prior to coronary stenting in clopidogrel group.
METHODS: Data were retrospectively collected from medical charts of patients who had undergone coronary stenting and received either clopidogrel with or without loading 300 mg followed by 75 mg/d (n=58), or 200 mg/d cilostazol (n=72) for 1 year, between January 2000 and May 2002. All patients received aspirin 200mg/d throughout the study. The primary endpoints at 7, 30, 180 and 365 days were the composite of death, MI, stroke, angina, and revascularization in the intent to treat population and restenosis at follow up angiography. The secondary endpoint was incidence of bleeding complications at 7, 30, and 365 days, and durg adverse effects at 365 days.
RESULTS: At 180 and 365 days, the combined primary endpoint was significantly reduced in clopidogrel plus aspirin(relative risk 0.39; 95% CI 0.17 to 0.92; p=0.021, RR 0.43; 95% CI 0.22 to 0.84; p=0.0085, respectively). However, the combined primary endpoint was not significantly different between the two groups at 7 and 30 days (p=1.00, p=0.79, respectively). Angiographic restenosis rate was 14.3% in clopidogrel plus aspirin and 32.1% in cilostazol plus aspirin (p=0.19). 300 mg of clopidogrel loading dose did not significantly reduce the combined primary endpoint at 30 days (RR 0.14; 95% CI 0.01 to 2.65; p=0.23). The rate of bleeding complications and drug adverse effects were not different between the two groups.
CONCLUSIONS: In patients undergoing intracoronary stenting, clopidogrel plus aspirin therapy is more beneficial than cilostazol plus aspirin in reducing major adverse cardiac events with similar rate of bleeding complication. A loading dose of clopidogrel did not lead to a statistically significant reduction in major adverse cardiac events.
Presented at the Midyear Clinical Meeting of the American Society of Health-System Pharmacists, New Orleans, LA, December 7-11, 2003.

15E. Assessment of lipid management in an academic VA medical center. *Alexandria A. Piotrowski, Pharm.D.*[1], Lonnie K. Wen, R.Ph., Ph.D.[2], Thane Erwin, R.Ph.[1], William D. Linn, Pharm.D[1], Nicole L. McMaster, Pharm.D., BCPS.[1]; (1)South Texas Veterans Health Care Administration, University of Texas at Austin, San Antonio, TX; (2)Pfizer, Inc., San Antonio, TX.

PURPOSE: Evidence suggests that treatment of hypercholesteremia is suboptimal. Less than 20% of patients with established coronary heart disease (CHD) have achieved the low-density lipoprotein (LDL) goal specified by the NCEP Adult Treatment III Panel. The purpose of this investigation was to examine the reason(s) why high-risk patients have not achieved LDL goals.
METHODS: Computerized medical records (CPRS) were used to identify patients with coronary heart disease (CHD), diabetes, or both who have not attained the VA-specified low-density lipoprotein (LDL) goal (100mg/dL and 120mg/dL for CHD and diabetes, respectively). Eligible patients received care at the VA Internal Medicine Clinic between December 10, 2003 and December 13, 2004. Patients were excluded if the LDL goal was attained at time of evaluation, or the diagonosis of either heart disease or diabetes could not be confirmed. Documentation from the most recent physician-patient encounter was used to determine whether an appropriate intervention was made and the possible reasons for not attaining lipid goals.
RESULTS: Data from 124 veterans were included in the analysis. Ninety-nine (79.8%) of patients had diabetes, 58 (46.8%) patients had CHD and 33 (26.6%) had both diabetes and CHD. Overall, mean LDL-cholesterol was 139.0mg/dL ± 30.4 in this cohort of high-risk patients. Despite not attaining the LDL goal, no intervention was made in 55% of the physician-patient encounters examined. An appropriate intervention was made in 41% of the encounters studied, while an inappropriate intervention was made 4% of the time. Reasons for no intervention included: lack of laboratory data at time of physician-patient encounter (47% of those in whom no intervention was made), non-adherence (16%), adverse drug effects and patient refusal of therapy.
CONCLUSIONS: Patient-, provider- and healthcare system-related factors were identified as potential barriers to optimal lipid management.
Presented at the Alcalde XIX of the Texas Society of Health-System Pharmacists, Austin, TX, April 7-9, 2005.

16. Comparison of oral N-acetylcysteine versus intravenous sodium bicarbonate in contrast-induced nephropathy treatment [CONVICT Trial]. *Stanley Hill, Pharm.D.*[1], Steven Fowler, M.D.[2], Harminder Sikand, Pharm.D.[1], Paul Phillips, M.D.[2]; (1)Scripps Mercy Hospital/Cardinal Healthcare, San Diego, CA; (2)Scripps Mercy Hospital, San Diego, CA.

PURPOSE: Contrast induced nephropathy (CIN) is a leading cause of acute renal failure. Independent studies suggest that sodium bicarbonate ($NaHCO_3$) and *N*-acetylcysteine (NAC, Mucomyst®) can reduce the incidence of CIN. The study objective was to evaluate the efficacy of intravenous $NaHCO_3$ versus oral NAC to prevent CIN in patients undergoing cardiac catheterization.
METHODS: A prospective, randomized, open-label trial in patients with serum creatinine of ≥1.5 mg/dL or GFR <60 mL/min, who received either 600 mg NAC orally every 12 hours x4 doses and IV 0.45% NaCl at 1 mL/kg/hr 12 hours before and 12 hours after contrast administration or an infusion of 150 mEq/L $NaHCO_3$ at 3 mL/kg/hr 1 hour prior to contrast and 1 mL/kg/hr during and 6 hours after contrast. Serum creatinine levels are monitored at baseline and 48 hours after contrast. Endpoints include the incidence of CIN, change in serum creatinine, and treatment related complications.
RESULTS: Preliminary results in sixteen patients indicate that there are no significant differences between patient groups. The mean serum creatinine is 1.70 ± 0.29 mg/dL in NAC patients and 1.73 ± 0.36 mg/dL in $NaHCO_3$ patients (p=0.85). The incidence of CIN is 14.3% in NAC patients and 11.1% in $NaHCO_3$ patients (p= 1.0). The mean increase in serum creatinine is 0.43 mg/dL in NAC patients and 0.07 mg/dL in $NaHCO_3$ patients (p=0.42). An analysis of pooled data reveals a linear relationship between pre- and post-contrast serum creatinine (R^2 = 0.79). No patients in either treatment arm have experienced any treatment related complications.
CONCLUSIONS: Our data suggests that $NaHCO_3$ is as effective as NAC in preventing CIN in high-risk patients. The cost, ease of administration, and duration of treatment for $NaHCO_3$ is appealing in patients receiving contrast.

17E. Intrathecal clonidine reduces the risk of ischemic ventricular arrhythmias in a post-infarction heart failure canine model. Ziad Issa, MD[1], *Michael R. Ujhelyi, Pharm.D.*[2], Keith R. Hildebrand, DVM, PhD[2], Josh Rosenberger, BS[1], William J. Groh, MD[1], John M. Miller, MD[1], Douglas P. Zipes, MD[1]; (1)Indiana University, Indianapolis, IN; (2)Medtronic, minneapolis, MN.

PURPOSE: Intrathecal clonidine (ITC) effectively manages neuropathic pain. ITC has sympatholytic actions and could have beneficial cardiac effects such as preventing ischemia induced ventricular arrhythmias (VT/VF).
METHODS: We studied 10 mongrel dogs with healed anterior myocardial infarction and heart failure induced by rapid ventricular pacing. ITC was locally delivered via catheter to the spinal dorsal T3-T4 segments to inhibit cardiac sympathetic outflow. ITC was dosed (100-750 µg) to reduce HR by ≥ 20-25%. Electrophysiologic (EP) study was performed before and after ITC dosing. After baseline EP study, transient (4-min) myocardial ischemia was induced via left circumflex coronary artery occlusion on 2 separate occasions (control and ITC) to provoke VT/VF. Ischemia episodes were separated by 1-2 days and dogs were randomly assigned to receive ITC or control prior to the first or second ischemic episode.
RESULTS: ITC produced significant changes in several EP measurements but had no effect on blood pressure (Table). VT/VF was reduced from 8/10 (control) to 2/10 dogs during ITC (p=0.023). ITC blunted ischemia-induced heart rate increase (24.3 ± 9.9 BPM vs. 6.3 ± 3.8; $p<0.05$).
CONCLUSION: ITC reduced ischemia-induced VT/VF by 75%. EP data demonstrated a reduction in cardiac sympathetic activity from the spinal cord; ITC had no effect on blood pressure. Hence, ITC administration may be a novel method to prevent VT/VF associated with increased sympathetic activity.

	Baseline *(Mean ± SD)*	**ITC** *(Mean ± SD)*
MAP *(mmHg)*	88 ± 16	97 ± 17
HR *(bpm)*	103 ± 22	71 ± 23*
PR interval *(ms)*	122 ± 26	149 ± 34*
QTc interval *(ms)*	307 ± 24	336 ± 18*
HV interval *(ms)*	36 ± 4	35 ± 5
Wenckebach Cycle Length *(ms)*	315 ± 91	698 ± 237*
Atrial ERP *(ms)*	159 ± 23	189 ± 21*
Ventricular ERP *(ms)*	178 ± 12	194 ± 11*

Presented at the 2004 Scientific Sessions of the American Heart Association, New Orleans, LA, November 7-10, 2004.
*p<0.05

18. Atorvastatin reduces endothelial cell IL-6 release in a dose-dependent fashion with no effect on IL-10. *Issam Zineh, PharmD*[1], Xiaoping Luo, MD[2], Gregory J. Welder,[1], Amy E. DeBella,[1], Nasser Chegini, PhD[2]; (1)Department of Pharmacy Practice, University of Florida College of Pharmacy, Gainesville, FL; (2)Department of Obstetrics and Gynecology, University of Florida College of Medicine, Gainesville, FL.

PURPOSE: Atherosclerosis is characterized by the complex interplay between vascular endothelial cells, pro-inflammatory cytokines, and anti-inflammatory cytokines. We investigated whether atorvastatin affects human umbilical vein endothelial cell (HUVEC) elaboration of pro-inflammatory interleukin 6 (IL-6) or anti-inflammatory IL-10 in a dose-dependent way.
METHODS: HUVECs were treated with atorvastatin 1 uM, 5 uM, 10 uM, and

50 uM ± mevalonate and cultured for 24 hours. Experiments were performed in duplicate. Cell culture media were then collected, and IL-6 and IL-10 concentrations were simultaneously measured by flow-based immunofluorescent multiplex. Differences were compared by ANOVA with significance set at p<0.05.
RESULTS: Concentrations of IL-6 ± SE in control, 1uM, 5uM, 10uM, and 50uM atorvastatin groups were 20.1 ± 2.6 pg/ml, 15.6 ± 0.4 pg/ml, 10.1 ± 0.8 pg/ml, 7.7 ± 0.6 pg/ml, and 4.6 ± 0.7 pg/ml, respectively. This represented a significant, graded reduction of IL-6 concentrations with increasing atorvastatin dose (Range 22% to 77%, p<0.001 for dose effect). There was no effect of atorvastatin on IL-10 concentrations. The anti-inflammatory effect of atorvastatin on IL-6 was abolished upon exposure to mevalonate.
CONCLUSIONS: Atorvastatin reduced the production of the prototypical pro-inflammatory cytokine IL-6 from basal-state HUVECs in a dose-dependent fashion. These effects were dependent on HMG-CoA reductase inhibition. There was no drug effect on IL-10.

19. Evaluation of clinical outcomes of anticoagulation during percutaneous coronary intervention. *Kristin Zerumsky, Pharm, D*[1], Amy L. Seybert, PharmD[2], Melissa I. Saul, M.S[2], Joon Sup Lee, MD[2], Sandra L. Kane-Gill, Pharm, D, MSc[2]; (1)Uninversity of Maryland, Belair, MD; (2)University of Pittsburgh, Pittsburgh, PA.

PURPOSE: The Randomized Evaluation of Percutaneous Coronary Intervention (PCI) Linking Angiomax to Reduced Clinical Events (REPLACE-2) trial, demonstrated that bivalirudin with provisional glycoprotein IIb/IIIa (Gp) inhibitors is not inferior to unfractionated heparin (UFH) plus planned Gp inhibitors in preventing ischemic complications in non-high risk PCI patients. Decreased Gp inhibitor use and bleeding were shown with bivalirudin. The purpose of this study is to compare outcomes and Gp inhibitor use in a real-world setting between PCI patients who received bivalirudin or UFH.
METHODS: One thousand and seventy-five adult patients were identified retrospectively from April 2003–April 2004 through an electronic medical record repository using ICD-9 codes for PCI and pharmacy charges for bivalirudin or UFH following IRB approval. Demographics, co-morbidities, laboratory values, radiology and cardiac catherization reports and discharge summaries were obtained. Outcomes evaluated include mortality, length of stay (LOS) and bleeding (REPLACE-2 and TIMI criteria). Chi-square, Mann-Whitney U, *t*-test and Fisher exact tests were applied.
RESULTS:

	UFH group (n=536)	Bivalirudin group (n=539)	P value
Age, mean ± SD, y	63.0 ± 11.9	65.5 ± 12.3	0.001*
Female (n,%)	160(45.5)	192(54.5)	0.044*
Caucasian (n,%)	410(76.5)	455(84.4)	0.003*
Gp inhibitor use (n,%)	336(62.7)	147(27.3)	<0.001*
Mortality (n,%)	21(3.9)	7(1.3)	0.007*
REPLACE major bleed (n,%)	69(12.9)	29(5.4)	<0.001*
REPLACE minor bleed (n,%)	33(6.2)	32(5.9)	0.880
TIMI major bleed (n,%)	52(9.7)	27(5.0)	0.003*
TIMI minor bleed (n,%)	32(6)	9(1.7)	<0.001*
LOS mean ± SD, days	3.5 ± 4.1	2.8 ± 3.0	<0.001*

*Statically significant

CONCLUSIONS: Bivalirudin improves mortality, bleeding rates and shortens LOS compared to UFH in PCI patients in the real-world setting; however, further analysis considering confounding variables is needed. The use of Gp inhibitors is reduced in the bivalirudin group potentially contributing to the reduction in bleeding events compared to the UFH group.

20E. Use of 24-hour ambulatory blood pressure monitoring to assess antihypertensive efficacy: a comparison of olmesartan medoxomil and amlodipine besylate. *Thomas C. Marbury, MD*[1], Tonous Silfani, PhD[2]; (1)Orlando Clinical Research Center, Orlando, FL; (2)Sankyo Pharma Inc., Parsippany, NJ.

PURPOSE: Ambulatory blood pressure monitoring (ABPM) is a useful tool for monitoring antihypertensive drug efficacy throughout the 24-hour dosing interval, and often distinguishes effects of these agents when clinic BP measurements fail to do so.
METHODS: This 12-week, randomized, double-blind, placebo-controlled study used ABPM to compare efficacy of the recommended starting doses of olmesartan medoxomil (20mg) and amlodipine besylate (5mg) monotherapy in patients with essential hypertension (seated cuff diastolic BP [SeDBP] ≥100 and ≤115 mmHg and mean daytime DBP ≥90 and ≤119 mmHg). After a 4-week placebo run-in, patients were randomized to olmesartan medoxomil 20 mg/day (n=171), amlodipine besylate 5 mg/day (n=172) or placebo (n=54) for 8 weeks.
RESULTS: Patient demographics were similar between the treatment groups. Change from baseline in mean seated cuff systolic BP (SeSBP)/SeDBP, mean 24-hour BP, and mean daytime and nighttime BP at week 8 were previously reported (Chrysant et al. *J Hum Hyper* 2003;17:425). Both treatments produced significant and similar mean reductions versus placebo for SeSBP/SeDBP and daytime, nighttime and 24-hour BP at week 8. However, this secondary analysis showed that significantly more patients receiving olmesartan medoxomil achieved ABP goals of mean 24-hour ABP <130/80 and <130/85 mmHg, mean daytime ABP <130/80 and <135/85 mmHg, and mean nighttime ABP <120/75 and <130/85 mmHg at week 8 (Table).
CONCLUSION: Although mean reductions in clinic and 24-hour BP were similar, the proportion of hypertensive patients reaching ABP goals was significantly greater with olmesartan medoxomil than amlodipine besylate at their respective recommended starting doses.

Ambulatory BP goal, mmHg	Patients, % olmesartan medoxomil	amlodipine besylate	p-value
24-hour			
<130/80	18	7	0.002
<130/85	30	14	<0.001
Daytime			
<130/80	8	3	0.033
<135/85	16	6	0.003
Nighttime			
<120/75	18	8	0.003
<130/85	44	32	0.023

Published in Am J Hypertens 2005;18(5):68A.

21E. Resource use during hospitalization for acute decompensated heart failure. *Sandra L. Kane-Gill, Pharm, D, MSc*, Amy L. Seybert, PharmD, Jessica Spates, P.A, Melanie Shatzer, R.N., Melissa I. Saul, M.S, Levent Kirisci, Ph.D., Srinivas Murali, M.D.; University of Pittsburgh, Pittsburgh, PA.

BACKGROUND: Since hospitalization costs account for the largest share of the total cost of heart failure (HF) care, we sought to evaluate hospitalization resource use for acute decompensated HF.
METHODS: Adult patients were identified retrospectively over 1 year in an electronic repository using DRG 127 and ICD-9 429 for HF. Patients admitted for implantation of cardiac defibrillator, pacemaker placement or cardiac surgery were excluded. Data obtained for 331 patients (420 admissions) included demographics, de-identified admission and discharge summaries and ratio of cost to charge for hospital resources. Patients were categorized into new onset HF (documented new onset in the electronic chart), known HF (known HF diagnosis in the past but not hospitalized within previous year), HF readmission (HF hospitalization in the previous year). Average costs used for patients with >1 admission. Comparisons were made using chi-square, ANOVA for log transformed costs and post-hoc Scheffe test.
RESULTS:

	New Onset HF n = 60	Known HF n = 171	HF Readmission n = 100	*P* Value
Age (mean ± SD), yrs	68 ± 17	73 ± 14	70 ± 13	0.088
Gender	53% Female	49%Female	55% Female	0.875
Length of stay, days	3.8 ± 2.2	4.0 ± 2.0	4.1 ± 2.2	0.813
Average Total Cost	$4200	$4479	$4584	0.740
Cost per Day	$1109	$1146	$1176	0.568
Echocardiogram (ECHO)**	$136	$133	$76	0.001*
Electrophysiology (EP)**	-	$269	$69	0.001
Emergency Department**	$350	$318	$313	0.682
Dialysis**	$1692	$1867	$3275	0.229
Pharmacy Department**	$121	$200	$271	0.002#

SIGNIFICANT PAIRWISE COMPARISONS: *Known HF vs HF readmission (*P*<0.001) or New onset HF vs HF readmission (*P*<0.001); #New onset HF vs HF readmission (*P*=0.002)
**Mean data are presented; sample size varied depending on patients using resources.
CONCLUSIONS: 1)Total HF hospitalization costs are the same whether it is a new diagnosis, known diagnosis or readmission. 2) New onset HF uses more resources from ECHO and less from pharmacy departments compared to HF readmission.
Published in Circulation 2005; 20:e342.

22. Pharmacist intervention in risk reduction. *William M. Semchuk, BSP, M.Sc., Pharm.D.*[1], Jeffrey G. Taylor, BSP, M.Sc., Ph.D.[2], Michelle Deschamps, BSP, M.Sc.,[1], Linda A Sulz, BSP, Pharm.D.[1]; (1)Regina Qu'Appelle Health Region, Regina, SK, Canada; (2)University of Saskatchewan, Saskatoon, SK, Canada.

PURPOSE: The Pharmacist intervention in risk reduction study was designed to compare two education strategies for training community pharmacists to identify and educate high risk vascular patients on the benefits of medications known to decrease cardiovascular risk and to collaborate with the patient's primary care physician to achieve best care. The primary endpoint was the composite measure of change in pharmacologic risk reduction strategies implemented through the study period between groups.
METHODS: Sixty-one pharmacists from 40 pharmacies were randomized to: In-depth training group (all-day session including role playing) OR Standard

training group(an evening program). Following obtainment of consent, pharmacists interviewed and educated patients on risk factors for vascular disease. If opportunity for medication optimization existed, pharmacists completed a physician information and referral form containing information on CHD risk factors, medication history, and recommendations, and faxed it to the patient's primary care physician and referred the patient to that individual for further assessment and intervention as appropriate. Patient follow-up occurred at four, 16, and 24 weeks to determine if further medications had been initiated. Beginning December 2001, 216 high risk patients were enrolled and followed for 24 weeks. Pharmacists were reimbursed $30 per patient accrued.
RESULTS:Enhancement in risk reduction therapies occurred in 76/119 patients (63.9%) in the intervention group vs. 49/97 patients (50.5%) in the standard training group (p=0.04). Throughout the study period, aggregate use of ASA increased from 51.9% to 76.9% of patients (p<0.05); lipid-lowering therapy increased from 39.8% to 49.1% (p<0.05) and a nonsignficant increase in the use of ACE inhibitors, other antihypertensive agents, smoking cessation agents and antiobesity agents occurred from study entry to end.
CONCLUSIONS: Although underpowered, this trial demonstrates the positive impact that community pharmacists can have on the utilization of risk reduction therapies when working in collaboration with primary care physicians and patients.

23. Two-year safety and efficacy of once-daily extended-release niacin/lovastatin in patients with hypercholesterolemia. Moti L. Kashyap, M.D.[1], *Eric J. Stanek, Pharm.D.*[2], Phillip D. Simmons, M.S.[2], Mark E. McGovern, M.D.[2]; (1)Veteran's Affairs Healthcare System, Long Beach, CA; (2)Kos Pharmaceuticals, Inc., Cranbury, NJ.

PURPOSE: To assess the safety and efficacy of fixed-dose combination extended-release niacin/lovastatin (ERN/L) during treatment for up to 2 years.
METHODS: Adults with type IIA or IIB hyperlipidemia and non-optimal LDL cholesterol (LDL-C) were enrolled in an open-label trial of ERN/L 500/10 mg qhs titrated to a maximum of 2000/40 mg qhs over 16 weeks. This dose was maintained through trial completion at 52 weeks, after which patients were eligible to continue in a 48-week extension. Change in LDL-C from baseline was the primary efficacy measure, and secondary efficacy parameters included changes in total cholesterol (TC), HDL cholesterol (HDL-C), triglyceride (TG), lipoprotein (a); Lp(a), and nonHDL-C. Compliance and safety were assessed at each visit, and included clinical chemistry, hematology, coagulation, and urinalysis testing.
RESULTS: Of the 814 patients enrolled, 550 completed 52 weeks, 454 entered the 48-week extension, and 397 completed 100 weeks. Demographics: mean age 59 years, 64% male, 88% white, coronary heart disease 38%, diabetes mellitus 11%. Compliance by tablet count averaged 94%.

Lipids, mg/dL	Baseline N=814	Week 52, % change N=550	p value	Week 100, % change N=397	p value
TC	283 (1.5)	-30 (0.5)	<0.05	-30 (0.6)	<0.05
LDL-C	195 (1.4)	-43 (0.7)	<0.05	-42 (0.7)	<0.05
HDL-C	48 (0.4)	+34 (1.1)	<0.05	+31 (1.3)	<0.05
TG	199 (3.3)	-40 (1.2)	<0.05	-40 (1.3)	<0.05
NonHDL-C	236 (1.5)	-43 (0.7)	<0.05	-43 (0.7)	<0.05
Lp(a), median	23	-25%	<0.05	N/A	—-

Table values are mean (S.E.). Changes in LDL-C and other lipids were statistically greater in women and in patients ≥65 y/o. Flushing was reported by 65% of patients, resulting in discontinuation by 11% over 100 weeks. Five patients (0.6%) had transient elevations in liver function enzymes >3 times the upper limit of normal and there were no cases of confirmed myopathy.
CONCLUSION: ERN/L is safe and produces significant, sustained improvements in multiple lipid and lipoprotein parameters for up to 2 years.

24. Impact of intensive pharmaceutical care on uncontrolled hypertension in ambulatory patients in Hong Kong. *Moses S.S. Chow, PharmD*, S. Y. Tsang, MClinPharm, Y.S. Wong, MClinPharm; School of Pharmacy, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong SAR, China.

PURPOSE: This study evaluated the impact of "intensive pharmaceutical care" provided by the pharmacist on blood pressure (BP) control, drug cost and patient satisfaction in ambulatory patients with uncontrolled hypertension. Method: Adult patients with uncontrolled hypertension at 2 outpatient hospital clinics were randomized to receive intensive pharmaceutical care (IPC) or usual care (UC). IPC involved interviewing, assessing and counseling of patients as well as recommending medication changes to the physician. UC involved routine dispensing service and counseling. All BP were measured independently by nurse using a standard device. After a mean follow up period of 12 weeks, % target BP (as per JNC7) attained, BP reduction from baseline, and daily drug cost were assessed. In addition, a satisfaction survey was carried out in the IPC patients.
RESULTS: Of the 45 IPC and 43 UC patients completed the study, 47% and 5% (P<0.001) respectively achieved the target BP. The mean systolic/diastolic BP was reduced by 27.8/10.0mmHg and 2.6/2.1mmHg in the IPC and UC group (p<0.001) respectively. Furthermore, evaluation of 23 patients who had 3 months of UC post IPC was found to maintain similar target BP and BP reduction. No significant change in the daily drug cost was found in either group. The patient satisfaction survey showed satisfied (51%) or strongly satisfied (49%) rating in receiving the IPC.
CONCLUSION: IPC was significantly more effective in achieving target BP as compared to UC and the effect lasted beyond the IPC period. Also, providing IPC can lead to high patient satisfaction without an increase in the drug cost.

25E. Coronary heart disease events and associated costs in U.S. adults with uncontrolled hypertension and multiple cardiovascular risk factors. *Joshua S. Benner, PharmD, ScD*[1], Timothy W. Smith, BA[1], Allison A. Petrilla, BA[1], David Klingman, PhD[1], Simon Tang, MPH[2]; (1)ValueMedics Research, LLC, Falls Church, VA; (2)Pfizer Inc US Outcomes Research, New York, NY.

PURPOSE: To determine the prevalence of uncontrolled hypertension (HTN) with multiple risk factors in US adults, and the clinical/economic burden of coronary heart disease (CHD) events in these patients.
METHODS: Prevalence of uncontrolled HTN (SBP ≥160 or DBP ≥100 mmHg if untreated; SBP ≥140 or DBP ≥90 mmHg if treated) was calculated using NHANES III-Phase 2 and 2000 census data. Risk factors assessed included left ventricular hypertrophy, abnormal ECG, diabetes, previous stroke/TIA, male, age ≥55 years, microalbuminuria/proteinuria, smoking, total:HDL cholesterol ratio ≥6, and family history of premature CHD. Framingham risk equations were used to calculate the 4-year risk of any CHD event; first-year direct costs were calculated using literature-based values.
RESULTS: 7031 NHANES III subjects (upweighted to 201 million US adults) were included. The weighted prevalence of uncontrolled HTN was 16.3 million (8.1%). Of those with uncontrolled HTN, 86% were free of CHD (35% with ≥3 CV risk factors, 27% with 2, 19% with 1, and 4% with 0). Mean 4-year risk of CHD was 18% in those with uncontrolled HTN and CHD. Among those with HTN and no CHD, 4-year risk of CHD ranged from 2% in those with 0 to 13% in those with ≥3 additional risk factors. Over 1.5 million CHD events were predicted within 4 years among patients with uncontrolled HTN (first-year direct medical costs $19.0 billion); 732,000 ($8.5 billion) were in primary prevention patients with ≥3 risk factors.
CONCLUSIONS: Among patients with uncontrolled HTN, those with ≥3 CV risk factors but no CHD (like those in the ASCOT trial) were predicted to incur more CHD events and higher direct costs than any other subgroup studied; 1 in 8 will experience a CHD event within 4 years. Intensive efforts by all healthcare professionals are needed to screen/treat patients without CHD but with multiple risk factors.
Published in Am J Hypertens 2005 18;(5 suppl1):A224.

26E. Accuracy of uncorrected vs corrected QT interval for prediction of drug-induced torsades de pointes. *James E. Tisdale, PharmD*[1], Beth L. Cariera, PharmD[1], Deming Mi, MD, MS[2], George P. McCabe, PhD[2], Christopher Lisek, PharmD[1], Richard Kovacs, MD[3]; (1)Purdue University, 1001 West 10th Street, Indianapolis, IN; (2)Purdue University, West Lafayette, IN; (3)School of Medicine, Indiana University, Indianapolis, IN.

PURPOSE: Determine if uncorrected QT interval (QTu) is more accurate than rate-corrected QT interval for predicting drug-induced torsades de pointes (TdP).
METHODS: This was a retrospective analysis of a previously reported case-control study of risk factors for haloperidol-induced TdP; 46 critically ill patients who received intravenous haloperidol for sedation and had no other TdP risk factors were included; 7 patients developed TdP. QT intervals were measured manually by one investigator from ECGs performed prior to and during haloperidol therapy. Logistic regression analysis for prediction of TdP was performed, incorporating on-treatment QTu and QT intervals corrected using Bazett's (QTB) and Fridericia (QTFr) methods, as well as RR interval. Receiver operating characteristics (ROC) curves were constructed. The logistic model probability of TdP occurring at the widely accepted high-risk QTB interval of 500 ms was 0.044; this corresponded to a QTu of 436 ms and a QTFr of 485 ms. Sensitivity and specificity of QT interval methods for prediction of TdP were calculated at this probability.
RESULTS: Demographics were similar in the TdP vs non-TdP groups, except for a higher prevalence of diabetes and longer pretreatment QTFr values in the TdP group. QTu was associated with the highest R≤ (Table). QTu and QTFr were associated with the largest areas under the ROC curve (AUROC). QTu was the most specific method for prediction of TdP.
CONCLUSION: Compared with QTB and QTFr, QTu is the best predictor of haloperidol-induced TdP in critically ill patients. Further study is required to determine the predictive accuracy of QTu vs QTB and QTFr for TdP associated with other drugs in other populations, as well as other methods of QT interval correction.

	R2	AUROC	Sensitivity	Specificity
QTu	0.44	0.97	100%	82%
QTFr	0.39	0.97	100%	72%
QTB	0.31	0.93	100%	64%
RR	0.17	0.79	—	—

Published in Circulation 2004;110:III-580.

27E. Efficacy of olmesartan medoxomil and olmesartan/hydrochlorothiazide in achieving blood pressure control and normalization in stage 2 systolic hypertension. *Joseph Izzo, MD*[1], Joel M. Neutel, MD[2], Robert Dubiel, R.Ph.[3], Findlay Walker, MD[3]; (1)State University of New York at Buffalo, Buffalo, NY; (2)Orange County Research Center, Tustin, CA; (3)Sankyo Pharma Inc., Parsippany, NJ.

PURPOSE: This open-label titration study evaluated the efficacy of olmesartan medoxomil alone and in combination with hydrochlorothiazide to control blood pressure (BP) (<140/90 mmHg) and to normalize BP (<120/80 mmHg) in stage 2 systolic hypertension.
METHODS: After a placebo run-in, 169 patients with systolic BP (SBP) ≥160 and <200 mmHg and diastolic BP (DBP) <110 mmHg received olmesartan 20 mg/day for 3 weeks. Up-titration occurred at 3-week intervals if BP remained ≥120/80 mmHg according to the schedule: olmesartan 40 mg/day; combination with hydrochlorothiazide 12.5 mg/day; hydrochlorothiazide 25 mg/day. If BP remained ≥120/80 mmHg at 12 weeks, hydrochlorothiazide was titrated to 50 mg/day for 4 weeks. Primary endpoint was changed from baseline in mean trough SBP after 12 weeks of treatment. Secondary endpoints included BP changes from baseline at the end of each titration period and the proportion of patients achieving BP control and normalization.
RESULTS: Marked reductions in BP were seen at the end of each titration step (Table; p<0.001 compared with baseline for SBP and DBP at all times analyzed). At week 12, with olmesartan/hydrochlorothiazide 40/25 mg/day, 70% of patients achieved BP control and 15% achieved normal BP. Increasing hydrochlorothiazide to 50 mg/day allowed additional reductions in SBP leading to 78% achieving BP control and 27% achieving normal BP.
CONCLUSION: Olmesartan monotherapy is effective in reducing SBP and DBP, and hydrochlorothiazide provides additional BP reductions resulting in substantial proportions of patients achieving BP control and normalization.

Week	3	6	9	12	16
Olmesartan, mg/day	20	40	40	40	40
Hydrochlorothiazide, mg/day	–	–	12.5	25	50
Mean ΔSBP, mmHg	–16.9	–18.4	–30.3	–34.7	–38.3
Patients, %					
SBP <140 mmHg	17.8	30.8	58.0	75.1	81.1
SBP/DBP <140/90 mmHg	15.4	29.0	55.6	70.4	77.5
SBP <120 mmHg	1.2	1.2	6.5	16.0	27.8
SBP/DBP <120/80 mmHg	1.2	1.2	5.9	15.4	27.2

Published in Am J Hypertens 2005;18(5):64A.

28E. Metabolic effects and safety of hydrochlorothiazide in combination with olmesartan medoxomil in stage 2 systolic hypertension. *Joseph Izzo, MD*[1], Joel M. Neutel, MD[2], Robert Dubiel, R.Ph.[3], Findlay Walker, MD[3]; (1)State University of New York at Buffalo, Buffalo, NY; (2)Orange County Research Center, Tustin, CA; (3)Sankyo Pharma Inc., Parsippany, NJ.

PURPOSE: This study evaluated metabolic consequences and safety of an open-label titration regimen of the angiotensin receptor blocker olmesartan alone and in combination with hydrochlorothiazide in stage 2 systolic hypertension.
METHODS: After a placebo run-in, 169 patients with systolic BP (SBP) ≥160 and <200 mmHg and diastolic BP (DBP) <110 mmHg received olmesartan 20mg/day for 3 weeks. Up-titration occurred at 3-week intervals if BP remained ≥120/80 mmHg according to the schedule: olmesartan 40mg/day; olmesartan 40mg/day+hydrochlorothiazide 12.5mg/day; olmesartan 40mg/day+hydrochlorothiazide 25mg/day. If BP remained ≥120/80 mmHg at 12 weeks, hydrochlorothiazide was titrated to 50mg/day for 4 weeks. Primary endpoint was changed from baseline in mean SBP after 12 weeks of treatment. Adverse events (AE) and metabolic data were tabulated for all patients who received ≥1 dose of study medication.
RESULTS: Mean age was 60 years; patients were 46% male and 84% non-black. Mean baseline BP was 171/95 mmHg. Both agents were well tolerated with a low incidence of AEs across the dosing range (Table). Symptomatic hypotension occurred in 1 olmesartan/hydrochlorothiazide 40mg/12.5mg recipient and 1 olmesartan/hydrochlorothiazide 40mg/50mg recipient. Serum potassium, glucose and uric acid levels remained within normal limits for all olmesartan/hydrochlorothiazide combinations; no incidents of gout occurred. There were similar small changes in glucose and uric acid across all hydrochlorothiazide doses, while serum potassium did not change.
CONCLUSION: The addition of hydrochlorothiazide to olmesartan does not appreciably increase AEs or cause significant metabolic disturbances across the hydrochlorothiazide dosing range of 12.5–50mg/day.

Drug-related AEs occurring in ≥2% of patients	Olmesartan/hydrochlorothiazide mg/day				
	20/0	40/0	40/12.5	40/25	40/50
	% patients				
Dizziness	<2	<2	3.8	4.9	5.7
Fatigue	0	0	<2	2.1	<2
Increased:					
g-glutamyl transferase	0	0	0	2.1	<2
serum uric acid	0	0	0	<2	7.6
serum creatinine	0	0	0	2.1	5.7
serum urea nitrogen	0	0	0	0	7.6

Published in Am J Hypertens 2005;18(5):64A.

29E. Comparison of ascending doses of olmesartan medoxomil, losartan potassium and valsartan in patients with stage 2 essential hypertension. *Thomas D. Giles, MD*[1], Suzanne Oparil, MD[2], Tonous Silfani, PhD[3], Findlay Walker, MD[3]; (1)Louisiana State University School of Medicine, New Orleans, LA; (2)University of Alabama School of Medicine, Birmingham, AL; (3)Sankyo Pharma Inc., Parsippany, NJ.

PURPOSE: This 12-week study compared the efficacy of olmesartan medoxomil with valsartan and losartan potassium across recommended doses and regimens.
METHODS: Patients with stage 2 hypertension (n=723) were randomized to once-daily olmesartan 20 mg, valsartan 80 mg, losartan 50 mg or placebo. At week 4, daily doses were titrated to olmesartan 40 mg, valsartan 160 mg or losartan 100 mg. At week 8, olmesartan remained at 40 mg/day (maximum recommended dose) for another 4 weeks, valsartan was titrated to 320 mg/day, and losartan to 50 mg twice daily. The primary endpoint was mean change in seated diastolic blood pressure (SeDBP) from baseline to week 8. Secondary endpoints included mean change in seated systolic BP (SeSBP). Secondary analyses were done to determine BP goal rates.
RESULTS: Olmesartan 40 mg, valsartan 160 mg and losartan 100 mg significantly reduced mean SeDBP and SeSBP from baseline (p<0.001) versus placebo (p<0.01) at week 8. Mean SeDBP reduction with olmesartan (-13.1 mmHg) was significantly greater than losartan (-9.6 mmHg; p<0.001) and placebo (-6.8 mmHg; p<0.001) and numerically greater than valsartan (-11.8 mmHg; p=0.078). Mean SeSBP reduction with olmesartan (-15.1 mmHg) was significantly greater than losartan (-11.0 mmHg; p=0.001) and placebo (-6.2 mmHg; p<0.001) and numerically greater than valsartan (-12.8 mmHg; p=0.054). BP <140/90 mmHg was achieved by more patients with olmesartan (40.3%) than valsartan (28.5%; p=0.016), losartan (20.1%; p<0.001), or placebo (12.2%; p<0.001) at week 8. At 12 weeks, mean SeSBP and SeDBP reductions were similar for each active treatment arm. However, the proportion of patients achieving BP <130/85 mmHg with olmesartan (18.0%) was numerically greater than valsartan (10.9%; p=0.057) and losartan (11.2%; p=0.069) and significantly greater than placebo (2.3%; p<0.001).
CONCLUSION: Olmesartan is an effective antihypertensive agent and allowed more patients to achieve BP goals compared with valsartan and losartan at week 8.
Published in Am J Hypertens 2005;18(5):59A.

30E. Effects of olmesartan medoxomil and valsartan on the renin-angiotensin-aldosterone system in healthy normal subjects. *Michael Jones, PhD*[1], Jean Sealey, DSc[2], John Laragh, MD[2]; (1)Sankyo Pharma Inc., Parsippany, NJ; (2)Cardiovascular Center, Department of Cardiothoracic Surgery, Weill Medical College of Cornell University, New York, NY.

PURPOSE: Angiotensin II receptor blockers lower BP by blocking the binding of Angiotensin II to the AT_1 receptor. Renin-angiotensin-aldosterone system (RAAS) blockade at the AT_1 receptor causes a compensatory rise in plasma renin activity (PRA). This 5-way crossover study measured the increase in PRA achieved with olmesartan medoxomil and valsartan to compare the degree and persistence of receptor blockade with the two agents.
METHODS: Mean PRA increase (DPRA)over 24 hours, following single doses of placebo, olmesartan (20 and 40mg) or valsartan (80 and 160mg), was measured in normal volunteers (n=20), with a 7-day washout period between doses.
RESULTS: All doses of olmesartan and valsartan increased PRA compared with placebo. At 24 hours post-dose (Table), DPRA was significantly higher with olmesartan 20 and 40mg and valsartan 160mg versus placebo (p=0.002, p<0.001, p=0.029, respectively) and significantly higher with olmesartan 40mg than with olmesartan 20mg (p=0.004) or either valsartan dose (p<0.001). Changes at 24 hours were not significant for valsartan 80mg. At 4 hours post-dose, DPRA was similar for olmesartan and valsartan at all doses. With olmesartan, there was a clear relationship between dose and DPRA at 8, 16 and 24 hours: olmesartan 40mg achieved a significantly greater DPRA than olmesartan 20mg (p=0.002, p=0.016, p=0.004 at 8, 16 and 24 hours, respectively). There were no significant differences in DPRA at these times between valsartan 80 and 160mg. 24-hour urine aldosterone excretion rates were significantly lower than placebo with olmesartan 20mg (p=0.008) and

40mg (p=0.040) and valsartan 160mg (p=0.036)but not with valsartan 80mg (p=0.689).
CONCLUSION: These results demonstrate more prolonged AT_1 receptor blockade with olmesartan 40mg than with either dose of valsartan.
24-hour DPRA (all completed subjects, n=20)

	Mean (SEM), ng/mL/hour
Placebo	–0.1 (0.3)
Olmesartan 20mg	4.1 (1.2)
Olmesartan 40mg	8.0 (1.9)
Valsartan 80mg	1.7 (0.5)
Valsartan 160mg	2.9 (0.7)

Published in Am J Hypertens 2005;18(5):65A.

31E. Achievement of blood pressure goals using an angiotensin receptor blocker-based regimen. *Joel M. Neutel, MD*[1], David Smith, MD[2], Tonous Silfani, PhD[3], Yonghee Lee, PhD[4], Michael Weber, MD[5]; (1)Orange County Research Center, Tustin, CA; (2)Memorial Research Medical Clinic, Long Beach, CA; (3)Sankyo Pharma Inc., Parsippany, NJ; (4)Forest Research Institute, Jersey City, NJ; (5)State University of New York Downstate College of Medicine, Brooklyn, NY.

PURPOSE: This study evaluated the efficacy of an olmesartan medoxomil-based treatment algorithm for patients with stage 1 hypertension (systolic blood pressure [SBP] 140-149 or diastolic BP [DBP] 90-99 mmHg) and stage 2 hypertension (SBP≥160 or DBP≥100 mmHg).
METHODS: Patients (baseline SBP<200/DBP 90-109 mmHg) enrolled in a 24-week, open-label study followed a 6-step titration starting with olmesartan 20mg/day, modified every 4 weeks until patients attained BP ≤130/85 mmHg according to the schedule: olmesartan 40mg/day; add hydrochlorothiazide 12.5mg/day; hydrochlorothiazide 25mg/day; add amlodipine 5mg/day; amlodipine 10mg/day. Automated BP devices were used to ensure objectivity of measurements.
RESULTS: In stage 1 patients (baseline BP 149.7/94.7 mmHg), 80% and 56% achieved BP goals of ≤140/90 and ≤130/85 mmHg, respectively, with olmesartan alone (94% and 89% with olmesartan plus hydrochlorothiazide) (Table). Amlodipine increased goal rate achievement to 98% and 96%, respectively. In stage 2 patients (baseline BP 169.8/98.1 mmHg), 42% and 19% achieved BP goals of ≤140/90 and ≤130/85 mmHg, respectively, with olmesartan alone (75% and 54% with olmesartan/hydrochlorothiazide). Amlodipine increased goal rate achievement to 90% and 81%, respectively.
CONCLUSION: Goal achievement was driven by large decreases in mean SBP/DBP. A treatment algorithm that included olmesartan alone and with hydrochlorothiazide controlled a majority of patients with stage 1 and 2 hypertension to the more aggressive goal of ≤130/85 mmHg.

Week	Algorithm step	Mean SBP/DBP reduction, mmHg[1]	Patients achieving goal BP, % ≤140/90 mmHg[2]	130/85 ≤mmHg[2]
Stage 1 hypertension (n=85)				
8	olmesartan	16.7/11.6	80	56
16	olmesartan/hydrochlorothiazide	24.8/15.8	94	89
24	olmesartan/hydrochlorothiazide/ amlodipine	26.4/16.5	98	96
Stage 2 hypertension (n=113)				
8	olmesartan	18.4/10.0	42	19
16	olmesartan/hydrochlorothiazide	32.7/16.3	75	54
24	olmesartan/hydrochlorothiazide/ amlodipine	39.1/19.4	90	81

[1]last observation carried forward [2]Analysis of evaluable cohort (stage 1: n=79; stage 2: n=100); excluded patients not given opportunity to reach target BP and those withdrawing early.
Published in Am J Hypertens 2005;18(5):70A.

32E. Barriers to appropriate anticoagulation with warfarin in orthopedic surgery. Juan Blackburn, M.D.[1], Glen Schumock, Pharm.D.[1], Jerry Bauman, Pharm.D.[1], Joseph Caprini, M.D.[2], *Edith A. Nutescu, PharmD*[1]; (1)University of Illinois at Chicago, Chicago, IL; (2)Evanston Northwestern Healthcare, Evanston, IL.

OBJECTIVE: The aim of this study is to describe challenges associated with oral anticoagulant use in real life clinical practice by evaluating the use of warfarin as the preferred method of thromboprophylaxis after major orthopedic surgery (MOS).
METHODS: Data was collected retrospectively from medical records of patients who underwent MOS, received thromboprophylaxis with warfarin, and were monitored in a centralized Antithrombosis Center between 1998 and 2002.
RESULTS: A total of 202 patients were evaluated who underwent total hip replacement (45.5%) or total knee replacement (54.5%). Most patients were female (73.3%) with a mean age of 58.95 ± 12.8 (mean ± SD). The mean number of clinic visits for warfarin dose-adjustment was 6.13 ± 2.7. The mean length of therapy was 50 ± 19.7 days, and 44 ± 12.7 days when excluding outliers. Patient compliance (self-reported) with therapy was 59%. The mean time required to reach therapeutic range was 8.26 ± 8.6 days. The average time spent in therapeutic range was 35 ± 20.7% and significantly lower in non-compliant patients 28.3 ± 16.8% (p= 0.002). The mean time spent below therapeutic range was 56.6 ± 24.7%; however, for non-compliant patients it was significantly higher 63 ± 22.3% (p=0.01). Adverse outcomes associated with warfarin use were documented in 15 (7.4%) patients: 3 (1.5%) major bleeding, 10 (5%) minor bleeding, and 2 (1%) objectively confirmed, symptomatic venous thromboembolic events (VTE).
CONCLUSION: In this cohort of orthopedic patients, despite close monitoring in a centralized Antithrombosis Center, the use of warfarin was plagued by poor patient compliance and a high number of clinic visits for dose adjustments. In addition, delayed time (> 1 week) to reach therapeutic anticoagulation and significant periods of time spent below acceptable anticoagulant levels were also observed. These latter two observations have resulted in a high rate of VTE events in past large clinical trials.
Presented at the 20th Congress of the International Society of Thrombosis and Haemostasis, Sydney, Australia, August 6-12, 2005.

33. Treatment guidelines for acute decompensated heart failure associated with improved outcomes. *Heather M. Eyrich, PharmD*, Robert J. DiDomenico, PharmD, Deidre Fontana, RN, BA, George T. Kondos, MD, Glen Schumock, Pharm.D.; University of Illinois at Chicago, Chicago, IL.

PURPOSE: Acute decompensated heart failure (ADHF) is associated with considerable morbidity, mortality, and resource consumption. We developed ADHF treatment guidelines and compared ADHF patient outcomes before and after their implementation.
METHODS: A treatment algorithm and timeline for assessments and treatment initiation was constructed and implemented on January 1, 2004. Patients hospitalized for ADHF were identified via the Acute Decompensated Heart Failure Registry (ADHERE) and evaluated retrospectively. Treatment periods included the 12 months prior to (PRE) and the 11 months following guideline implementation (POST). Outcome measures included the use of intravenous vasoactive drugs (IVVAD), need for intensive care unit (ICU) monitoring, and length of stay (LOS).
RESULTS: 739 patients were included (389 PRE, 350 POST). IVVAD were administered to 76 patients PRE (19.5%) and 81 patients POST (23.1%, p=0.23); more patients received nesiritide following guideline implementation (9.0% PRE vs.14.9% POST, p<0.02). Duration of IVVAD decreased by 44% with guideline utilization (4.1 ± 5.6 days PRE vs. 2.3 ± 1.5 days POST, p<0.02). ICU monitoring was required in 46 patients PRE (11.8%) compared to 31 patients POST (8.9%, p=0.19). In patients treated with IVVAD guideline usage reduced the need for ICU monitoring by 46% (36.8% PRE vs. 19.8% POST, p<0.02). Significantly shorter ICU LOS was observed (5.9 ± 8.4 days PRE vs. 2.9 ± 2.9 days POST, p=0.03). In patients treated with IVVAD, LOS in the ICU was 55% lower (8.4 ± 10.2 days PRE vs. 3.8 ± 3.4 days POST, p=0.09) and overall hospital LOS was 1.8 days less (9.7 ± 10.0 days PRE vs. 7.9 ± 7.5 days POST, p=0.2).
CONCLUSIONS: Use of ADHF treatment guidelines led to increased nesiritide use, but decreased duration of IVVAD therapy. IVVAD use was associated with decreased need for ICU monitoring. Trends toward reduced ICU LOS and reduced overall LOS were observed. Adherence to ADHF treatment guidelines may lead to clinical improvements and more efficient resource utilization.

34E. Economic evaluation of a fixed-dose combination of isosorbide dinitrate and hydralazine in blacks with heart failure: results from the African-American Heart Failure Trial (A-HeFT). *Judy W. Cheng, Pharm.D.*[1], Walter T. Linde-Zwirble, BS[2], S. William Tam, PhD[3], Manuel Worcel, MD[3], Michael L. Sabolinski, MD[3], Jalal K. Ghali, MD[4], Derek C. Angus, MD, MPH[5]; (1)Long Island University, New York, NY; (2)ZD Associates LLC, Perkasie, PA; (3)NitroMed, Inc., Lexington, MA; (4)Louisiana State University, Shreveport, LA; (5)University of Pittsburgh School of Medicine, Pittsburgh, PA.

PURPOSE: Combination of isosorbide dinitrate/hydralazine (ISDN/HYD, BiDil® 40mg/75mg tid) in addition to standard therapy, improved survival and reduced hospitalization for NYHA class III/IV heart failure (HF) patients in the African-American Heart Failure Trial (A-HeFT). Its cost effectiveness was evaluated.
METHODS: Hospital and other care resources use were obtained from A-HeFT and corresponding costs from Medicare data. Costs for medications were obtained from 2004 Redbook. Cost effectiveness was modeled over a life-time Reference Case from societal perspective.
RESULTS: The ISDN/HYD group (N=518) had an increased survival of 21.6 days (95% confidence interval [CI], 3.1–39.4 days, p=0.01) per patient per year compared to placebo (N=532). ISDN/HYD group incurred fewer heart-failure-related hospitalizations (0.33 vs. 0.47 per subject, p=0.002) and shorter mean hospital stays (6.7 vs. 7.9 days, p=0.006). Number needed to

treat for one year was 16.9 to gain one year of life, 7.6 to avoid one HF-related hospitalization and 5.1 to avoid an any-cause hospitalization. Excluding ISDN/HYD cost, the average HF cost per ISDN/HYD patient was $2,950 less per year (95%CI, $283-$5,078), and all healthcare cost $4,381 less per year (95%CI, $482-$6,603). Average wholesale price for BiDil® is not determined yet. Based on the within-trial average daily dose consumed (4.2 tablets) and compliance (85.4%), ISDN/HYD will be dominant (save cost and lives) if ISDN/HYD cost up $8.05 daily (cost for 6 tablets: $13.52) considering HF costs, and $12.00 daily (cost for 6 tablets: $20.06) for all healthcare costs. Cost-effectiveness of ISDN/HYD using HF-related costs (assuming $5 ISDN/HYD daily) was projected to be $6,900/life-year at 2 years post-enrollment, $26,000/life-year at 5 years, and $31,000/life-year over lifetime (Reference Case).
CONCLUSION: ISDN/HYD improved clinical outcomes and reduced resource use in blacks with HF. Adopting this therapy should be a dominant strategy over a wide range of cost for the therapy itself and cost-effective long-term.
Presented at the 9th Annual Scientific Meeting of the Heart Failure Society of America, Boca Raton, FL, September 18-21, 2005.

35E. Amphetamine treatment of ADHD in adults with primary essential hypertension. Timothy E. Wilens, MD[1], Joseph Biederman, MD[2], Thomas J. Surman, MD[3], Thomas J. Spencer, MD[2], David A. Mays, PharmD, MBA, BCPS[4], *Paul Hodgkins, PhD, RAC*[5]; (1)Massachusetts General Hospital and Harvard Medical School, Boston, MA; (2)Harvard University and Massachusetts General Hospital, Boston, MA; (3)Division of Cardiology, Boston, MA; (4)Shire Pharmaceuticals Inc., Wayne, PA; (5)Shire Pharmaceutical Inc., Wayne, PA.

OBJECTIVE: To assess the cardiovascular safety and tolerability of mixed amphetamine salts extended release (MAS XR) in successfully treated hypertensive adults with ADHD.
METHODS: Adults with clinical hypertension (BP>140/9) and ADHD were recruited for this study. Each was required to be normotensive (BP<135/85, treated) at entry. All patients had to be currently treated for hypertension (one or two FDA-approved antihypertensives with an ending BP<135/85. MAS XR was administered for a 6-week period. Medication was titrated to a target maximum dose of 60 mg/d. Following the study period, patients were taken off MAS XR. They remained on their previous antihypertensive therapy regimen and were followed over a 2-week period. The ADHD Symptom Checklist Severity Scale was used weekly to assess symptoms of ADHD.
RESULTS: A total of 7 patients took 60 mg/d MAS XR (maximum dose) at end dose. Five patients attempted higher dosing but experienced AEs that were not related to BP. One patient experienced complete alleviation of symptoms at 20 mg. No patients had increased adjustments in their antihypertensive therapy regimen during the study. There was no significant difference among all weeks in mean systolic BP (SBP), including baseline (P=0.18). There was no significant difference in mean diastolic BP (DBP) among all weeks, including baseline (P=0.63). No new development of clinical significant electrocardiographic (ECG) changes was found during the study. There were no significant changes in mean PR, QRS, or QTc between baseline values and Week 6. There was a significant difference in mean QT interval between baseline and Week 6.
CONCLUSIONS: MAS XR may be used in adult patients with hypertension controlled with antihypertensive medication. BP changes were minimal in adult patients with ADHD whose hypertension was treated. MAS XR is efficacious for ADHD when used in conjunction with antihypertensive medications.
Presented at the Annual Meeting of the American Psychiatric Association, Atlanta, GA, May 24, 2005.

36. Spironolactone-induced hyperkalemia in patients with heart failure. *Zachary A. Stacy, Pharm.D., BCPS*[1], Shannon L. Dobson, Pharm.D.[1], Paul P. Dobesh, Pharm.D., FCCP, BCPS[2]; (1)St. Louis College of Pharmacy, St. Louis, MO; (2)University of Nebraska Medical Center, Omaha, NE.

PURPOSE: In the RALES trial, spironolactone demonstrated a 30% relative reduction in mortality in patients with severe heart failure, with a minimal increased risk of hyperkalemia. Literature suggested that the incidence of hyperkalemia may be greater in general practice due to less aggressive and structured monitoring, and more liberal use of spironolactone compared to the RALES trial. We conducted a retrospective analysis to determine if the incidence of serious hyperkalemia in our multidisciplinary Heart Failure Clinic (HFC) patients was different than in the RALES trial.
METHODS: We performed a historical cohort study which included all HFC patients whom received spironolactone from 10/99 to 10/04 (n=74). Data collection included patient demographics, hyperkalemic risk factors, concomitant medications, serious hyperkalemic events (potassium ≥6 mEq/mL), and all potassium levels during the first year of therapy. These data from our HFC were compared with those reported in the RALES trial. Serious hyperkalemia was compared using the Fisher's exact test.
RESULTS: Patient demographics, presence of risk factors, and concomitant medications were similar between both groups, except the baseline New York Heart Association (NYHA) class and b-blockers use. There were more patients with NYHA class I and II (45.9% vs. 0.5%; p<0.001) and less NYHA classes III and IV (54.1% vs. 99.5%; p<0.001) in our HFC than those in the RALES trial. b-blockers were used more often in our HFC patients compared to the RALES trial (73% vs. 11%; p<0.001). The incidence of serious hyperkalemia was not different between the groups (2.7% in HFC and 1.7% in RALES; p=0.14).
CONCLUSIONS: Despite more liberal use of spironolactone in our HFC, the incidence of serious hyperkalemia was similar to that reported in the RALES trial.

37E. Cardiovascular safety of MAS XR treatment in patients with ODD. Daniel Connor, MD[1], Thomas J. Spencer, MD[2], David A. Mays, PharmD, MBA, BCPS[3], Paul Hodgkins, PhD, RAC[3], *Jennifer Robinson, PharmD*[3]; (1)UMass Memorial Medical Center, Worcester, MA; (2)Harvard University and Massachusetts General Hospital, Boston, MA; (3)Shire Pharmaceuticals Inc., Wayne, PA.

OBJECTIVE: The objective of this study was to assess the cardiovascular safety of once-daily MAS XR (10 mg/d–40 mg/d) in children and adolescents with ODD with or without comorbid ADHD.
METHODS: The cardiovascular safety of MAS XR in the treatment of school-aged children and adolescents (6–17 years of age) with ODD was examined in this multicenter, randomized, double-blind, parallel-group, placebo-controlled, forced–dose-escalation study. Key inclusion criteria were normal blood pressure, an electrocardiogram (ECG) within normal range, and no comorbid illness that could affect the efficacy or tolerability of MAS XR. Pulse rate, systolic blood pressure (SBP), and diastolic blood pressure (DBP) were measured at each visit, and 12-lead ECGs were completed at screening and endpoint or early termination.
RESULTS: Of the 308 randomized patients, 262 completed the study. Demographic characteristics were comparable across treatment groups, with most patients being male and white. Most of the patients diagnosed with ODD with comorbid ADHD. Overall changes in pulse, SBP, DBP, and ECG measurements were not clinically significant, and there did not appear to be an association between treatment with MAS XR and any changes in these parameters. There were no apparent trends and no notable differences among treatment groups with respect to the percentage of patients with cardiovascular changes. Only 2.1% of the patients had a pulse increase of ≥25 bpm from baseline to endpoint. Only 4.5% of patients had an increase in SBP of ≥20 mm Hg from baseline to endpoint. No serious cardiovascular adverse events or deaths occurred during this study.
CONCLUSIONS: MAS XR was shown to have a safe cardiovascular profile. Overall changes in laboratory values, ECGs, and vital signs were not clinically significant, no trends were seen, and an association between MAS XR and changes or abnormalities was not apparent.
Presented at the Annual Meeting of the American Academy of Child and Adolescent Psychiatry, Toronto, ON, Canada, October 18-23, 2005.

38E. Cardiovascular safety of mixed amphetamine salts XR in childhood ADHD. Joseph Biederman, MD[1], Paul Hodgkins, PhD, RAC[2], David A. Mays, PharmD, MBA, BCPS[2], M. Alex Michaels, MD[3], *Jennifer Robinson, PharmD*[2]; (1)Harvard University and Massachusetts General Hospital, Boston, MA; (2)Shire Pharmaceuticals Inc., Wayne, PA; (3)Shire Pharmaceutical Development Inc., Rockville, MD.

OBJECTIVE: The objective of this study was to assess the cardiovascular safety of once-daily dosing (10–40 mg/d) of MAS XR in children aged 6–12 years with ADHD.
METHODS: This was a prospective, open-label, noncomparative, community-based study designed to determine the cardiovascular safety of once-daily MAS XR dosing. Subjects were children 6–12 years of age (N=2968) diagnosed with ADHD by DSM-IV-TR‘ criteria, in good physical health, whose symptoms were well controlled with stimulant medication. Following the initial screening period and baseline visit, patients meeting eligibility requirements were converted from their current treatment regimen to equivalent doses of MAS XR. Systolic blood pressure (SBP), diastolic blood pressure (DBP), and pulse rate were measured at each study visit. A 12-lead electrocardiogram (ECG) was performed at screening and at the end of the extension phase or upon early termination.
RESULTS: After screening, 2968 patients were enrolled and treated at 365 sites; of those patients, 2280 completed the initial phase. Of the 1407 patients who entered the extension phase, 293 discontinued therapy, 673 were terminated, and 441 completed therapy. The mean increase in SBP and DBP from baseline to final visit was <1 mm Hg, and the mean increase in heart rate was 1.5 bpm. The magnitude of change from baseline in SBP, DBP, and pulse rate was similar among patients treated with 10, 20, 30, and 40 mg/d MAS XR. Mean changes in ECG parameters were statistically, but not clinically, significant and were within age-specific normal ranges.
CONCLUSION: The cardiovascular effects of MAS XR treatment in children 6–12 years of age appear to be minimal. Few cardiovascular AEs, no serious

cardiovascular AEs, and no deaths were reported. There were no clinically significant or dose-related changes in SBP, DBP, or pulse rate.
Presented at the Annual Meeting of the American Academy of Child and Adolescent Psychiatry, Toronto, ON, Canada, October 18-23, 2005.

39. Efficacy of coronary stents: bare metal versus drug-eluting stents. *Tera D. Moore, Pharm.D.*[1], J. Nile Barnes, Pharm.D.[2], Robert A. O'Rourke, M.D.[1], William D. Linn, Pharm.D.[1]; (1)University of Texas Health Science Center at San Antonio/ South Texas Veterans Health Care System, San Antonio, TX; (2)The University of Texas College of Pharmacy, Austin, TX.

PURPOSE: This historical cohort study compared hard clinical outcomes in patients who underwent percutaneous coronary intervention (PCI) using bare metal stents (BMS) vs. drug-eluting stents (DES). Our hypothesis is that there are no differences between the two cohorts.
METHODS: Medical records of 172 patients who underwent PCI at the South Texas Veterans Health Care System (STVHCS) between 2002 and 2003 were reviewed. In 2002 all patients received BMS and in 2003, DES were used exclusively. The dataset included vital signs, lipid values, current medications, past cardiac history, coronary anatomy, ventricular function, vessels intervened on, type of stent(s) used, costs of stents per PCI, and 9 months of post-procedure follow-up. Data collected during the follow-up included death from any cause, cardiac events, need for revascularization, and risk factor modification. Rates of major adverse cardiac events (MACE) for the two groups were compared.
RESULTS: Ninety-five patients underwent PCI with BMS in 2002 versus 77 patients with DES in 2003. At baseline, the BMS cohort was older (mean age 71 versus 62 years) and more likely to have uncontrolled diabetes [mean HbA 1C 8.4 (n=46) versus 6.8 (n=45)] than the DES cohort. After 9 months of follow-up, rates of MACE were 8.4% for the BMS and 10.4% for the DES cohorts. Cardiac admissions were higher in the DES cohort (10.5% BMS vs. 14.3% DES). In-stent restenosis was similar in both groups (8.4% BMS vs. 7.8% DES).
CONCLUSION: These data are consistent with emerging data that DES provide no advantage over BMS in terms of hard clinical outcomes. Unfortunately, DES have become the "standard of care" imposing a significant economic burden. Importantly, neither BMS nor DES have been proven superior to optimized medical therapy in decreasing MACE in patients with chronic ischemic heart disease.

40E. Safety of atorvastatin in the elderly patient population. Judith Hey-Hadavi, MD, Erik Kuntze, MD, Don Luo, PhD, Paul Silverman, PharmD, Donald Pittman, PharmD, Barbara LePetri, MD, *Margaret Noyes Essex, Pharm.D.*; Pfizer Global Pharmaceuticals, New York, NY.

PURPOSE: CV disease is the leading cause of death in the US. Of those who die of CHD and/or experience a stroke, 85% are ≥65 yrs. Sub-analyses suggest that statins benefit pts ≥65 yrs similarly to younger pts. Elderly may not receive evidence-based therapies, like statins, because of safety concerns. Method: This was an age-defined subgroup analysis of safety data in pts ≥65yrs from 50 randomized atorvastatin (Atv) trials completed by Sept 15, ë04. The analysis included treatment-associated adverse events (AEs), serious AEs and musculoskeletal, hepatic and renal AEs in Atv 10-80 mg dose range and placebo (Pbo).
RESULTS: A total of 5924 pts ≥65 yrs at the time of study enrollment were categorized in Atv 10mg (n=2042), 20mg (n=667), 40mg (n=522), 80mg (n=1698) and Pbo (n=995). Overall AE profiles for all Atv groups and Pbo were similar. Most frequent treatment-associated AEs were related to the digestive system (>7.5% all groups). Serious AEs were rare and seldom led to withdrawal. Pts with persistent elevation of LFTs (>3xULN) were 2(0.2%), 3(0.2%), 0, 1(0.2%), and 7(0.4%), in Pbo, Atv 10mg, 20mg, 40mg, and 80mg, respectively. Persistent CPK elevations (>10xULN) were not observed in any treatment group. The incidence of treatment-associated myalgia was low. Hematuria was rare (1 pt in Pbo and Atv 80mg). There were no cases of treatment-related albuminuria and no cases of rhabdomyolysis.
CONCLUSION: The overall incidence of AE in Atv-treated elderly did not increase with dose and was similar to that observed with Pbo. The incidence of LFT elevations (>3xULN) was slightly higher in 80mg group, and specific musculoskeletal and hepatic AEs were rare. The results of this analysis support the positive benefit to risk profile of atorvastatin and should be taken in consideration when managing the CV risk in the elderly.
Presented at the 2nd International Symposium on Triglycerides and High-Densiy Lipoproteins, New York, NY, July 14-17, 2005.

41. Impact of formulary changes on the care provided to Medicaid patients with hyperlipidemia. *L. Brian Cross, PharmD, CDE*[1], Natalie A. Christy, PharmD[1], Andrea S. Franks, PharmD, BCPS[1], John E. Delzell, MD, MSPH[1], James K. Eddlemon, PharmD[2]; (1)University of Tennessee, Memphis, TN; (2)Pfizer Pharmaceuticals, Inc, Memphis, TN.

PURPOSE: The objectives of this study were to assess low-density lipoprotein (LDL) goal attainment, the percent change in Framingham 10-year CHD risk, appropriate dosage conversions, and follow-up monitoring after a statewide Medicaid formulary change from atorvastatin to simvastatin in an academic family medicine clinic.
METHODS: A retrospective chart analysis was conducted in patients identified via ICD-9 codes for hyperlipidemia. Adult patients were included if their change from atorvastatin to simvastatin was a direct result of the formulary change in September 2003. Data were collected for a 9-month period from September 2003 to June 2004. Data collected included: demographic data, change in lipid values, and appropriate dosage conversion and follow-up after formulary changes. Prior to formulary changes, no dosing conversion recommendations were provided by Medicaid.
RESULTS: Sixty-one of 900 patients with hyperlipidemia met study inclusion criteria. There was no significant difference in LDL goal attainment or change in Framingham 10-year CHD risk for all study patients converted from atorvastatin to simvastatin. However, for the highest risk patients with an LDL goal of <100 mg/dL, there was a significant difference in LDL goal attainment favoring atorvastatin (55%) versus simvastatin (26%) [p=0.0139]. Fifty percent of patients were dose converted incorrectly, with 90% of those receiving a lower dose equivalent. The mean atorvastatin dose was 21.5 mg pre-conversion, with a mean simvastatin dose of 30.9 mg post-conversion. A direct correlation was found between those appropriately dose converted and LDL goal attainment (p=0.0472). Finally, twenty of 61 patients (33%) had no follow-up lipid panel and 63% had no liver function test (LFT) monitoring during the 9-month data collection period.
CONCLUSIONS: This study identifies problems, specifically in the highest risk patients, with a Medicaid formulary conversion of statin therapy.

42. Adherence to guidelines for lipid management on admission for unstable angina. *Amy L. Seybert, PharmD*, Sandra L. Kane-Gill, PharmD, Melissa I. Saul, MS, Daniel Edmundowicz, MD; University of Pittsburgh Medical Center, Pittsburgh, PA.

PURPOSE: To describe lipid goal attainment in patients admitted for unstable angina (UA) and to assess adherence to ACC/AHA guidelines for managing patients admitted for UA, focusing on recommendations for lipid therapy in those being treated with statins.
METHODS: This was a retrospective cross-sectional analysis of patients admitted with UA at a tertiary care hospital from July 1, 2001 and July 1, 2004. Patients were included in analysis if they were on a statin upon admission and a lipid panel was obtained within 24 hours. Lipid goals and thresholds were set using NCEP ATP-III guidelines (LDL-C <100 mg/dL, HDL-C >40 mg/dL). Patients were stratified into four categories of LDL-C and HDL-C goal combinations. Adherence to UA guidelines for lipid-altering therapy was assessed using pharmacy charge codes and electronic medical records.
RESULTS: There were 1458 admissions in 1385 patients during the study period. On admission, 674 (49%) were receiving statins. Only 390 (58%) patients had a lipid panel within 24 hours. Despite treatment with a statin, 40% were at goal LDL-C upon admission. In patients at goal LDL-C, 63% had suboptimal HDL-C. Evaluation of adherence to UA guidelines is being finalized. Lipid goal categories and clinical outcomes are described in the table.

Outcome[a]	LDL≥100, HDL≤40 n=97	LDL<100, HDL>40 n=95	LDL≥100, HDL>40 n=58	n=140	p-value
PCI	48	55	27	70	0.494
CABG	10	17[b]	2[b,c]	21[c]	0.048
AMI	26	39	16	39	0.099

[a]not powered to detect differences
[b]p=0.006, difference between LDL≥100, HDL≤40 and LDL<100, HDL>40
[c]p=0.014, difference between LDL<100, HDL>40 and LDL≥100, HDL>40

CONCLUSION: Among statin-treated patients admitted for UA, the majority are not reaching goal LDL-C. In those patients at goal LDL-C, two-thirds have suboptimal HDL-C. This represents an opportunity for intervention to improve adherence to UA management guidelines with respect to lipids that may improve quality outcomes.

43. Anti-factor Xa profiles in cardiac patients receiving enoxaparin therapy. Mei E. Tse, Pharm., D.[1], May Mak, Pharm., D.[1], *Gladys H. Mitani, Pharm., D.*[1], Pamela Pickens, Pharm., D.[2], Paul M. Beringer, Pharm., D.[1], Jane Tran Tesoro, Pharm., D.[1], Radha Sarma, M.D.[2], Stan Louie, Pharm., D.[1]; (1)USC School of Pharmacy, Los Angeles, CA; (2)LAC+USC Medical Center, Los Angeles, CA.

PURPOSE: Low-molecular weight heparins (LMWHs) are widely used in the treatment and prophylaxis of thromboembolic events. The need for routine anti-factor Xa (aFXa) level monitoring remains controversial; however, data on this subject are scarce. Guidelines for dosing LMWHs in the prophylaxis of cardiac patients at high risk for thromboembolic events are also limited. This study describes and evaluates aFXa profiles in cardiac patients who received subcutaneous (SQ) enoxaparin (Enox) bridging during initiation of

anticoagulation therapy with warfarin or prophylaxis during perioperative periods.
METHODS: This study was a retrospective study of 47 aFXa levels obtained in 38 patients who received Enox bridge therapy with standard prophylactic doses (30mg SQ q 12 h or 40mg SQ daily) or higher doses targeted to achieve therapeutic aFXa levels between 0.5-1.0 IU/ml at four and six hours post SQ injection.
RESULTS: The average dose for patients receiving standard prophylactic regimens was 0.48mg/kg/dose. Forty-five percent of the samples achieved aFXa levels between 0.5–1.0 IU/ml in these patients. For patients who received higher doses, average Enox doses of 0.76mg/kg/dose achieved the therapeutic target or higher in 100% of the samples at four hours post injection; and an average dose of 0.83mg/kg/dose achieved the therapeutic target or higher in 90.9% of the samples at six hours. Correlation of aFXa levels vs mg/kg and mg/BMI doses at six hours were 0.678 and 0.826 respectively ($p<0.0003$). There were no thromboembolic complications but two minor bleeding complications.
CONCLUSION: Most cardiac patients required less than 1mg/kg/dose of Enox to achieve aFXa levels between 0.5-1.0 IU/ml at 4-6 hours. aFXa levels vs mg/BMI dose showed the best correlation at 6 hours post injection.

44. Dietary potassium intake and potassium use with spironolactone. Courtney Krueger, Pharm.D.[1], *Lisa Rene, Pharm.D., candidate*[2], Kathryn Momary, Pharm.D.[1], Vicki Groo, Pharm.D.[1], Deidra Fontana, RN, BA[3], Paul Vaitkus, M.D.[3], Larisa Cavallari, Pharm.D., BCPS[1]; (1)University of Illinois at Chicago, College of Pharmacy, Chicago, IL; (2)University of Illinois at Chicago, College of Pharmacy, Chicago, IL; (3)University of Illinois at Chicago, Chicago, IL.

PURPOSE: Spironolactone is recommended for patients with severe heart failure based on evidence that it improves clinical outcomes in this population. Spironolactone increases potassium (K) concentrations, and guidelines recommend stopping or reducing K supplements when spironolactone is started. However, we previously found that a large number of patients still require K supplementation with spironolactone therapy. The objective of this study was to determine whether dietary K intake contributes to the need for K supplementation with spironolactone in heart failure patients.
METHODS: Heart failure patients taking spironolactone in addition to standard therapy were enrolled. Participants completed a survey designed to assess dietary K intake. Demographic characteristics, medical history, concomitant medications, and laboratory measurements of serum K and creatinine were also obtained. Survey results and patient characteristics were compared between patients on and not on K supplements with spironolactone.
RESULTS: Thirty-two subjects were enrolled; 15 were taking K supplements in addition to spironolactone and 17 were not. Demographic characteristics, heart failure severity, heart failure therapy, and renal function were similar between groups. The median (range) K supplement dose was 30 (20-60) mEq/day, equivalent to 8,211 (5,474-16,421) mg/week. Subjects on K supplements had lower K concentrations [median (range) 4.2 (3.5-4.8) vs. 4.5 (3.6-5.1) mmol/L; p=0.03]. Dietary K intake was 10,150 (7,559-16,398) mg/week in subjects taking K supplements and 11,980 (5,183-22,565) mg/week in those not on supplements; p=0.13.
CONCLUSION: Subjects on K supplements had lower K concentrations than those not taking K supplements despite consuming a similar amount of K in their diet. These data do not support a major role for dietary K intake as a determinant of the need for K supplementation with spironolactone in heart failure.

45. Improving the treatment of risk factors for coronary heart disease in the community setting. *Kathryn M. Uchida, Pharm.D.*, Noreen T. Wong, Pharm.D.; Pfizer, Inc., Pasadena, CA.

PURPOSE: The study assessed management of risk factors for coronary heart disease (CHD) in the community setting in order to: 1) identify risk factors for developing CHD, 2) identify treatment gaps compared to national guidelines, and 3) evaluate prescribing trends for patients with dyslipidemia and hypertension.
METHODS: Cardiovascular health screenings, which included full lipid panels, blood pressure and glucose monitoring, were conducted for 2,923 patients at 26 physician offices in the Western United States. Patients completed a cardiovascular risk assessment form documenting demographic information and risk factors for developing cardiovascular disease. CHD risk factors were calculated based on the patient responses. Blood pressure, HbA1c, blood glucose and lipid panel results (HDL, LDL, Total cholesterol and triclycerides) were documented.
RESULTS: While 26.2% of the participants had a history of hypertension, 79.0% were taking medications and 40.3% achieved their blood pressure goals. Approximately one-fourth (25.8%) of the participants had a history of high cholesterol with only 57.2% taking medications and 69.0% achieving their LDL goals. Approximately 45.0% of the participants with no documented history of dyslipidemia had total cholesterol levels greater than 200 mg/dL. The percent of participants at LDL goal was 42.5%, 60.4% and 85.5% for participants with CHD or CHD risk equivalents, 2+ risk factors and 0-1 risk factors, respectively.
CONCLUSION: Patients with a history of hypertension were more likely treated with medications than patients with hyperlipidemia. Early detection and treatment of dyslipidemia are essential for the management of CHD risk. This study provides further evidence that awareness of cholesterol management should be increased among providers and patients.

46E. Impact of aggressive treatment with atorvastatin on renal function in managed care patients with coronary heart disease: the ALLIANCE study. Michael Koren, MD[1], Michael Davidson, MD[2], Robert Mendes, MD[3], *Margaret Noyes Essex, Pharm.D.*[3]; (1)Jacksonville Center for Clinical Research, Jacksonville, IN; (2)Chicago Center for Clinical Research, Chicago, IL; (3)Pfizer Global Pharmaceuticals, New York, NY.

PURPOSE: Previous data suggest atorvastatin may have nephroprotective effects, possibly as a result of vascular disease benefits. The ALLIANCE study, a prospective, randomized trial, demonstrated that aggressive lipid lowering with atorvastatin significantly reduced coronary events compared with usual care in patients with coronary heart disease (CHD) enrolled in managed-care organizations and VA settings. We retrospectively analyzed whether or not treatment with atorvastatin versus usual care improved renal function in this population.
METHODS: 2442 CHD patients with dyslipidemia were randomized to either aggressive treatment, using atorvastatin, or usual care. Atorvastatin-treated patients were titrated to an LDL-cholesterol goal of <80 mg/dL or a maximum atorvastatin dose of 80 mg/d. Patients randomized to usual care continued their baseline lipid treatment, with any further changes in therapy directed by their primary attendant physician. Renal function was compared at baseline and 48 months, using creatinine clearance (CrCl) calculated using the Cockroft-Gault formula.
RESULTS: CrCl was similar in the two groups at baseline (mean [SD] CrCl = 88.6 [30.8] mL/min in the atorvastatin group and 87.2 [28.8] mL/min in the usual care group; P=0.32). After 48 months, there was a mean (SE) decline in CrCl of 4.4% (0.75) in the usual care group (mean = 83.0 mL/min; P=0.0001 versus baseline). Over the same time period, CrCl did not change in the atorvastatin group (-0.06% [0.67]; mean = 88.3 mL/min; P=0.93 versus baseline). The difference in mean change from baseline between the atorvastatin and usual care groups was highly significant (P=0.0001). There were no significant interactions between treatment and gender, age, or race. BP control was equivalent between groups. Safety and tolerability were similar in the two groups.
CONCLUSION: In addition to improved lipid control and reductions in coronary events, aggressive treatment with atorvastatin prevents deterioration in renal function compared with usual care in patients with CHD.
Presented at the 54th Annual Scientific Session of the American College of Cardiology, Orlando, FL, March 6-9, 2005.

47. Evaluation of quality of care in heart failure hospitalization. *Corinne Chahine, M.S., Pharm.D.*, Yvonne Terceros, Pharm.D., Sherri Sochaski, RN, Marcel Forsythe-Thomas, RPh, Elie Chakhtoura, MD; Saint Michael's Medical Center, Newark, NJ.

PURPOSE: To evaluate the impact of the implementation of standardized multidisciplinary and discharge instructions forms on the quality of care provided for heart failure (HF) patients, based on the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) core measures.
METHODS: The data were collected and analyzed retrospectively on 2 cohorts of patients: Group 1 (G1) consisted of HF patients admitted between October-December 2003 prior to the standardized forms implementation; and Group 2 (G2) of those admitted between October-December 2004 following the forms implementation. Data collection assessed compliance with four JCAHO core measures: left ventricular ejection fraction (LVEF) assessment, ACE-inhibitors use in patients with LVEF < 40%, discharge instructions, and counseling for smoking cessation. Data analysis was performed using descriptive statistics and the Chi-Square test.
RESULTS: G1 consisted of 103 patients (62 males, mean age 69 ± 14 years) and G2 of 147 patients (77 males, mean age 68 ± 14 years). The mean length of stay was 9 ± 6 days for both groups. Assessment of LVEF was performed in 92 patients (89%) in G1 vs 141 patients (96%) in G2 ($p<0.05$). Fifty-four of 66 patients (82%) with LVEF<40% were treated with ACE-inhibitors in G1, as compared to 64 of 67 patients (96%) in G2 ($p<0.025$). Alert patients were evaluated for the receipt of discharge instructions (98 in G1 and 129 in G2). Instructions were given to 83 patients (85%) in G1 vs 129 patients (100%) in G2 ($p<0.001$). All smokers in both groups received appropriate counseling on smoking cessation.
CONCLUSIONS: The implementation of our standardized forms significantly improved the quality of care provided for our HF patients, particularly the use

of ACE-inhibitors which carry a considerable improvement in survival. Further improvements may be obtained through a standardized admission order form that will encompass more diagnostic criteria and therapeutic measures.

48. Predictors of excess dosing of injectable antithrombotics in patients with non-ST-segment elevation acute coronary syndromes. *Sarah Spinler, PharmD*[1], Karen P. Alexander, MD[2], Anita Y. Chen, MS[2], Matthew T. Roe, MD[2], W. Brian Gibler, MD[3], E. Magnus Ohman, MD[4], Eric D. Peterson, MD[2]; (1)Philadelphia College of Pharmacy, University of the Sciences in Philadelphia, Philadelphia, PA; (2)Duke Clinical Research Institute, Durham, NC; (3)University of Cincinnati, Cincinnati, OH; (4)University of North Carolina at Chapel Hill, Chapel Hill, NC.

PURPOSE: CRUSADE is a national registry and quality initiative designed to evaluate the application of evidenced based medicine in patients with non-ST-segment elevation acute coronary syndromes (NSTE ACS). Previous analyses indicate that excessive dosing of unfractionated heparin (UFH), enoxaparin (LMWH) and glycoprotein IIb/IIIa inhibitors (GPI) was associated with an increased risk for major bleeding. This report characterizes variables which are independent predictors of excess dosing.
METHODS: Multivariate analysis was performed to identify predictors of excess dosing of UFH, LMWH and GPI in 30,316 patients enrolled in CRUSADE between 01/04 and 9/04. Excessive dose was defined as UFH >70U/kg bolus or >15 U/kg/hr infusion, LMWH >1.05 mg/kg and GPI >package insert dose and not adjusted for renal insufficiency. Overall, 25.3% received an excessive dose of at least 1 agent.
RESULTS: Predictors of excess dose are shown (Table). Values are adjusted OR (95% confidence interval).

Variable	UFH (N=8944)	LMWH (N=9988)	GPI (N=10,379)
Weight (per 5 kg decrease)	1.28(1.22-1.35)	1.25(1.23-1.28)	1.02(1.00-1.04)
Female (vs male)	0.92(0.80-1.06)	0.73(0.63-0.84)	3.74(3.29-4.25)
Age 65-75 yrs (vs < 65 yrs)	0.93(0.79-1.11)	0.76(0.65-0.89)	4.23(3.67-4.86)
Age ≥75 yrs (vs < 65 yrs	0.81(0.68-0.96)	0.75(0.63-0.89)	14.39(12.24-16.90)
Diabetes	1.04(0.93-1.16)	1.16(1.03-1.31)	1.35(1.20-1.51)
Academic (vs non-academic hospital)	1.02(0.66-1.58)	1.26 (1.03-1.54)	0.93(0.76-1.15)
Cardiologist (vs non-cardiologist)	0.90(0.77-1.06)	1.17 (1.02-1.34)	0.94(0.82-1.06)
Renal Insufficiency	1.25(1.07-1.46)	0.82(0.67-1.00)	4.12(2.95-5.75)
Overall adherence to guideline medications score (per 5% increase)	0.89(0.77-1.03)	0.98(0.93-1.3)	0.94(0.89-0.99)
Hospital size (per 100 beds)	1.16(1.03-1.31)	1.01 (0.97-1.05)	0.98(0.94-1.03)

Variables included in the model but not presented were insurance status and positive biomarkers.

CONCLUSIONS: Excess dosing increases the risk for major bleeding and transfusion. Patients who are of lower weight or with abnormal renal function are at heightened risk of excess dosing. Pharmacists should be aware of these factors and help with determining correct doses of UFH, LMWH and GPIs. Education is needed to heighten awareness of importance of dosing practice.

49. Pharmacy-directed, multidisciplinary practice to improve compliance with published guidelines and quality indicators in post-CABG patients. *Felix K. Yam, Pharm.D.*, Wendell S. Akers, Pharm.D., Ph.D., Kelly M. Smith, Pharm.D., Jeremy D. Flynn, Pharm.D.; University of Kentucky Chandler Medical Center, Lexington, KY.

PURPOSE: Lifestyle modification and appropriate medication therapy can influence morbidity and mortality in patients with coronary artery disease requiring coronary artery bypass graft (CABG) surgery. We previously evaluated our compliance with American Heart Association (AHA)/American College of Cardiology (ACC) guidelines and found opportunity for significant improvement with angiotensin converting enzyme (ACE) inhibitor initiation. We hypothesized that implementation of a pharmacy-directed, multi-disciplinary practice would improve compliance with published guidelines.
METHODS: In this prospective, historical control study of CABG patients, we implemented a systematic method of care through patient education, documentation of medication histories, and continuous medication review. The multidisciplinary team included a physician, nurse, dietician, physical therapist and a clinical pharmacist. The primary outcome was to achieve at least an 80% compliance rate with initiation of ACE inhibitors. Secondary endpoints were to achieve 100% compliance with other quality indicators: pharmacotherapy (beta-blocker, aspirin, and lipid-lowering agents) and lifestyle modification (dietary, physical activity, and smoking cessation).
RESULTS: A total of 100 patients were included in this study, 50 historical controls and 50 prospective patients. Compliance rates with pharmaco-therapy indicators between the control and intervention groups were: beta-blockers (98% vs. 96%, p=0.32), HMG-CoA reductase inhibitors (76% vs. 96%, p=0.006), ACE inhibitors (42% vs. 84%, p<0.001), and aspirin (92% vs. 100%, p=0.04), respectively. Compliance rates with lifestyle modification counseling between the control and intervention groups were: dietary (49% vs. 91%, p<0.001), physical activity (54% vs. 87%, p<0.001) and 100% for smoking cessation counseling, respectively. Documentation for smoking cessation counseling in the control group patients could not be found in the medical record.
CONCLUSIONS: A pharmacy-directed multidisciplinary program can increase ACE inhibitor initiation at discharge and improve compliance with currently accepted AHA/ACC guidelines and quality indicators in patients following CABG surgery.

50E. Transfusion rates associated with excess dosing of antiplatelet and antithrombin agents in patients with non-ST-segment elevation acute coronary syndromes. *Sarah Spinler, PharmD*[1], Karen P. Alexander, MD[2], Anita Y. Chen, MS[2], Matthew T. Roe, MD[2], W. Brian Gibler, MD[3], E. Magnus Ohman, MD[4], Eric D. Peterson, MD[2]; (1)Philadelphia College of Pharmacy, University of the Sciences in Philadelphia, Philadelphia, PA; (2)Duke Clinical Research Institute, Durham, NC; (3)University of Cincinnati, Cincinnati, OH; (4)University of North Carolina at Chapel Hill, Chapel Hill, NC.

PURPOSE: Antithrombotic agents reduce death/MI in patients with non-ST-segment elevation acute coronary syndromes (NSTE ACS) yet may cause bleeding. While dosing algorithms exist, the degree to which they are followed in practice and the relationship between dose and red blood cell (RBC) transfusions is unknown.
METHODS: We explored initial antithrombotic dose in 30,316 NSTE ACS patients enrolled in the CRUSADE Initiative from 1/04 to 9/04. Excess was defined as unfractionated heparin (UFH) >70 U/kg bolus or >15 U/kg/hr infusion, low-molecular-weight heparin (LMWH) >1.05 mg/kg, and GP IIb/IIIa inhibitors not adjusted for patient CrCl. The relationship between excess dose and transfusion (excluding CABG patients) was determined before and after adjustment for age, renal function, sex, CHF, and systolic blood pressure.
RESULTS: 25.3% received at least one antithrombotic in excess (among treated: 32.8% for UFH, 13.8% for LMWH, and 26.8% for GP IIb/IIIa). Advanced age was strongly associated with excess dosing (p<0.0001 for all agents), as was female sex. Transfusion occurred in 9% overall, but was associated with excess doses even after accounting for pt factors (Table). Among those receiving heparin and GP IIb/IIIa inhibitor, transfusions ranged from 4% when both given as recommended to18% when both given in excess.

Agent (N treated)	Transfusion (%) Excess vs. no excess	Transfusion Adj OR (95% CI)
LMWH (n=7484)	8.8 vs. 6.7	1.22 (0.94, 1.57)
UFH (n=6924)	10.4 vs. 8.0	1.13 (0.96, 1.34)
GP IIb/IIIa (n=8085)	13.3 vs. 4.4	1.38 (1.08, 1.76)
Any Heparin or GP IIb/IIIa (n=6148)	10.6 vs. 4.1	1.41 (1.10, 1.80)

CONCLUSION: Excess dosing of antithrombotics is common, affecting 40% of NSTE ACS patients. These errors particularly affect women and elderly and result in an increase in transfusions. To maximize patient benefits, quality metrics must include how as well as whether evidence-based therapies are given.
Published in Circulation 2005;111:e310-e359.

51. Association between the use of glycoprotein (GP) 2b-3a Inhibitors, bleeding events, and creatinine clearance (CrCl) in patients undergoing percutaneous coronary intervention (PCI). *Sarah A. Spinler, PharmD*[1], Kathleen A. Stringer, PharmD[2], Ann K. Wittkowsky, PharmD[3], Sallie K. Young, PharmD[4], Marianne McCollum, Ph.D., R.Ph.[2]; (1)Philadelphia College of Pharmacy, University of the Sciences in Philadelphia, Philadelphia, PA; (2)University of Colorado School of Pharmacy, Denver, CO; (3)University of Washington, Seattle, WA; (4)Penn State Milton S. Hershey Medical Center, Hershey, PA.

PURPOSE: Use of anticoagulants is commonly associated with bleeding. In particular, patients with renal impairment who undergo PCI are prone to bleeding complications. The objective of this study was to evaluate the association between the use of GP 2b-3a inhibitors and bleeding events and CrCl in patients undergoing PCI procedures.
METHODS: Medical records of consecutive PCI patients who received GP 2b-3a inhibitors at two university-affiliated hospitals were reviewed concurrently to document bleeding. Patients with active bleeding disorders were excluded. Bleeding was determined using two prospectively defined sets of criteria; Thrombolysis in Myocardial Infarction (TIMI) criteria and investigator criteria (INV) defined as intracranial, retroperitoneal, intraocular or clinically overt bleeding associated with a decrease in hemoglobin ≥ 3 g/dL from baseline or any clinically overt bleeding (e.g., groin oozing, groin hematoma, blood in urinary catheter). Associations between use of GP 2b-3a inhibitors and bleeding events and CrCl were estimated using multiple logistic regression analysis that was performed at a third study site.
RESULTS: Medical records from 423 post-PCI patients were reviewed; 229 patients experienced a major or minor bleed by either TIMI or INV criteria (or both). Results of multivariate analysis indicate that use of GP 2b-3a inhibitors was associated with bleeding events (OR 2.00, 95% CI 1.32, 3.05, p<0.01) and CrCL (OR 0.99, 95% CI 0.99, 1.00, p=0.05). No other adjusting

variables were significant (age, sex, diabetes, hypertension, pre-PCI hematocrit or hemoglobin, concomitant use of low molecular weight heparin, thrombolytic therapy, or heparin).
CONCLUSIONS: Use of GP 2b-3a inhibitors was significantly associated with bleeding events in patients undergoing PCI procedures. In addition, CrCL is an independent predictor of bleeding risk in these patients. Based on these results, the risk-benefit of GP 2b-3a inhibitors in patients with impaired renal function should be considered before initiating therapy.

52. Discharge quality indicators in patients with acute heart failure admitted to the coronary care unit and step-down unit at a tertiary medical center. *May I. Achi, Pharm.D.*[1], Cynthia A. Sanoski, Pharm.D.[1], Simon De Denus, MSc, (Pharm)[2], Mariell Jessup, MD[3], Sarah Spinler, PharmD[1]; (1)Philadelphia College of Pharmacy, University of the Sciences in Philadelphia, Philadelphia, PA; (2)University of Montreal, Montreal, QC, Canada; (3)University of Pennsylvania, Philadelphia, PA.

PURPOSE: Implementation of JCAHO discharge quality indicators (DQI) for patients with acute heart failure (AHF) reduces mortality and rehospitalization. The objective of this study is to report compliance data for patients admitted to a CCU/CICU in a tertiary care center and to compare characteristics associated with performance.
METHODS: Data were extracted from medical records of consecutive patients admitted to the CCU/CICU with AHF who were enrolled in the Acute Decompensated Heart Failure National Registry (ADHERE) between 3/11/02 and 4/12/03. The proportion of patients meeting each DQI and prescription of beta-blockers (BB) and angiotensin receptor blockers (ARBs) at discharge were assessed. Parametric and non-parametric statistics were employed. A p-value<.05 was considered significant.
RESULTS: 338 patients (61% white, 61.8% male, mean age 63.2 yrs) were included. At admission, 84.6% had a history of HF, 51.8% had a history of coronary artery disease (CAD), and 75.4% had LVEF<40%. For evaluation of DQIs, 85.3% of patients received medication and diet instructions, 96.4% had LVEF evaluated, 65.7% (of those with LVEF<40% and without contraindication) were prescribed ACEI at discharge and 10.9% of smokers received smoking cessation counseling. At discharge 89.5% (without contraindication) were prescribed BB and 72.5% of patients (without contraindication) were discharged on either ACEI or ARB. 52.1% of patients met all 4 DQIs. Neither history of renal insufficiency, race nor gender significantly impacted discharge prescription of ACEI. Neither race, history of CAD, nor gender significantly influenced discharge prescription of BB. The mean age of patients prescribed ACEI at discharge was significantly lower than patients not prescribed ACEI (61.3 years vs 65.3 years; p=0.03).
CONCLUSIONS: With the exception of smoking cessation counseling documentation, performance of other JCAHO DQIs meets or exceeds other similar institutions in ADHERE. Gender and race did not impact ACEI and BB prescribing. Proper documentation of smoking cessation counseling is warranted.

53. Amiodarone monitoring: adherence to current recommendations. *Anne P. Spencer, PharmD*[1], Courtney L. Bickford, PharmD[2]; (1)Medical University of South Carolina, Charleston, SC; (2)The University of Texas MD Anderson Cancer Center, Houston, TX.

PURPOSE: The purpose of this study is to quantify the Medical University of South Carolina's (MUSC) adherence to published recommendations for baseline monitoring parameters when initiating inpatient amiodarone therapy, and to determine if appropriate outpatient monitoring of chronic amiodarone therapy (≥ 6 months) is occurring at MUSC.
METHODS: A retrospective review of the medical records of patients initiated on or receiving chronic amiodarone therapy were reviewed. Data are reported using descriptive statistics.
RESULTS: Over a 6-month period, there were 277 adult patients who received oral amiodarone as an inpatient at MUSC. Out of the 277 total patients identified, 45 patients were initiated on chronic amiodarone therapy during their admission at MUSC. Baseline chest x-rays (CXR), liver function tests (LFTs), and thyroid function tests (TFTs) occurred as recommended in 80–90% of patients. Baseline pulmonary function tests (PFTs) occurred in only 24% of patients, 60% of which included a diffusion capacity (D_LCO). Twenty patients with available outpatient records for review were identified as receiving chronic amiodarone therapy. Baseline assessment of LFTs, TFTs, and CXRs occurred in 80–90% of patients, and PFTs occurred in only 30% of patients, 83% of which included a D_LCO. Chronic monitoring at recommended time intervals of LFTs and TFTs occurred in 35% and 20% of patients, respectively, while annual CXRs were performed appropriately in 50% of patients.
CONCLUSION: The adherence rate to published recommendations was between 80-90% for baseline parameters such as LFTs, TFTs and CXRs. Baseline pulmonary function tests were obtained in < or equal to 30% of patients. Serial monitoring of laboratory and radiographic parameters is occurring < or equal to 50% of the time. These data may be utilized to develop an evidence-based protocol for amiodarone monitoring.

54E. Beta 2-mediated glucose production during carvedilol and metoprolol titration in heart failure. *Kai I. Cheang, Pharm.D.*[1], Orly Vardeny, Pharm.D.[2], James Zebrack, MD[3], Mark A. Munger, Pharm.D., FCCP[4], Edward Michael Gilbert, MD[3]; (1)Virginia Commonwealth University, Richmond, VA; (2)University of Wisconsin School of Pharmacy, Madison, WI; (3)University of Utah, Salt Lake City, UT; (4)Department of Pharmacotherapy, University of Utah College of Pharmacy, Salt Lake City, UT.

PURPOSE: Metoprolol and carvedilol are commonly used in heart failure. Previous studies in hypertension indicate worsening of insulin sensitivity with metoprolol but not with carvedilol. However in heart failure, their relative effects on glucose production have not been directly compared. This study compares fasting glucose and β2-mediated glucose production during metoprolol and carvedilol titration in heart failure patients.
METHODS: From a previous heart failure cohort whose metoprolol or carvedilol were titrated to maximally tolerated doses (up to metoprolol 200mg/d or carvedilol 25mg twice daily) in 5 visits, we analyzed fasting glucose and glucose AUC0-180min upon a β2-agonist (terbutaline) infusion in nondiabetic individuals.
RESULTS: Fasting glucose (mg/dL) in the metoprolol group (n=9) decreased from 91.1 ± 2.6 (baseline) to 86.9 ± 2.0 (end of titration) while it increased from 91.8 ± 3.1 to 95.7 ± 2.6 with carvedilol (n=6) (p=0.0273, ANCOVA for the comparison between groups). AUC0-180 (mmol/L x 180 min) upon terbutaline infusion decreased from 5.6 ± 0.3 to 4.8 ± 0.1 with metoprolol, and from 5.8 ± 0.3 to 5.0 ± 0.1 with carvedilol (p=NS). AUC0-180 for both metoprolol and carvedilol decreases as drug dosages increase (p=0.0006, repeated measure ANOVA), with a trend toward bigger reduction with metoprolol.
CONCLUSIONS: Metoprolol and carvedilol at clinically relevant doses do not impair fasting glucose. As beta blockade increases, β2-mediated glucose production is reduced.
Presented at the Annual Meeting of the American Society of Clinical Pharmacology & Therapeutics, Orlando, Florida, March 5, 2005.

55. SSRI use in acute coronary syndromes: effect on major adverse cardiac events and bleeding complications. *William Alvarez Jr., Pharm.D., BCPS*, Jennifer Meuchel, M.D., Madiha Latif, B.S., Neela Dasgupta, B.S., Brett D. Thombs, Ph.D., Roy C. Ziegelstein, M.D.; The Johns Hopkins Hospital, Baltimore, MD.

PURPOSE: To determine whether use of selective serotonin reuptake inhibitors (SSRIs) is associated with differences in major adverse cardiac events (MACE) or bleeding complications in patients with acute coronary syndrome (ACS) who are receiving glycoprotein IIb/IIIa (GP IIb/IIIa) inhibitors, including other antiplatelet therapies.
METHODS: Medical records of patients with ACS admitted to The Johns Hopkins Hospital who had received GP IIb/IIIa inhibitors between April 1, 2001 and April 1, 2004 were examined for use of SSRIs, use of other medications known to affect platelet activation or coagulation, MACE (cardiac death, nonfatal myocardial infarction, or unplanned revascularization), and major or minor bleeding.
RESULTS: Interim analysis of 1151 patients in a planned review of 1,500 medical records shows that MACE were experienced by 23/155 patients receiving an SSRI during the hospitalization vs. 202/996 not receiving an SSRI (14.8% vs. 20.2%, RR 0.73, 95% CI 0.49–1.09, p=0.11). Major or minor bleeding occurred in 57/155 SSRI patients vs. 319/996 patients not receiving an SSRI (36.8% vs. 32.0%, RR 1.22, 95% CI 0.97–1.55, p=0.10).
CONCLUSIONS: This interim analysis suggests that SSRI use in patients with ACS already receiving antiplatelet therapy including GPIIb/IIIa inhibitors may be associated with further reductions in MACE at the expense of an additional bleeding risk. If these results are confirmed by additional data analysis, we suggest that prospective randomized trials carefully address bleeding and MACE in patients with ACS treated with SSRIs.

56E. Experimental sleep apnea decreases myocardial infarction size. *John M. Dopp, Pharm.D.*[1], Nicholas A. Wiegert, B.S.[1], Robert M. Twieg, B.S.[1], E. Burt Olson Jr., Ph.D.[1], J. Jason Sims, Pharm.D.[2]; (1)University of Wisconsin, Madison, WI; (2)Medtronic, Minneapolis, MN.

INTRODUCTION: Obstructive sleep apnea (OSA) is characterized by intermittent hypoxemia and has been linked to the development and progression of cardiovascular disease. OSA worsens ischemic heart disease and could subsequently lead to poorer outcomes after myocardial infarction (MI). However, the survival rate in patients with OSA following myocardial infarction is similar to the survival rate in patients without OSA, suggesting OSA may provide a cardioprotective effect. We hypothesized that intermittent hypoxia that mimics sleep apnea would decrease MI size similar to myocardial preconditioning.
METHODS: We randomized adult male Sprague-Dawley rats to either two

weeks of intermittent hypoxia (n=10) that mimics sleep apnea (alternating 21% and 10% oxygen every two minutes for twelve hours per day) or control treatment (no hypoxia) (n=8). Two additional groups were assigned to hypoxia (n=8) or control (n=8) and received ischemic preconditioning (five minutes of left coronary artery (LCA) occlusion followed by five minutes reperfusion for three cycles) prior to induced MI. In all groups, MIs were induced by occlusion of the LCA for 30 minutes followed by 60 minutes of reperfusion. Hearts were stained and excised for infarct size analysis. Infarct size was calculated as a ratio of the infarcted area to area at risk determined by computer morphometry of Evans blue/tetrazolium stained sections.
RESULTS: Control rats had a mean infarct size of 39 ± 4% of the area at risk (AAR). Rats exposed to intermittent hypoxia had a reduced mean infarct size of 29 ± 3% of AAR (p=0.04 vs control). Infarct size in hypoxia rats was similar to rats that received ischemic preconditioning (26 ± 3% for both preconditioning groups) (p=NS).
CONCLUSIONS: Exposure to intermittent hypoxia prior to MI reduces infarct size similar to myocardial preconditioning through an unexplored mechanism. Therefore, myocardial protection from intermittent hypoxia may offset some of the detrimental myocardial effects of OSA.
Presented at the 19th Annual Meeting of the Associated Professional Sleep Societies, Denver, CO, June 18-23, 2005.

57E. Phosphodiesterase-5 inhibition enhances sympathetically mediated vascular tone. *John M. Dopp, Pharm.D.*[1], Aye-Thandar Win, M.D.[2], Christine A. Sinkey, R.N.[2], William G. Haynes, M.D.[2], Bradley G. Phillips, Pharm.D.[2]; (1)University of Wisconsin, Madison, WI; (2)University of Iowa, Iowa City, IA.

BACKGROUND: Phosphodiesterase type-5 (PDE-5) inhibition causes vasodilation and sympathetic activation. The contribution of each of these on resting vascular tone has not been studied. We tested the hypothesis that PDE5 inhibition contributes to increased sympathetically mediated vascular tone.
METHODS: We studied 9 healthy males (44 ± 2 years), randomized in a double-blind, crossover fashion to sildenafil 100 mg or placebo. Blood pressure and forearm vascular resistance (FVR) were determined at rest, after study drug administration and during intra-brachial infusion of norepinephrine (NE) 480 pmol/minute (to test alpha-receptors), adenosine (ADEN) 300 µg/minute (control), isoproterenol (ISO) 250 ng/minute (to test beta receptors) and phentolamine (PHEN) 120 µg/minute (to test sympathetically-mediated vascular tone). Norepinephrine was measured at baseline and 1 hour after study drug administration.
RESULTS: Mean arterial blood pressure increased slightly after placebo (p=0.06) but was unchanged after sildenafil. FVR responses to NE, ADEN, ISO were similar (table; p=NS for all). FVR was reduced during PHEN following sildenafil compared to placebo (*p=0.002). Plasma norepinephrine increased by 84 ± 31% and 30 ± 12% following sildenafil and placebo (p=0.05).
CONCLUSIONS: PDE-5 inhibition significantly increased sympathetically mediated vascular tone compared to placebo in healthy, middle-aged men: this vasoconstriction offsets the vasodilatory effects of PDE-5 inhibition.

Study Drug	NE (% ΔFVR)	ADEN (% ΔFVR)	ISO (% ΔFVR)	PHEN (% ΔFVR)
Sildenafil	64 ± 15	-80 ± 2	-77 ± 3	-73 ± 3*
Placebo	56 ± 14	-78 ± 2	-72 ± 3	-63 ± 3

Published in Clin Pharmacol Ther 2005;77(2):P10.

58. A determination of the reasons why patients discontinue statin therapy. *Kari L. Olson, Pharm.D.*, David W. Brand, MSPH, Brandy McGinnis, Pharm D, David Magid, MD, MPH; Kaiser Permanente Colorado Region, Aurora, CO.

PURPOSE: Data, derived mainly from retrospective analysis of pharmacy claims, suggest that approximately 50% of patients receiving statin therapy discontinue at one year. Typically, these data do not focus on patient specific reasons for discontinuation. The purpose of this study was to determine if there were documented reasons for discontinuing statin therapy and to compare characteristics of patients who do and do not discontinue therapy.
METHODS: All patients with an initial statin prescription within 01/01/2004 and 03/31/2004 were identified through pharmacy claims. "Discontinuers" were those with no statin dispensed for 6 months plus the days supply. For each discontinuer, a "continuer" with a statin dispensed within 2 months of data pull, was identified. Chart reviews were conducted to determine if there were documented reasons for statin discontinuation. Subsequently, telephone surveys addressing satisfaction with care, statin knowledge, general and mental health, social support, and communication were conducted for both continuers and discontinuers. χ^2 analysis was used to compare dichotomous data between groups.
RESULTS: Full results will be presented at ACCP. A total of 1413 patients had an initial statin dispensed. A convenience sample of 434 patients (223 continuers and 211 discontinuers) was identified over a year. One-third of discontinuers had a valid and documented reason for stopping the statin. Fewer discontinuers had a follow-up with a provider within 6 months of statin start. Surveys revealed significantly (P<0.001 for all comparisons) fewer discontinuers than continuers knew why they were taking the statin (91.1% vs. 95.0%), trusted their providers (78.2% vs. 94.2%), or felt the statin was of benefit (18.4% vs. 60.7%). Significantly more discontinuers did not tell their provider if they missed statin doses (32.7 vs. 15.0%, P< 0.001).
CONCLUSIONS: Statin adherence may be overestimated using pharmacy claims records alone. Interventions to improve adherence should focus on patient communication, education, and follow-up.

59. Effectiveness and tolerability of concomitant beta blocker-amiodarone therapy to prevent postoperative atrial fibrillation after cardiac surgery. *Brian J. Barnes, PharmD*, Dennis W. Grauer, PhD, Patricia A. Howard, PharmD, FCCP, BCPS (AQ CV), Erin A. Kirkland, PharmD, Michael E. Gorton, MD, Gregory F. Muehlebach, MD, Jeffrey B. Kramer, MD; University of Kansas Medical Center, Kansas City, KS.

PURPOSE: Post operative atrial fibrillation (POAF) occurs in 32.3% of patients after cardiac surgery and increases morbidity, mortality, and resource utilization. Clinicians frequently use beta-blockers (BB) and/or amiodarone prophylaxis (AMP) to decrease the risk of POAF. We examined the efficacy and hemodynamic tolerability of combined AMP/BB prophylaxis compared to monotherapy with either agent or no prophylaxis.
METHODS: A retrospective observational analysis of 509 patients who underwent cardiac surgery was conducted. Data sources included The Society of Thoracic Surgeons national database and medical/medication administration records. Patients with chronic atrial fibrillation were excluded. AMP and BB use was defined as patients receiving ≥ 1 day of therapy between postoperative days 0–4. The number of days patients experienced heart rates <50bpm (HR<50), and systolic blood pressures <90mmHg (SBP<90) were recorded. χ^2 tests, odds ratios with 95% confidence intervals, and number needed to treat calculations were performed.
RESULTS: The mean patient age was 63 ± 13.4 years, 27% were female, 80% underwent CABG, and 29% underwent valve surgery. POAF occurred in 36.2% (25/69) of patients receiving no prophylaxis, 28.3% (39/139) receiving only BB, 25.5% (26/102) receiving only AMP, and 20.5% (41/200) receiving both AMP and BB. When compared to patients not receiving prophylaxis, POAF was significantly reduced in the combination therapy group (ARR=16%, OR 0.45, 95%CI 0.25–0.82, p=0.014, NNT=6). However, significant reductions in POAF were not observed with AMP monotherapy (ARR=11%, OR 0.60, 95%CI 0.31–1.16, p=0.182) or BB monotherapy (ARR=8%, OR 0.69, 95%CI 0.38–1.28, p=0.312). Patients receiving combination therapy experienced the same frequencies of HR<50 and SBP<90 when compared to those receiving BB monotherapy or no prophylaxis.
CONCLUSIONS: In this cohort, combination therapy with AMP/BB was effective in reducing the occurrence of POAF and was hemodynamically well tolerated. Prophylactic strategies should routinely incorporate combination therapy.

60. Assessment of cardiovascular health status in a predominantly Hispanic population. *Noreen T. Wong, Pharm.D.*, Kathryn M. Uchida, Pharm.D.; Pfizer, Inc., Pasadena, CA.

PURPOSE: This study was designed to evaluate the cardiovascular risk of participants in largely Hispanic communities within a designated area. The study followed a marketing campaign in the same areas to improve health communications and preventative care for Hispanic patients related to cardiovascular disease.
METHODS: Cardiovascular risk assessment data was collected at community outreach events from June 2004 through May 2005. Each participant completed a health assessment questionnaire and received testing for blood pressure, cholesterol, and glucose. Information on health insurance and physician visits was also collected.
RESULTS: Assessments were completed on 2,611 participants, with Hispanics comprising 75% of the participants. In comparison to Hispanic population data from the Centers for Disease Control (CDC), the Hispanic participants in this study had a lower incidence of cardiovascular risk factors such as elevated cholesterol, smoking, diabetes, high blood pressure and obesity. Results from blood pressure screening showed 51.9% of patients diagnosed with hypertension and receiving treatment had elevated blood pressure. In addition, 52% of diabetic patients had an elevated blood pressure above 130/80 mm/Hg. Over 40% of participants had an elevated cholesterol level (i.e., elevated total cholesterol, triglycerides and/or LDL). Of the participants previously diagnosed with elevated cholesterol, 28% were receiving treatment.
CONCLUSION: According to the National Health and Nutrition Examination Survey III (NHANES III), 1988-1994, Centers for Disease Control/National Center for Health Statistics, while dyslipidemia is the most prevalent cardiovascular risk factor in both Hispanics and non-Hispanic whites, Hispanics are less likely to be diagnosed and treated for their condition. While some participants in this study were diagnosed with cardiovascular disease, the number actually receiving treatment was less than 30%. In addition, the study showed that despite being diagnosed and treated for

cardiovascular disease, patients are not attaining goals as recommended by national guidelines.

Critical Care

61. Antimicrobial use in critically-ill ventilated patients with pseudomonal pneumonia. *Michael J. Peeters, PharmD, BCPS*, Charles F. Seifert, PharmD, FCCP, BCPS; Texas Tech University Health Sciences Center School of Pharmacy, Lubbock, TX.

PURPOSE: Recent 2005 guidelines suggest combination antimicrobial therapy for P. aeruginosa ventilator-associated pneumonia (VAP) based on limited non-VAP evidence. We reviewed antimicrobial use in patients with P. aeruginosa VAP within our tertiary teaching institution, to evaluate patient factors, antimicrobial selection, and outcomes.
METHODS: Intubated patients with a P. aeruginosa sputum culture, infiltrate on chest x-ray, and increased white blood cell count were retrospectively enrolled. Collected data identified illness acuity using the Simplified Acute Physiology Score (SAPS), antimicrobial use and sensitivity, and patient survival at hospital discharge.
RESULTS: Fifty-nine patients were analyzed between January 2003 and November 2004. Average age was 57 ± 15.7, BMI of 28.5 ± 6.1, and SAPS of 45.1 ± 13.7. Survival was significantly higher among patients on 2 culture-sensitive antimicrobials (23/28, 82%) versus <2 agents (12/31, 39%; p=0.0018). Almost all patients who received the B-lactam and aminoglycoside (BL&A) combination survived (15/16; p=0.0015). While fewer severely ill patients lived (SAPS>54; p=0.0029), none were on the BL&A combination. Lower survival was seen among obese patients (BMI >30; p=0.0043), but 5/6 obese patients on BL&A survived (p=0.0237). Patients >64yo were more often on 2 appropriate antimicrobials (p=0.0143) and had a higher survival (p=0.0241). More acutely ill patients had a lower survival (p=0.0029) and were less often on appropriate antimicrobials (p=0.0143). Unfortunately, we found a lack of culture follow-up, as only 60% (30/50) of inappropriate antimicrobials were switched to sensitive agents.
CONCLUSIONS: Our results emphasize the need to use combination aminoglycoside and B-lactam antimicrobials for P. aeruginosa VAP as guidelines suggest, and to ensure that antimicrobials are optimized based on culture results.

62. Emergency department-based sepsis protocol in a teaching hospital: evaluation using sepsis bundles. *Claire McManus, BSc., Pharm.D.*, Gerard Hayes, MD, Luis Lobon, MD, Virginia Mason, RN, PhD, Patricia Masters, BSc., Pharm.D.; Caritas St. Elizabeth's Medical Center, Boston, MA.

PURPOSE: Early recognition and treatment of septic shock is associated with an increase in survival. We noted from a previous institutional database that there were delays in the identification and fluid resuscitation of septic patients and in the placement of CV catheters. A sepsis protocol based on the emergency department (ED)-centric model was instituted. The aim of this study is to provide an initial evaluation of the protocol after 3 months.
METHODS: Twelve patients were treated using the sepsis protocol over 3 months. Performance was evaluated by assessing predefined goals, using sepsis bundles. Data were recorded from time of entry into the ED to the time the event was measured.
RESULTS: The median time to perform treatment-related events was within the goal for all 6h bundles: CVP access was achieved in 3.98h (range 1–6.2h); lactate level was measured in 2.13h (0.25–6.87h); cortisol level was measured in 5.85h (0.25–8.75h); antibiotics were administered in 2.17h (0.58–3.58h) and blood cultures were drawn within 1.62h (0.1–6.42). In the 24h bundles, there was good compliance for evaluation of steroid and APC therapy. APC was not given in 5 patients due to rapid response after fluid resuscitation. Glucose control was inadequate at 24h in 4 patients. Initial fluid resuscitation was aggressive with a median of 5L administered in the first 6h and 12.85L over 72h.
CONCLUSION: Implementation of a sepsis protocol based on an ED-centric model had a high rate of success in achieving the 6h and most of the 24h goals in this small study. It introduced an effective strategy for the early recognition and therapy of septic patients that was achieved through interdisciplinary co-operation. The protocol is easy to operate and has the potential to be expanded hospital-wide.

63E. Pharmacologic predictors of QTc prolongation and proarrhythmia in the adult intensive care unit. *Tien M. Ng, PharmD*[1], Keith M. Olsen, PharmD[2], Megan A. McCartan, PharmD[3], Katie M. Speidel, PharmD[2], Melissa A. Miller, PharmD[2]; (1)University of Southern California, 1985 Zonal Ave, Los Angeles, CA; (2)University of Nebraska Medical Center, Omaha, NE; (3)The Nebraska Medical Center, Omaha, NE.

PURPOSE: Despite their high-risk for proarrhythmia, intensive care unit (ICU) patients are often prescribed pharmacologic agents which are known to delay ventricular repolarization. The purpose of this study was to determine the resulting incidence of QTc prolongation and proarrhythmia associated with QT prolonging medications in ICU patients.
METHODS: In a prospective, observational study, all adult ICU patients prescribed pre-specified QT prolonging medications were followed for effect on QTc duration and incidence of new onset ventricular ectopy. The primary endpoint was the combined incidence of QTc >500ms at anytime, QTc increase >60ms above baseline, or new onset ventricular ectopy. Secondary endpoints were QTc >470 or 450ms (females or males, respectively) at anytime, QTc increase >20ms, drug discontinued for QTc prolongation, mean increase in QTc at 48 hours, and medication predictors of QTc prolongation.
RESULTS: Over 3 months, 267 consecutive patients (64 ± 18 years, 50.2% female, 72.3% Caucasian, baseline QTc 398 ± 147ms) were prescribed a QT prolonging medication. The primary endpoint occurred in 46.6% of the patients (QTc >500ms 38.6%, QTc increase >60ms 29.0%, new onset ventricular ectopy 11.0%). Greater than half of the patients experienced a QTc >470 or 450ms (59.5%) or an increase in QTc >20ms (52.6%). Mean increase in QTc at 48 hours was 131.2 ± 205.6ms. Despite these electrophysiologic effects, drugs were discontinued in only 5.2% of patients. Upon multivariate analysis, moxifloxacin [OR 2.54, 95% CI (1.34, 4.81), p=0.0041] and amiodarone [2.63 (1.33, 5.21), p=0.0056] were associated with an increased risk for the primary endpoint, while beta-blockers [0.42 (0.23, 0.75), p=0.0035] were associated with a risk reduction.
CONCLUSIONS: Increased risk of proarrhythmia, as assessed by QTc prolongation, occurs in the majority of ICU patients prescribed medications with electrophysiologic properties. Increased vigilance is warranted in this patient population, especially in those prescribed moxifloxacin or amiodarone.
Published in Crit Care Med 2004;32(suppl):A40.

64. Which is the optimal formula to estimate glomerular filtration rate in critically ill patients? *Laura Gratacos, Resident*, Dolors Soy, Ph.D., Patricia Dominguez-Tordera, Resident, Carles Codina, Ph.D., Jose Ribas, Ph.D.; Pharmacy Service. Hospital Clinic Barcelona, BARCELONA, Spain.

PURPOSE: To assess whether the formula from the Modification of Diet in Renal Disease (MDRD) study is a better choice than the Cockroft- Gault (CG) formula, for estimating the glomerular filtration rate (GFR), in intensive Care Unit (ICU) patients.
METHODS: Serum creatinine (SC) and 24h-urinary creatinine levels were measured and used to calculate the real GFR ($CrCl_{24h}$). These values were compared to those obtained from the aforementioned formulae: $CrCl_{CG}$ and $CrCl_{MDRD}$. Correlation coefficients were estimated to evaluate the relationship between true values and $CrCl_{CG}$ or $CrCl_{MDRD}$. Bland-Altman plots, bias and precision were performed to contrast all creatinine clearance estimates. All data were first analyzed as a whole. Later, they were split into different subgroups according to the mean urea binding nitrogen (BUN), serum albumin (Alb) and SC values.
RESULTS: 125 samples corresponding to 62 ICU patients (35 male; 27 female) were recruited from May to December 2004. The population included patients with different medical diagnoses: polytrauma, nosocomial pneumonia, etc. Their median age was 65 (Interquartile ratio: 51-76). From total data analysis: when comparing $CrCl_{CG}$ and $CrCl_{MDRD}$ values against $CrCl_{24h}$, the later presented a better correlation (r=0.68;IC95:0.57-0.76) than the former (r=0.61;IC95:0.49-0.71), but non-statistically significant (p=0.348). Both methods lacked precision and overestimate $CrCl_{24h}$; nevertheless, $CrCl_{MDRD}$ showed a statistically significant lower bias than $CrCl_{CG}$. From subgroup analysis: pearson coefficients offered no significant differences, but CG formulae always exhibited a superior correlation with $CrCl_{24h}$ than MDRD equation.
CONCLUSION: In our UCI population both formulae may be indistinctly used to estimate GFR. Depending on the available data one or other can be applied.

65. Evaluation of bivalirudin treatment for heparin-induced thrombocytopenia (HIT) in critically ill (ICU) patients with hepatic and/or renal dysfunction. *Tyree H. Kiser IV, Pharm.D.*; University of Colorado Health Sciences Center, Denver, CO.

PURPOSE: Evaluate the use of bivalirudin for treatment of HIT in ICU patients with hepatic and/or renal dysfunction.
METHODS: ICU patients with hepatic and/or renal dysfunction diagnosed with HIT and treated with bivalirudin between January 1, 2004 and March 31, 2005 at the University of Colorado Hospital were retrospectively evaluated. Patients receiving bivalirudin for percutaneous coronary intervention were excluded. Patients were assessed for dose and duration of bivalirudin therapy, thrombosis, and clinically significant adverse effects.
RESULTS: Eighteen patients were identified. Twelve patients had both hepatic and renal dysfunction (group 1), 4 patients had hepatic dysfunction (group 2), and 2 patients had renal dysfunction (group 3). Demographics were

similar between groups. Patients were 54 ± 15 years old, 82 ± 14 kg, 67% male, 83% Caucasian, and 50% were on renal replacement therapy. Bivalirudin doses were 0.06 ± 0.15 mg/kg/hr (median 0.03 mg/kg/hr), 0.14 ± 0.05 mg/kg/hr (median 0.14 mg/kg/hr), and 0.05 ± 0.01 mg/kg/hr (median 0.05 mg/kg/hr) for patients in groups 1, 2, and 3 respectively. Nine patients on continuous venovenous hemofiltration ± dialysis had mean doses of 0.04 ± 0.03 mg/kg/hr (median 0.03 mg/kg/hr). Mean bivalirudin duration was 15 ± 17 days. Mean activated partial thromboplastin times (aPTT) were 69 ± 22 seconds. Supratherapeutic aPTTs were most common on days 1 (22%) and 2 (28%) when bivalirudin doses were highest. Mean INR values were 2.2 ± 0.8. Clinically significant bleeding did not occur in any patient. Thrombosis on bivalirudin occurred in 6% of patients.
CONCLUSION: ICU patients with hepatic and/or renal dysfunction require low doses of bivalirudin to achieve aPTT values 1.5-2.5 times baseline. Bivalirudin can be initiated safely at 0.14 mg/kg/hr in patients with hepatic dysfunction, 0.03–0.05 mg/kg/hr in patients with renal or combined hepatic and renal dysfunction, and 0.03–0.04 mg/kg/hr in patients receiving continuous renal replacement therapy.

66. Comparison of selected utilization variables in critically ill patients with anemia who received weekly recombinant human erythropoietin (rHuEPO) or no rHuEPO. *Eric Wittbrodt, Pharm.D.*[1], Fernando Rodriguez, Pharm.D.[1], John Medendorp III, R.N., B.S.N.[2], Michael Sherman, M.D.[2]; (1)University of the Sciences in Philadelphia, Philadelphia, PA; (2)Drexel University College of Medicine, Philadelphia, PA.

PURPOSE: To retrospectively evaluate the impact of rHuEPO on selected outcomes in an intensive care unit population.
METHODS: The case cohort consisted of adult patients admitted to the Medical or Surgical Intensive Care Unit, anemic upon admission (hemoglobin < 10 g/dL), and who received at least one dose of rHuEpo 40,000 units SC. The control cohort met the case cohort criteria but did not receive rHuEpo. Cases were matched to controls by APACHE II score (±3) and by admitting service. Selected outcome variables including pRBCs transfused, lengths of stay, and organ failure (SOFA) scores were calculated from data retrospectively collected from the records of discharged patients. Adjusted means that controlled for SOFA and APACHE II scores at admission were compared using analysis of covariance. Unadjusted mortality was compared using chi-square; logistic regression was used for multivariate analysis (alpha = 0.05, two-tailed).
RESULTS: The data of 56 patients were collected (28 cases, 28 controls). Multivariate analyses demonstrated that patients who received rHuEpo had significantly greater SOFA scores two weeks after admission for cases (6.0 vs. 4.0, p=0.0447) and experienced significantly longer hospital (23.3 vs. 18.3 days, p=0.0419) and ICU lengths of stay (19.5 vs. 12.4 days, p=0.0053). Total pRBC transfused were not significantly different between groups (21 units for cases vs. 15 units for controls, p=0.3318). Mortality was not significantly different between cases and controls (21.8% vs. 16.8 %, p=0.61).
CONCLUSIONS: Lengths of ICU and hospital stays were significantly prolonged in a small group of moderately ill predominantly male trauma patients who received rHuEpo versus no rHuEpo. Use of rHuEpo produced no impact on mortality or the number of pRBC transfusions in the study population. Further studies are necessary to affirm the transfusion-sparing effects of rHuEpo administration.

67. A retrospective evaluation of the efficacy of HMG-CoA reductase inhibitors in sepsis. *Christopher Martin, PharmD*[1], Robert L. Talbert, Pharm.D.[1], David S. Burgess, Pharm.D.[1], Jay I. Peters, M.D.[2]; (1)University of Texas College of Pharmacy/UT Health Sciences Center San Antonio, San Antonio, TX; (2)University of Texas Health Sciences Center at San Antonio School of Medicine, San Antonio, TX.

PURPOSE: Severe sepsis is a devastating condition of infection and immune system dysregulation with a high mortlity rate for which mostly symptomatic treatments are currently available. HMG-CoA reductase inhibitors (statins) have broad immunomoduatory properties which may be efficacious in sepsis.
METHODS: A retrospective cohort study was conducted of patients diagnosed with sepsis between October 1, 2003 and September 30, 2004 at University Hospital, San Antonio, TX. Patients were identified by ICD-9 code and were separated into two cohorts: those who took a statin prior to admission and those who did not take a statin. Data was collected from the electronic medical record. Baseline characteristics including past medical history, laboratory parameters and vitals were collected, and an APACHE III score was calculated, for each patient. The primary endpoint of the study was the incidence of severe sepsis as defined by the American College of Chest Physicians and the Society of Critical Care Medicine guidelines. Secondary endpoints were in-hospital mortality and the incidence of organ dysfunction.
RESULTS: A total of 53 patients were evaluated including 16 in the statin group and 37 in the no statin group. Statins were associated with a 30% lower incidence of severe sepsis (56% vs. 86%, p<0.02). There was no difference between the cohorts in terms of in-hospital mortality. The incidence of cardiovascular dysfunction (hypotension requiring vasopressors) was significantly lower in the statin group (38% vs. 73%, p<0.02). There was no difference between the cohorts with regard to the other organ dysfunction categories (pulmonary, renal, hematologic and metabolic)
CONCLUSIONS: Statins may be protective against progression to severe sepsis in patients with sepsis. Prevention of hypotension requiring treatment with vasopressors may explain the efficacy of statins in this setting.

68. Pharmacological management of constipation in the critically ill. *Asad E. Patanwala, Pharm.D.*, Jacob Abarca, Pharm.D., M.S., Yvonne Huckleberry, Pharm.D., Brian L. Erstad, Pharm.D.; University of Arizona, Tucson, AZ.

PURPOSE: The purpose of this study was to compare the effectiveness of common laxatives in producing a bowel movemenr (BM) among patients admitted to a medical intensive care unit (MICU).
METHODS: Medical records of 95 patients admitted to the medical intensive care unit (MICU) between July 1 and October 31, 2004 were retrospectively reviewed. A total of 50 patients satisfied inclusion criteria. Patient specific data was recorded during the first 96 hours of admission. Logistic regression analysis was used to compare patients who had a bowel movement to those that did not.
RESULTS: Of the 50 patients studied and included, 25 patients did not have a bowel movement during the first 96 hours of MICU admission. Patients that were given a stimulant (senna, bisacodyl) and/or an osmotic (lactulose, milk of magnesia) laxative were more likely to have a bowel movement (OR=26.6; CI 3.2, 221). Of these, the most frequently used laxative was senna. Opioid use, expressed as logarithmic morphine equivalents, was negatively associated with a BM (OR=0.76; CI 0.59, 0.97). Severity of disease, as determined by APACHE II score, was also negatively associated with a BM (OR=0.84; CI 0.7, 0.99).
CONCLUSION: Critically ill patients have a high incidence of constipation and opiate use is a significant risk factor. Routine use of stimulant and/or osmotic laxatives in this patient population should be considered.

69. Costs associated with a continuous insulin infusion protocol in critical care. *Scott R. Bolster, PharmD*[1], Therese Conner, PhD[1], Sandy Rankin, RN, CCRN[1], Gretchen Inman, MSN, CNS[1], Karen Rascati, PhD[2]; (1)Brackenridge Hospital, Austin, TX; (2)University of Texas–College of Pharmacy, Austin, TX.

INTRODUCTION: Normalization of blood sugar (BS) in critically ill patients via continuous insulin infusion (CII) has become standard of care secondary to literature demonstrating beneficial outcomes. However, the criteria for CII initiation is unclear; for example, one recent study reported benefits when CII was initiated at BS >110mg/dL, while another reported benefits when initiated for BS >145 mg/dL. This analysis sought to compare the overall costs of implementing CII by different admission BS thresholds.
METHODS: Both retrospective chart review and time-in-motion (TIM) observations were conducted. Chart review included ICU patients >16 years old receiving mechanical ventilation for at least 12 hours. Patients with diabetes were excluded. Data collection included frequency of CII activities per patient day. TIM observations recorded the time involved for staff to perform activities associated with a CII protocol. Costs were calculated in 2005 $US from the hospital perspective.
RESULTS: In 2004, 540 charts met criteria; of those 82 (15%) randomly-selected charts were reviewed. The sample was representative of the population among multiple patient variables, but had a higher % of medical versus surgical cases (p<0.05). Activities associated with protocol implementation and time to perform each activity will be discussed. Data revealed 77.6% of patients had admission BS >110mg/dL and 43.4% had admission BS >145mg/dL. Calculations demonstrated that CII cost $5.61/patient day in labor and supplies. Therefore, if CII is initiated on all patients with admission BS >110mg/dL, cost per 100 patient days is $435.34 and if CII is initiated on all patients with admission BS >145mg/dL, cost is $243.
CONCLUSIONS: Implementing CII at a lower BS threshold almost doubled costs from a hospital perspective. Cost-effectiveness studies using different implementation BS thresholds to compare both outcomes and costs may better define the optimal BS to initiate CII in ICU patients.

70. Impact of an intensive insulin nomogram in the critically ill. *Jared M. Freml, PharmD*, Kelly M. Smith, PharmD, Craig Martin, PharmD, P. Shane Winstead, Pharm.D., Aaron M. Cook, PharmD; University of Kentucky Chandler Medical Center, Lexington, KY.

PURPOSE: Maintaining blood glucose levels within 80–110 mg/dL has been shown to significantly reduce morbidity and mortality in critically ill patients. Our primary objective was to assess the percentage of blood glucose values within 80-110 mg/dL during utilization of a newly instituted insulin infusion nomogram. Secondary objectives were used to determine safety and identify areas for nomogram improvement by monitoring the mean time to first goal

blood glucose, overall mean blood glucose, and incidence of hypoglycemia.
METHODS: Concurrent, observational study of 60 consecutive adult ICU patients receiving treatment with an insulin infusion nomogram between October 9, 2004 and March 2, 2005 in the adult ICUs of a 473 bed academic, tertiary care center. Patients were monitored for blood glucose control, hypoglycemia, nutrient intake, and concomitant medication utilization.
RESULTS: The total number of blood glucose values obtained in the 60 patients was 4613. Blood glucose values were within the goal range 37.2% (n=1716) of the time. An extended analysis also showed the following percentage of blood glucose values within each range: 60–130 mg/dL, 66.5% (n=3068); 60–143 mg/dL, 75% (n=3460); and 60–186 mg/dL, 90% (n=4152). Secondary objectives found the mean time to first goal blood glucose to be 10.2 ± 9.2 hours, overall mean blood glucose value was 130.6 mg/dL, and that safety was maintained by the low rate of hypoglycemia (<60 mg/dL), 1.3% (n=62).
CONCLUSION: Although our nomogram did not achieve the predefined goal range for percentage of blood glucose values at goal, this study identified modifications to insulin infusion nomogram that have been implemented to maintain simplicity and improve overall efficacy.

71. Sedation with dexmedetomidine versus propofol in coronary artery bypass grafting. *Michelle Turner, PharmD*, Jackie Roh, BSPharm, Debra Britt, RN, BSN; Moses Cone Health System, Greensboro, NC.

PURPOSE: Dexmedetomidine may offer advantages over propofol when used for sedation given it has analgesic effects and produces less respiratory depression. This evaluation was conducted to determine if dexmedetomidine is a reasonable alternative to propofol in the coronary artery bypass grafting (CABG) surgical population with regards to cost, clinical outcomes, and impact on patient management.
METHODS: Patients received dexmedetomidine or propofol as their primary sedating agent based on the surgeon performing the CABG. Prospective data was collected to evaluate drug cost. Secondary outcomes included the amount of anesthetics/analgesics, ICU length of stay, time on ventilator, and nursing questionnaires assessing patient's management. Appropriate parametric and nonparametric statistical analyses were used.
RESULTS: 111 patients were evaluated between January 17 and March 23, 2005; 61 received dexmedetomidine and 50 received propofol. Use of dexmedetomidine cost $48 more per patient than propofol ($91.33 vs. $43.33, p<0.01). Dexmedetomidine patients received more midazolam (10.3 mg vs. 8.3 mg, p<0.02) and less fentanyl (1503 µg vs. 1752 µg, p<0.02) than propofol patients. There was no statistically significant difference with regards to adjunctive medication use in the ICU, ICU length of stay, or mechanical ventilation time. Nurses gave dexmedetomidine patients better scores on the Nurse Assessment Rating Questionnaire regarding sedation rating, patient communication, and patient management (p values <0.05).
CONCLUSIONS: Dexmedetomidine is a more expensive agent for sedation in CABG than propofol. This cost differential was not offset by changes in secondary outcomes. However, nurses taking care of CABG patients rated dexmedetomidine patients as easier to manage as compared to propofol patients. Positive feedback from nursing staff indicates patients may receive improved postoperative care when receiving dexmedetomidine.

72. Insulin infusion protocols improve glycemic control, or do they? *Jennifer A. Norberg, PharmD*[1], Almut G. Winterstein, PhD[2], Thomas E. Johns, PharmD, BCPS[1], Aimee C. LeClaire, Pharm.D.[1]; (1)Shands at the University of Florida, Gainesville, FL; (2)Department of Pharmacy Health Care Administration, University of Florida, Gainesville, FL.

PURPOSE: Aggressive glycemic control improves morbidity and mortality in critically ill adults; however, implementation of such a strategy can be logistically difficult. This observational study evaluated compliance with an insulin infusion protocol, and its potential impact on glycemic control in a Surgical Intensive Care Unit (SICU).
METHODS: Two cohorts of SICU patients at risk for developing hyperglycemia were compared. Patients in the control group received insulin infusions with target blood glucose (BG) ranges based on physician's preference. Insulin was titrated upon nurse's discretion. Patients in the insulin protocol group received an insulin infusion adjusted using a standardized protocol with a defined target BG range of 110-140 mg/dL. Nursing documentation and daily flow sheets from a random sample of patients were used to evaluate compliance, expressed as the percentage of correct actions taken according to the guidelines established by the protocol. Effectiveness was measured by comparing the percentage of time spent within the target BG range between cohorts.
RESULTS: Patients in the protocol cohort maintained BG levels in the target range 42% of the time, compared to 41% in the control group. Overall compliance with insulin adjustments per protocol was highest with BG values in the 110-140 mg/dL range (80%). For BG values greater than 140 mg/dL, compliance with insulin adjustments was only 47%.
CONCLUSIONS: In the clinical trial setting, protocols have been consistently shown to enhance glycemic control in the ICU. However, this protocol was not able to improve BG control compared to previous non-standardized approaches. Reasons may include a difference between controlled conditions in a clinical trial environment and routine care as well as reluctance among nurses to maintain target BG ranges that pose a higher risk for hypoglycemia. More research examining protocol implementation strategies is needed.

Dermatology

73. Evaluation of sebum secretion, skin type, pH in humans with and without acne. *Myo-Kyoung Kim, Pharm.D., BCPS*[1], Sun-Young Choi, B.S., R.N.[2], Hee-Jin Byun, M.D.[2], Chang-Hun Huh, M.D., M.S.[2], Kyoung-Chan Park, M.D., Ph.D.[2], Rajul Patel, Pharm.D., Ph.D.[1], Annie Shinn, Pharm.D., Ph.D.[1], Sang-Woong Youn, M.D., Ph.D.[2]; (1)University of the Pacific, Thomas J. Long School of Pharmacy, Stockton, CA; (2)Department of Dermatology, Seoul National University, College of Medicine, Seongnam, Kyounggi-do, South Korea.

PURPOSE: This study assessed the differences in objective skin types (OST) and subjective skin types (SST) between subjects with acne (ACNE) and subject without acne (CONTROL). Secondly, this study also evaluated the difference in pH on five facial areas (forehead, nose, chin, right and left cheek) between the two populations. Lastly, the relationship between pH and sebum secretion was analyzed.
METHODS: Sebum casual levels (CL) of the five facial areas in 36 ACNE and 47 CONTROL were measured by using a Sebumeter SM 815® and subjects were classified into OST by CL. Subjects reported what type of skin they believed they had, which determined SST. The pH levels were measured by the Skin-pH-Meter PH 905®. Data was assessed with adequate statistical tests.
RESULTS: Among the five areas, the nose of ACNE showed a significantly higher CL, compared to CONTROL. OST did not differ between the two groups, but SST differed significantly. In addition, OST were significantly different than SST in ACNE, whereas the two skin types did not differ in CONTIRL. ACNE actually overestimated their skin types and stated their skin types were "oilier" than they were. In respect to pH, none of the five areas differed significantly between the two groups. Among the five sites in ACNE, CL showed a significant correlation with pH on the left (r=-0.34) and right (r=-0.39) cheeks, which resulted in a significant correlation on the U-zone (r=-0.38). In contrast, in CONTROL, there was a significant correlation between CL and pH on the forehead (r=-0.32) and chin (r=-0.40), which led to a significant correlation on the T-zone (r=-0.37).
CONCLUSION: It would be recommended to measure the objective skin types when skin care products are selected, rather than solely depending on the subjective feelings of the consumer, especially for subjects with acne.

Drug Information

74. Assessment of potentially inappropriate medications using the Beers criteria in an inpatient setting. *Sabrina W. Cole, PharmD*, Kelli L. Davis, PharmD, Holly M MacFall, PharmD, Nannette M. Berensen, PharmD, Marlea G Wellein, PharmD, Christopher R Fortier, PharmD, Jessica A Starr, PharmD, Sarah K. Ford, PharmD; Medical University of South Carolina, Charleston, SC.

PURPOSE: To evaluate patients 65 years and older who are receiving a potentially inappropriate medication (PIM) as defined by the Beers criteria.
METHODS: Patients were identified and eligible for enrollment based on medications in their active profile, at least 65 years of age, and admission to the adult internal medicine service. Patients receiving at least 1 PIM were introduced to the study by a pharmacist. If the patient was able to give informed consent, they were asked to participate in an additional interview to discuss PIM safety and tolerability. Data collected on all patients included demographics, length of stay, number of medications, and number of disease states.
RESULTS: Seventy-four patients were assessed. Of those, 25 (34%) patients had a PIM in their active profile, three of whom were prescribed more than 1 PIM. Of those prescribed a PIM, 3 patients gave informed consent to assess safety and tolerability of the PIM in a standardized format. Doxazosin, senna, and promethazine were the most commonly prescribed PIMs (n = 5, n = 4, and n = 3, respectively). The mean length of hospital stay was longer for patients who were prescribed a PIM compared with those not receiving a PIM (5.84 versus 4.6 days, respectively). On average, patients receiving a PIM had a greater number of medications in their active profile compared with patients who were not prescribed a PIM (12 versus 10, respectively). Patients in both groups had an average of 6 (range = 1 to 14) disease states.
CONCLUSION: The Beers criteria is a tool that can be used to identify agents that should be avoided in elderly patients. Prescribers should be educated about these criteria. Patients were reluctant to participate, which makes conducting research in the elderly population difficult.

75. Comparison of tertiary drug information databases. *Amy S. Peak, PharmD*, Aaron Girt, PharmD; Butler University, Indianapolis, IN.

PURPOSE: Although studies have been conducted comparing hand-held drug information databases, formal studies comparing online drug information databases have not been published. The objective of this study is to examine the completeness, clinical dependability, and ease-of-use of common tertiary online drug information databases.
METHODS: This prospective study compared Clinical Pharmacology, eFacts, ePocrates RX Online, Lexi-Comp Online, and Micromedex. One hundred drug information questions (20 categories, 5 questions each) were researched in each database. Databases were assessed in three ways. To determine completeness, databases were assigned points for each question: provided complete, correct answer (5 points), correct, but incomplete answer (2 points), no information (0 points) and incorrect answer (-5 points.) To determine clinical dependability, databases were evaluated based on providing a correct, incorrect, or no information. To determine ease-of-use, the number of screens viewed (past the original search screen) was evaluated.
RESULTS: Clinical Pharmacology achieved the highest completeness score (311) followed by Micromedex (284), Lexi-Comp (245), eFacts (191), and ePocrates RX Online (99). ePocrates Online and eFacts were the least clinically dependable databases, failing to provide information to answer 79 and 56 of the 100 questions, respectively. Very few incorrect answers were found in any database. None of the databases scored well in the cost or monitoring/laboratory categories. Lexi-Comp required the fewest number of screen viewed, followed by ePocrates, Clinical Pharmacology, eFacts, and Micromedex.
CONCLUSIONS: Although no database answers all drug information questions, Clinical Pharmacology provides the most complete and dependable information, closely followed by Micromedex and Lexi-Comp Online. ePocrates RX Online is the least complete and/or clinically dependable database. Micromedex requires the most steps to locate information. Lexi-Comp Online requires viewing the fewest number of screens; thus, healthcare providers may find this database easier to use.

Education/Training

76. Exposure to basic drug information earlier in the pharmacy curriculum: assessment of student perceptions and performance. *Christopher L. Cook, Pharm.D., Ph.D.*, Keith N. Herist, Pharm.D., S. Michelle McElhannon, Pharm.D., Henry H. Cobb III, R.Ph., Ph.D.; University of Georgia College of Pharmacy, Athens, GA.

PURPOSE: A curriculum change was implemented to expose students to basic drug information earlier. "Top 200 Drug Cards" tests were moved from the second professional year to the first year, allowing greater time to introduce, reinforce, and differentiate medications. Study objectives were to 1) assess two first year pharmacy class' perceived need for increased drug knowledge focus in the first year curriculum; 2) compare test results between first and second year classes; and 3) assess impact of curricular change on students.
METHODS: During the transition year of curriculum change, first and second year students took the same three exams. At end of semester, both pharmacy classes were surveyed. First year students completed the original survey which prompted the curricular change. Second year students completed a follow-up survey to re-assess their opinions of the change, their performance on the drug card tests, and whether the curriculum change should remain for future classes. Student performance was based on class grades and distribution of the test scores.
RESULTS: 87 of 120 (72.5%) first year and 83 of 123 (67.5%) second year students supported the curricular change. Second year class average was significantly higher on the first two exams; 86.6% vs. 83.1% ($p<0.001$) and 86.1% vs. 79.2% ($p<0.0001$) respectively. Third exam averages were not significantly different; 87.4% to 86.5% (p=NS). Perceived rigor of first year curriculum (7.13 vs. 7.14, p=NS) and hours studied per day (2.89 vs. 2.81, p=NS) did not differ significantly between first-year classes before and after the change.
CONCLUSIONS: Results indicated both first and second year students favor earlier exposure to medications. While second year scores were statistically higher on the first two exams, first year scores were acceptable. The evidence suggests no unreasonable burden was placed upon first year students and the curricular change was successful.

77E. Revising small group active learning sessions to enhance student knowledge of pharmacotherapy. *Susan P. Bruce, PharmD*, Michael R Brodeur, PharmD, Nicole M Stack, PharmD, Aimee F Strang, PharmD, Mario M Zeolla, PharmD; Albany College of Pharmacy, Albany, NY.

PURPOSE: The content and format of small group learning activities were revised to expand student opportunities for application of therapeutic knowledge and skills. Graded activities were minimized and greater focus was placed on case discussion and group-based problem solving to optimize comprehension of lecture material.
METHODS: The Pharmacists' Inventory of Learning Styles (PILS) was used to place P3 students in Pharmacotherapy into groups of 5 or 6. A faculty facilitated, small group therapeutic discussion was conducted six times throughout the semester. Student acceptance of the format change was evaluated through a survey administered at the end of the course. Student performance on recall and higher-order exam questions was retrospectively assessed and compared to the previous year.
RESULTS: The distribution of learning styles (n=139) was A (3.8%), B (59.6%), C (20%), D (5.6%), multiple learning styles (11%). Ninety-one percent of students felt recitation helped them better understand the therapeutic topic. Positive comments were received regarding class size, group work and the increased opportunity for discussion. Students would have preferred less grade weight on the final case, sessions that followed the lecture topics on a separate day, and an earlier time frame. There was no statistical difference in student performance on recall and higher-order exam questions.
CONCLUSIONS: Prospective evaluation of this curricular change will include mapping learning style to exam performance, analyzing benefits of group learning, and using the PILS survey to create groups.
Presented at the Annual Meeting of the American Association of Colleges of Pharmacy, Cincinnati, OH, July 9-13, 2005.

78. Does delivery method of lectures affect exam performance of Web-based pharmacy students in a therapeutics course? *Eric B. Hoie, Pharm.D.*, Gary Elsasser, Pharm.D., Mary Hayes, B.A.; Creighton University School of Pharmacy and Health Professions, Omaha, NE.

PURPOSE: Determine if the delivery method of lectures to web-based pharmacy students in a therapeutics course effects exam performance.
METHODS: All web-based pharmacy students enrolled in the first semester therapeutics course were given a compact disc containing handouts, slides, and synchronized presentation files of all lectures. The audio portions of the synchronized files consisted of recordings from the previous year's lectures or were recorded by faculty in their office prior to the semester. Before the second semester, all class notes and slides were placed on the course website. Recordings of lectures given to campus students were made available to the web-based students within 24 hours of the lecture. Campus students and web students took the same exams each semester. Exam performance of the two groups was compared and web-based students were surveyed for their preference of delivery methods used in the course.
RESULTS: Forty-seven students were enrolled in the web course and 25 completed the survey. Synchronized presentation files were preferred by 13 (52%) of the students with 12 (48%) of the students preferring recordings of campus lectures. Eighteen students (72%) said recordings of current semester's campus lectures better prepared them for exams while 7 (28%) students said presentation files were better preparation. Campus students scored significantly higher on 4 of the 5 first semester exams than campus students ($p<0.05$). Web students and campus students each scored significantly better on one second semester exam with no difference on the remaining three exams.
CONCLUSIONS: Recordings of the current semester's lectures given on campus appear to improve exam performance of web-based students. Different points of emphasis during a lecture, from one year to the next, may explain the difference in exam performance when comparing delivery of lecture material.

79. Pilot study evaluating the effects of academic detailing sessions on chief residents and fellows. *Sabrina W. Cole, PharmD*, Nannette M. Berensen, PharmD, BCPS; Medical University of South Carolina, Charleston, SC.

PURPOSE: To assess the effectiveness of pharmacist-led, one-on-one, academic detailing sessions on physicians and assess their knowledge of medication-related policies and practices.
METHODS: Chief residents and fellows were identified for participation through the Office of Graduate Medical Education at the Medical University of South Carolina. Four 15-minute academic detailing sessions were developed by the investigators on the following medication-related policies and practices: prohibited abbreviations, nonformulary medication process, adverse drug reaction reporting, and reimbursement and cost containment. The one-on-one sessions were led by a clinical pharmacist and occurred at weekly intervals. At the conclusion of each session, participants were asked to complete a questionnaire to assess their baseline knowledge of the policy or practice, the effectiveness of the detailing session, and their satisfaction with the interaction.
RESULTS: Nine physicians completed all 4 detailing sessions. Six (67%) physicians were chief residents and 3 (33%) were fellows. Of these, 100% agreed or strongly agreed that the stated objectives for each detailing session were met. When asked whether new information was learned during the sessions, 94% of participants agreed or strongly agreed. Two physicians were undecided whether new information was learned during the session on the

nonformulary medication process. Additionally, 94% of physicians responded that the information acquired during the sessions would impact the way they write medication orders and/or improve the quality of patient care. One physician was undecided whether the information presented during the session on the nonformulary medication process would impact his order writing habits, and 1 physician disagreed that the information would affect his prescribing patterns.
CONCLUSION: These results support that pharmacist-led, one-on-one, academic detailing sessions are an effective mechanism to communicate policy-related information that may improve patient care.

80. Students' perceptions of advanced practice experience evaluation instruments. *Jennifer W. Beall, PharmD*, Mary A. Worthington, PharmD; McWhorter School of Pharmacy, Birmingham, AL.

PURPOSE: The purpose of this study is to clarify students' expectations of scores on clinical performance evaluation instruments by utilizing student perceptions describing levels of performance.
METHODS: Currently, advance practice experience (APE) students are assessed on pre-identified learning objectives using a five-point scale. Scores are defined as: 1=unacceptable, 2= needs improvement, 3=competent, 4=good and 5=excellent. In the APE manual, students are provided a general rubric to explain the scoring criteria, but it is not tailored for individual APE's and their learning objectives. Students on adult medicine and pediatric clerkships provided preceptors with their interpretations of scores for the objectives on the specific evaluation instruments for these rotations. A form was provided to students to standardize their input, and they were given a two week period to complete the form.
RESULTS: In general, students noted difficulty in characterizing scores for individual objectives. They were able to identify performance criteria for the extremes of the grading scale, e.g., scores of 1 and 5. However, they showed limited ability in delineating differences between the middle scores, e.g., 2–4. Additionally, preliminary results indicate that students' responses demonstrated poor association between the criteria they used to define an objective and the objective itself. The majority of reporting students also used level of effort as a marker for grading in contrast to knowledge base or performance outcome. Finally, student responses showed little correlation with the general rubric provided in the APE manual. Data collected thus far have been from students completing their APE year. Currently students beginning their APE year are providing input. Data will be compared between these two groups for differences.
CONCLUSION: Students may lack a clear understanding of current performance evaluation. However, their input may be useful to develop specific rubrics that clarify communication of appropriate expectations as related to evaluation.

81. Perceptions of academic climate and turnover among pharmacy practice faculty. *Orly Vardeny, Pharm.D.*[1], Caren J. Frost, Ph.D., M.P.H.[2], Mark A. Munger, Pharm.D., FCCP[3]; (1)University of Wisconsin School of Pharmacy, Madison, WI; (2)Social Research Institute, College of Social Work, University of Utah, Salt Lake City, UT; (3)Department of Pharmacotherapy, University of Utah College of Pharmacy, Salt Lake City, UT.

PURPOSE: We previously demonstrated that female faculty resign more frequently compared to males in academic pharmacy. The purpose of this study was to ascertain potential reasons for faculty turnover, with an emphasis on gender differences, in this era of pharmacy workforce shortage.
METHODS: Pharmacy Practice Faculty from United States Colleges of Pharmacy were surveyed using an anonymous online questionnaire. The survey questioned mentoring and support, gender and ethnicity issues pertaining to academia, reasons for faculty turnover, and participant demographics.
RESULTS: A total of 202 faculty participated (53% female) with a mean age of 31-40 years. Institutions were categorized as public (59.9 %) or private (40.1 %). There was equal distribution between tenure and clinical track faculty; however, more male faculty held tenure track positions compared to females (53.8% versus 29.2%, p=0.002). Female faculty were less satisfied with job mentoring than male faculty (dissatisfaction: 37% females, 25% males, p<0.05), most pronounced in younger faculty. Gender and ethnicity biases relating to promotion and academic leadership position distribution were identified more commonly in females versus males (p=0.036). Faculty was content with opportunities for involvement in the department decision-making process, with a trend toward less satisfaction among female faculty. In this study sample, 14% admitted they planned to leave their current position in the next year (17.3% females, 10.5% males). The most common reason stated was job dissatisfaction, followed by alternative opportunities in academia for males and family responsibilities for females.
CONCLUSIONS: Females are significantly less satisfied with their academic careers. The most cited reasons were lack of job mentoring and involvement in departmental governance compared to male faculty. These results may be related to tenure track male dominance. Female faculty members are an important workforce component for academic pharmacy; therefore, importance for female faculty retention should be a priority strategic action item.

82. Behind academic dishonesty in pharmacy school: exploring characteristics, prevalence, attitudes and perceptions. *Suzanne M. Rabi, Pharm.D.*, Lynn R Patton, MS, RPh, BCNSP, Nancy Fjortoft, PhD, David P Zgarrick, RPh, PhD; Midwestern University–Chicago College of Pharmacy, Downers Grove, IL.

PURPOSE: Studies indicate that cheating rates have increased and that cheating perceptions have changed in students. Previous studies assessed medical and dental students' perceptions but not pharmacy students' attitudes. The objectives of this study were to ascertain background factors that influence pharmacy students' willingness to cheat, describe perceptions of methods of cheating, assess the prevalence of cheating, determine a relationship between cheating and demographics, and determine atmospheres that will aid in preventing academic dishonesty.
METHODS: Third professional year PharmD students at four institutions of varied types and locations were invited to participate in a survey administered by a class representative. Completed surveys were analyzed using descriptive statistics and χ^2 analysis.
RESULTS: Of 296 completed surveys, 16.3% admit to cheating in pharmacy school, yet 73.9% admit either they or classmates have worked on an individual assignment with a friend. Half of respondents (49.3%) admit either they or classmates copied directly from a reference without citing. Students agreed or strongly agreed with the following statements: not a single exam in pharmacy school goes by without a cheater (52.7%) and cheating is more likely to occur if a teacher has an intimidating style (68.3%). Students who cheated during high school or pre-pharmacy were more likely to cheat during pharmacy school, (p<0.0001), while those who possessed a BS degree prior to attending pharmacy school were less likely to cheat (p<0.0001). No relationship between cheating and gender or GPA was identified.
CONCLUSIONS: Academic dishonesty is prevalent among pharmacy students. While few respondents directly admit to cheating, many admit to activities traditionally defined as dishonest. Less cheating occurs among students who possess a prior BS degree and when faculty are approachable. Faculty and preceptors can take results into consideration in determining methods to decrease cheating.

83. Developing and delivering an instructional pharmacy residency program preceptors' conference. *Nannette M. Berensen, PharmD, BCPS*, Melissa M. Blair, PharmD, BCPS, CDE, Marc Lapointe, PharmD, BCPS, BCNSP; Medical University of South Carolina, Charleston, SC.

OBJECTIVE: To develop programming for a pharmacy residency program preceptors' conference and to deliver instructional content that would improve preceptor performance within an academic health sciences center.
METHODS: A workgroup convened to develop a pharmacy residency program preceptors' conference. The workgroup created a survey to assess preceptors' individual learning needs. The survey asked preceptors to rate potential pre-specified topics and to identify additional topics of interest. The survey also queried preceptors about conference format, frequency, attendance requirement, and an annual preceptor competency assessment. The survey was distributed electronically and responses were submitted online. Based on survey data, an agenda was developed. Speakers were selected based on their expertise and suggestions from preceptors and residents. Topics included an overview of program requirements, precepting rotation and nonrotation requirements effectively, giving meaningful evaluations, mentoring residents, and authorship. The 3-hour conference was presented on two occasions to increase attendance. At the conclusion, attendees were asked to complete a post conference evaluation.
RESULTS: Forty-three of 45 preceptors responded to the initial survey. Thirty-seven preceptors attended the conference (15 faculty, 14 clinical specialists, and 8 practice management/operations). Twenty-eight attendees (76%) completed a post conference evaluation. Post conference evaluation respondents had precepted a median of 5 residents in the last year (range 0 to15 residents) and had served as a residency preceptor for a median of 4.75 years (range 0 to18 years). All respondents who completed the post conference evaluation either agreed or strongly agreed that the instructional content was appropriate in scope and would be valuable to them when precepting residents.
CONCLUSIONS: Assessment of preceptors' individual learning needs was an effective mechanism to determine the instructional content for the pharmacy residency program preceptors' conference. Attendees who completed the post conference evaluations found the conference to be valuable and useful in their interactions with pharmacy residents.

84. Evaluation of patient case presentation by residents. *Marc M. Perreault, PharmD, BCPS*, Nathalie Turgeon, B.Pharm., ACPR; Faculté de Pharmacie–Université de Montréal, Montréal, QC, Canada.

PURPOSE: Evaluate pharmaceutical care competencies of residents through a

structured case oral presentation during clinical rotations.
METHODS: All residents (hospital and community) enrolled in the residency program from 2003 to 2005 participated in this study. They were each evaluated once during their program. A patient under their service was assigned to them one hour prior to meeting their preceptor, teaching coordinator, program coordinator and professor. After their one hour pharmacotherapy work up, the resident verbally presented the case in a structured approach. Residents were questionned with regards to the patient, the medical conditions and the pharmacotherapy. Formative evaluation was provided to the residents at the end of the case.
RESULTS: Forty-eight hospital residents and 4 community residents were evaluated over 2 years.The majority had difficulty presenting in a structured approach necessitating interventions from the evaluators. Patient interview was performed in about 66 % of the cases. Data collection was adequate in 62 % of the case presentations. Appreciation of the clinical condition of the patient was poorly demonstrated. Elaboration of the care plan was patient centered but often needed further clarification.The more precise was the care plan, the more proactive was the resident.
CONCLUSION: Further training of residents is recognized in order to master the skills required for case presentation. This can be achieved through increased frequency of this exercise.

85. Cultural competency needs analysis of pharmacy students. *Maisha K. Freeman, Pharm.D., BCPS*, D'Andrea F. Skipwith, Pharm.D.; Samford University, Birmingham, AL.

PURPOSE: Ethnic minorities and other special needs patients (e.g., visually/hearing impaired, illiterate, or limited English proficiency) comprise a significant portion of the Birmingham, Alabama metropolitan population; however, pharmacy students may not be exposed to enough of these patients to appropriately recommend therapy based on health beliefs. The purpose of this study was to determine the need for a cultural competency course for pharmacy students.
METHODS: A literature search was conducted via PubMed and IPA from April 15, 2005–May 10, 2005 to determine the availability of published cultural competence needs analyses conducted by schools of pharmacy. A 25-item pilot survey was developed and given to 8, fourth-year pharmacy students prior to class-wide administration. Pertinent suggestions were incorporated into the survey and were given to fourth year pharmacy students during exit interviews.
RESULTS: A total of 64 (54%) surveys were returned from the class (n=118). The majority of responders were white (78%), female (75%), between the ages of 24–30 years (74%), spent most of the time in the Southeast (100%), and planned to practice in a community pharmacy setting (75%). Approximately 64% of responders believed that pharmacists should incorporate patients' traditional/cultural health beliefs with evidence-based medicine whenever possible. The majority (81%) of students believed that all patients should have access to effective, understandable, respectful care that is compatible with their cultural health beliefs, practices, and preferred language and 91% of responders felt comfortable interacting with patients from different cultures. Approximately 47% of all students and 87% of the minority students felt that the school of pharmacy did not adequately address issues related to cultural competence. Approximately 66% of the student's surveyed felt cultural competence was needed in the curriculum.
CONCLUSION: The results of the survey indicate the need for incoroprating cultural competence in the pharamcy curriculum.

86. The impact of a community pharmacy experience in a family medicine residency-training program. *Julie A. Brousil, PharmD*, Tricia M. Berry, PharmD; St. Louis College of Pharmacy, St. Louis, MO.

The teaching and patient care roles of clinical pharmacists in family medicine residency programs are well established. However, the evolving role of community pharmacists, from a product-focus to a patient-focus, is less widely recognized. It is important for medical residents to understand community pharmacists' contributions to the healthcare team.
PURPOSE: This study evaluated the impact of a community pharmacy experience on family medicine residents' understanding of community pharmacists' roles/responsibilities.
METHODS: During the first year in a specific family medicine residency program, residents are required to complete one month in pharmacy/research. During this rotation, one-half day is spent in a community pharmacy to observe a variety of pharmacist-patient and pharmacist-provider interactions and pharmacy operations to better understand the roles/responsibilities of community pharmacists. Each resident completed a 7-question survey before and after the community pharmacy experience to assess his/her understanding using a 5-point Lickert scale (1=excellent through 5=no experience). Differences were evaluated using Wilcoxon Signed Rank Test, χ^2 and Fisher Exact Test using Sigma Stat.
RESULTS: Twenty family medicine residents were included in the study. The residents' understanding of the roles/responsibilities of community pharmacists, prescription errors and strategies to prevent them, and how community pharmacists can be utilized as resources to enhance patient care improved from adequate to excellent ($p \leq 0.001$) after the experience. Their understanding of the barriers to having prescriptions filled and the laws regarding prescriptions improved from adequate to good ($p \leq 0.001$). The residents' understanding of the technology and processes utilized within a community pharmacy improved from poor to good/excellent ($p \leq 0.001$). The residents' awareness of the community pharmacists' role in evaluating ($p=0.007$) and monitoring ($p=0.009$) drug therapy was enhanced.
CONCLUSION: A community pharmacy experience significantly improved family medicine residents' understanding of the roles/responsibilities of community pharmacists. This greater understanding may facilitate family physicians' utilization of community pharmacists to enhance patient care.

87. Fourth professional year pharmacy students in the ambulatory care setting: patient perceptions and satisfaction. *Rosalyn S. Padiyara, Pharm.D.*, Amie D. McCord, Pharm.D., BCPS, CDE, Patricia L. Lurvey, Ph.D.; Midwestern University–Chicago College of Pharmacy, Downers Grove, IL.

PURPOSE: Establishing a patient-provider relationship based on active participation and collaboration is implicit throughout health care professions. It is essential for pharmacy students to acquire skills that foster such active relationships. This study investigates how patients perceive: pharmacy student's role, satisfaction with services, patient care activities provided, and their advice to pharmacy students to become better health care professionals.
METHODS: Fourth year Pharm.D. candidates on clerkship at an ambulatory care clinic conducted medication histories with patients. Patients were surveyed to evaluate present and previous interactions with pharmacy students and demographic data. Surveys were analyzed using descriptive statistics, ANOVA, and qualitative analysis.
RESULTS: Thirteen students and 74 patients participated in this study. All 74 surveys were included in the data analysis; 55.5% of respondents were male and 82.4% were Caucasian. All respondents strongly agreed or agreed they enjoyed talking with the student, felt the student was professional, and felt comfortable discussing their medications. Ninety-three percent of respondents reported they were satisfied with services provided by the student, and 86.5% stated they would want to become a patient of the student's upon graduation. Respondents who had more activities performed by the student were more likely to think their time was well spent ($p<0.05$). Advice offered to students emphasized professionalism and empathy as important traits to gain in order to become better health care professionals.
CONCLUSIONS: In this ambulatory care setting, patients were satisfied with services fourth year Pharm.D. candidates provided, and felt the services added to their health care. Results may be used to communicate the benefits of pharmacy student interactions to clinical site administration at various organizations and to emphasize important areas for the professional development of students.

88. Prospective analysis of the impact of clinical clerkship experiences on the ethical development of pharmacy students. *Darren W. Grabe, PharmD*, Rowland J. Elwell, Pharm.D., George R. Bailie, PharmD, PhD, Michael R. Brodeur, PharmD; Albany College of Pharmacy, Albany, NY.

PURPOSE: The Early Patient-Oriented Care (EPOC) program is a competitive, elective, 3-semester long, early experiential clerkship offered to students during the second and third professional years. Students follow individual patients over a prolonged period. The primary aim of this study was to examine and compare the impact of EPOC on the ethical development of pharmacy students.
METHODS: This prospective, multi-phase, controlled study was open to students entering the second professional year. In phase one, participating students were administered the defining issues test (DIT) during the fall semester of their second professional year. The DIT is a standardized, validated, multiple-choice questionnaire. DIT scores (P-scores) are highly correlated with ethical development. In phases two and three, the DIT was completed 3 (completion of EPOC) and 5 semesters (completion of PharmD) later, respectively. P-scores at each phase of the study were compared. Results were analyzed using repeated measures ANOVA with significance defined as $p<0.05$.
RESULTS: Fifty-nine students (EPOC, n = 20) completed phase one. Forty students (EPOC, n = 17) completed phase two and 28 (EPOC, n = 14) completed phase three. The table outlines the P-scores at each phase in those students who completed all 3 phases and who had evaluable scores (n = 25).
Comparison of achieved P-scores at different phases

Students	Phase 1 [95% CI]	Phase 2 [95% CI]	Phase 3 [95% CI]
EPOC	31.7 [27.1, 36.4]	41.5 [33.3, 49.6]	44.6 [35.7, 53.6]
Non-EPOC	23.2 [18.4, 27.9]	33.8 [25.4, 42.1]	45.5 [36.4, 54.7]
All	27.4 [24.1, 30.8]	37.6 [31.8, 43.4]	45.1 [38.7, 51.5]*

*$p<0.001$ for phases 1–3

CONCLUSIONS: All students had an increase in ethical reasoning as

measured by the DIT. The EPOC program did not have a significant effect on the ethical development of pharmacy students.

89E. Clinical simulation of a family practice to support interprofessional practice. *Lisa R. Dolovich, BScPhm, PharmD, MSc*[1], Zubin Austin, PhD[2], Elaine Lau, BScPhm PharmD[1], Diana Tabak, BA[2], Connie Sellors, BScPhm[1], Natalie Kennie, BScPharm PharmD[2], Anthony Marini, PhD[3], Lisa McCarthy, BScPhm PharmD[1]; (1)Centre for Evaluation of Medicines McMaster University, Hamilton, ON, Canada; (2)University of Toronto, Toronto, ON, Canada; (3)University of Calgary, University of Calgary, Calgary, AB, Canada.

PURPOSE: With primary care reform, participation of pharmacists within family physicians' office practices expanding. The primary role of the pharmacist is to optimize prescribing and medication use. As part of the Integrating family Medicine and Pharmacy to Advance primary Care Therapeutics (IMPACT) project, pharmacists were placed within family physicians' offices. The objective of this study was to develop and evaluate a transitional training workshop focused on knowledge and skills required by a pharmacist to support collaborative, inter-professional practice.
METHODS: A workshop blueprint was developed through review of existing literature, competency/educational outcome statements, and standards of practice. An interprofessional standard-setting meeting was convened to review cases and assessments used in the workshop. The two-day workshop for IMPACT pharmacists involved an evidence-based review of patient charts on Day 1 and a full-day Family Practice Simulation on Day 2. The Family Practice Simulator involved real pharmacists and physicians working with simulated patients in a family practice setting to identify and resolve actual and potential drug related problems. Quantitative and qualitative post-workshop evaluations were undertaken and 2 weeks, 3 months and 7 months.
RESULTS: Post-workshop evaluations suggested that pharmacists and physicians perceive significant value to inter-professional clinical simulation to prepare pharmacists for integration in family physicians' offices. There was only moderate physician-pharmacist inter-rater reliability in assessment of pharmacists' performance suggesting that physicians and pharmacists may have differing expectations regarding the pharmacist's role. Areas for modification include increased formative feedback and opportunities for de-briefing, and curricular revision to support more formal discussion of team based practices and discourses.
CONCLUSIONS: The complexity of inter-professional work is significant, particularly for practitioners traditionally unaccustomed to face-to-face work. A transitional training workshop involving interprofessional clinical simulation provides a useful bootstrap for profession practitioners, and a novel method for clinical skills training and assessment.
Presented at the Interprofessional Education Conference, Toronto, ON, Canada, May 26–27, 2005.

Emergency Medicine

90. Emergency department management of pediatric asthma at a university teaching hospital. Cynthia Ly, Pharm., D., *Cathi E. Dennehy, Pharm., D.*; University of California, San Francisco, San Francisco, CA.

PURPOSE: We sought to compare the management of pediatric (ages 1 to 17) asthma in the University of California, San Francisco (UCSF) emergency department (ED) with National Asthma Education and Prevention Program (NAEPP) guidelines.
METHODS: We retrospectively reviewed all cases of pediatric asthma presenting to the UCSF ED between October 1, 2003 and October 31, 2004. Cases requiring hospital admission were excluded. We abstracted data pertaining to patient demographics, primary diagnosis (asthma or reactive airway disease), pharmacological management, diagnostic tests performed, and follow up plans. This information was then compared to NAEPP guidelines.
RESULTS: We identified 142 cases. Mean patient age was 5.8 years. Most patients were male (61.7%) and of African American ethnicity (31.9%). Asthma severity was typically mild (66.7%) or moderate (29.1%). In persons ≥ 6 years old, no Peak Expiratory Flow (PEF) or Forced Expiratory Volume in 1-second (FEV1) was performed on arrival in 74% of cases. Pulse oximetry, however, was always performed. Use of beta-agonists and steroids was appropriate in 97.2% and 66% of cases, respectively. At discharge, no steroid prescription was given in 40.4% of cases, no written action plan in 80% of cases, no formal device training in 67.3% of cases and no peak flow meter for persons ≥ 6 years old in 50% of cases.
CONCLUSION: The management of pediatric asthma in the UCSF ED frequently met NAEPP guidelines, regarding performance of pulse oximetry and in the pharmacological management of the exacerbation. Improvements could be made, however, in performing FEV1 and PEF measurements for persons ≥ 6 years old upon arrival and in the provision of formal device training, a written action plan and prescriptions for steroids and peak flow meters at discharge.

91. Emergency department medication administration record: reduction of medication errors. *Maria Rudis, PharmD*[1], Jacqueline Fu, BS[1], Jill M. Hara, PharmD[1], Sheila Mallett, RN[2], Crystal Cornell, PharmD[2], Mark Hollinger, RN[2], Kathryn Challoner, MD[2]; (1)USC School of Pharmacy, Los Angeles, CA; (2)LAC+USC Medical Center, Los Angeles, CA.

BACKGROUND: Emergency Department (ED) overcrowding and prolonged lengths of stay increase the risk of medication errors (ME). The existing ED chart does not accommodate ordering and documentation of the administration of ongoing medications.
PURPOSE: To evaluate the rate of ME before and after implementation of a new ED chart with a medication administration record (MAR).
METHODS: A concurrent pre- and post-evaluation study conducted in the ED of a large, urban, county, Level I trauma center. A multidisciplinary group reconfigured the ED chart with a designated area to prescribe scheduled and single orders of medications. Modifications were made to the RN flow sheet with distinct areas for documentation of all medications given during the ED stay. Multi-pronged educational efforts were conducted for the attending, nursing and resident staff regarding the new forms. Each data collection period (pre: 08/04 and post: 04/05) was conducted from 0800h-1600h over a consecutive 3-day period. Outcomes measures included errors in medication prescribing and medication administration and documentation. χ^2, Fisher's exact test or *t*-test was used to compare ME rates pre (08/04) and post (04/05) implementation.
RESULTS: At baseline, 104 ME were found among 85 doses received in 18 patients reviewed. Post implementation, 149 ME were found among 203 doses received in 31 patients reviewed. In terms of medication prescribing, there was a 91%, 84%, 49% and 35% improvement in ordering follow-up doses ($p=0.003$), use of unapproved abbreviations ($p=0.004$), and undated/timed orders ($p=0.03$), respectively, but no change in undocumented verbal orders. With respect to medication administration and documentation, there was a 100% and 91% reduction in missed doses ($p<0.001$) and undocumented administration times ($p<0.001$), respectively. There was no change in the number of delayed (>1hr) doses.
CONCLUSION: The new ED chart and MAR lowers ME and improves patient safety in a busy ED.

Endocrinology

92. Effect of conivaptan on serum AVP levels. *Neila Smith, MD*; Astellas Pharma US, Inc., Deerfield, IL.

Hyponatremia (serum [Na+] <135 mEq/L) is a common electrolyte disorder often associated with elevated vasopressin (AVP). Conivaptan (CNV) is a novel AVP receptor antagonist that produces aquaresis by blocking V2 receptors. The aquaretic effect of CNV was evaluated by determining changes in free and effective water clearance (FWC and EWC) in 3 randomized, double-blind, placebo (PBO)-controlled trials (1 intravenous [IV], 2 oral) in patients with hyponatremia ([Na+] 115 to <130 mEq/L). Eighty-four patients were randomized to receive a 20 mg intravenous (IV) loading dose of CNV or PBO, followed by infusion of CNV 40 or 80 mg/day for 4 days or PBO. Eighty-three and 74 patients were randomized to oral CNV 40 or 80 mg/day or PBO in 2 divided doses for 5 days. Treatment with CNV rapidly increased EWC and FWC. Increases from baseline FWC after 1 day of treatment with 20 or 40 mg IV CNV were 1953 and 1670 mL, respectively, versus -274 mL for placebo ($p=0.0004$ and 0.0007). The respective EWC values were 1984, 1759, and -322 ($p=0.0022$ and 0.0012). Oral CNV also promoted rapid aquaresis. In the first trial, increases from baseline FWC after 1 day of treatment with 20 or 40 mg CNV were 957 and 1307 mL, respectively, versus 48 mL for placebo ($p=0.0004$ and 0.0001). The respective values for EWC were 686, 662, and -72 mL ($p=.0006$ and .0001). In the second study, increases from baseline FWC after 1 day of treatment with 20 or 40 mg oral CNV were 669 and 1074 mL, respectively, versus -34 mL for placebo ($p=0.611$ and 0.021). The respective values for EWC were 922, 844, and -5 mL ($p=0.211$ and 0.053). The improvements in FWC and EWC with CNV were maintained for the duration of each study and were associated with significant increases in serum [Na+].

93. Two-year outcomes of a pharmacist-run teriparatide clinic. Shannon M. Rivers, Pharm.D.[1], *Michael P. Kane, Pharm.D.*[1], Asim M. Abu-Baker, Pharm.D.[2], Jeffrey Stroup, Pharm.D.[3], Robert A. Hamilton, Pharm.D.[1]; (1)Albany College of Pharmacy, Albany, NY; (2)LECOM College of Pharmacy, Erie, PA; (3)University of Oklahoma College of Pharmacy, Tulsa, OK.

PURPOSE: To report outcomes of patients referred to a pharmacist-run teriparatide clinic.
METHODS: Osteoporosis histories of referred patients from a private endocrinology practice were reviewed. One sample *t*-tests and paired *t*-tests were used to compare percent changes in bone mass density (BMD) and T-scores.

RESULTS: 148 patients were referred to the clinic. 107 patients subsequently started teriparatide therapy while 41 patients did not because of patient preference not to receive drug (n=19), contraindication to drug therapy (n=10), cost (n=6), or lack of follow-up (n=6). Among the evaluable patients, 97.2% were Caucasian, 88.8% were female, average age was 67.6 (+ 13.8) years, and 46.7% of patients reported a previous osteoporosis-related fracture. Baseline T-scores of the hip, lumbar spine, and wrist were -2.5, -2.4 and -2.2, respectively. Median duration of teriparatide therapy (June 1, 2005) was 394 (range 6-730) days. Twelve patients discontinued therapy because of displeasure with daily injections (n=7), side effect (n=3), or cost (n=2). At one year, BMD was assessed in 40 of 55 patients; there were significant increases in BMD of the hip (2.9%, p=0.0299) and lumbar spine (4.9%, p<0.0001). Wrist BMD did not change (-0.5%, p=0.6023). After 2 years (n=15), there was a continued increase in BMD (5.1%; p<0.0001) of the spine only (hip: 1.6%, p=0.3126; wrist: -1.4%, p=0.2338). Compared to baseline, T-scores of the hip significantly improved at one year (0.2, p=0.0052) but did not change at two years (0.3, p=0.116). T-scores of the spine were significantly increased at one year (0.35, p<0.0001) and 2 years (0.7, p<0.0001). Wrist T-scores at 1 (-0.1, p=0.3931) and 2 years (-0.4, p=0.6018) did not significantly change from baseline. No new osteoporosis-related fractures have occurred among the 107 patients during teriparatide treatment.
CONCLUSION: Teriparatide therapy was associated with improved hip and spine BMD and T-scores, and was generally well tolerated.

94E. Comparison of lipid and glycemic effects of pioglitazone and rosiglitazone in patients with type 2 diabetes and dyslipidemia. *Phil Naughten, PharmD*[1], Ronald Goldberg, MD[2], David Kendall, MD[3], Mark Deeg, MD, PhD[4], John Buse, MD, PhD[5], Anthony Zagar, MS[6], Jane Pinaire, PhD[6], Meng Tan, MD[6], Mehmood Khan, MD[1], Alfonso Perez, MD[7], Scott Jacober, DO[6]; (1)Takeda Pharmaceuticals North America Inc., Lincolnshire, IL; (2)University of Miami School of Medicine, Miami, FL; (3)Park Nicollet Institute, Minneapolis, MN; (4)Dept of Veterans Affairs and the Indiana University School of Medicine, Indianapolis, IN; (5)University of North Carolina School of Medicine, Chapel Hill, NC; (6)Eli Lilly and Company, Indianapolis, IN; (7)Takeda Global Research and Development Center, Lincolnshire, IL.

Diabetic dyslipidemia is a common cardiovascular risk in patients with type 2 diabetes (T2D). The thiazolidinediones, pioglitazone (PIO) and rosiglitazone (ROSI), have glucose-lowering and lipid-altering effects. Prior reports suggest that these agents may have different effects on lipid parameters. PIO and ROSI were compared in a randomized, double-blind, multicenter trial in patients with T2D (WHO criteria) and dyslipidemia (fasting TGs ≥150 and ≤600 mg/dL; fasting LDL-C ≤130 mg/dL). Subjects discontinued any prior T2D monotherapy and were randomized to receive placebo for 4 weeks followed by 24 weeks of PIO or ROSI monotherapy. At 12 weeks, PIO (30mg QD) and ROSI (4mg QD) were titrated to 45mg QD and 4mg BID, respectively. Patients received no other lipid-lowering therapies before or during the study. There were no clinically significant baseline differences between treatments. Mean change in HbA1c from baseline to week 24 was similar for PIO and ROSI (-0.7 ± 0.1% vs -0.6 ± 0.1%).
Week 24 Changes From Baseline

	PIO N=363		ROSI N=356	
	Mean change (SE)	% change	Mean change (SE)	% change
TG (mg/dL)	-51.9 ± 7.8*	-12.0%*	+13.1 ± 7.8	+14.9%
HDL-C (mg/dL)	+5.2 ± 0.5*	+14.9%*	+2.4 ± 0.5	+7.8%
Non-HDL-C (mg/dL)	+3.6 ± 1.9*	+3.8%*	+25.7 ± 2.0	+18.6%
LDL-C (mg/dL)	+12.3 ± 1.6*	+15.7%*	+21.3 ± 1.6	+23.3%
LDL particle conc. (nmol/L)	-50.5 ± 21.3*	+0.8%*	+110.5 ± 21.5	+12.0%
LDL particle size (nm)	+0.46 ± 0.04**	+2.4%**	+0.33 ± 0.04	+1.7%
Apolipoprotein B (g/L)	<0.01 ± 0.01*	+1.5%*	+0.11 ± 0.01	+11.5

*P<0.001,
**P=0.005, between groups.

This study demonstrates that PIO and ROSI exert different effects on plasma lipids. PIO is associated with significant improvements vs ROSI in TG, HDL-C, non-HDL-C, and LDL particle concentration and size, despite similar effects on glycemic control.
Presented at the 2004 Scientific Sessions of the American Heart Association, New Orleans, LA, November 7–10, 2004.

95E. Pioglitazone improves lipid levels in subjects with type 2 diabetes and dyslipidemia after treatment conversion from rosiglitazone while continuing stable statin therapy. *Philip Naughten, PharmD*[1], Mehmood Khan, MD[1], Paulos Berhanu, MD[2], Alfonso Perez, MD[3], Stuart Kupfer, MD[3], Seleshi Demissie, MSc, DrPH[3], Penny Fleck, MT[3]; (1)Takeda Pharmaceuticals North America Inc., Lincolnshire, IL; (2)Wayne State University School of Medicine, Detroit, MI; (3)Takeda Global Research and Development Center, Lincolnshire, IL.

PURPOSE: The current open-label study, "COMPLEMENT," was designed to determine whether lipid differences observed in a recent randomized, head-to-head, placebo-controlled trial in the absence of concomitant lipid-altering therapies would be similar when subjects converted from rosiglitazone to pioglitazone therapy while maintaining constant doses of existing statins and other lipid-altering therapies. The primary outcome measure was fasting TGs.
METHODS: In this multicenter, open-label study, 305 patients with type 2 diabetes and dyslipidemia (195 men, 110 women, aged 18-70 years, triglycerides 200-1000 mg/dL) who had been taking stable rosiglitazone and statin doses (>90 days) were converted to PIO 30 mg/day (titrated to 45 mg/day) at baseline and treated for 17 weeks while continuing existing statin and other lipid-altering regimens.
RESULTS: Changes in Glycemic and Lipid (mg/dL) Parameters

	Baseline Mean (SD) (n=304)	Week 17 Mean Change (SE) (n=280)	P Value
HbA1c (%)	7.3 (1.28)	+0.02 (0.887)	0.72
Triglycerides	303.3 (157.57)	-64.9 (6.43)	<0.0001
Total Cholesterol	198.5 (41.78)	-20.6 (1.55)	<0.0001
LDL-C	103.5 (32.74)	-2.6 (1.25)	0.040
HDL-C	42.4 (10.13)	0.0 (0.33)	0.93

At week 17 after conversion from ROSI to PIO, significant changes were observed in TGs (-21%), total cholesterol (-10%), and LDL-C (-1%), but no significant change in HDL-C was observed. HbA1c levels remained unchanged after conversion to PIO.

CONCLUSIONS: Replacing ROSI with PIO in subjects with type 2 diabetes while maintaining concomitant statin and other lipid-altering therapies resulted in significant improvements in TGs, total cholesterol, and LDL-C but no change in HDL-C levels. These combined improvements in lipid levels were independent of glycemic control.
Published in Diabetes 2005;54(Suppl 1):A137.

96. Twelve-week analysis of low-dose pioglitazone compared with low-dose rosiglitazone in patients with type 2 diabetes and dyslipidemia: results from a head-to-head trial. *Ken Johnson, PharmD*[1], Robert Spanheimer, MD[1], Alfonso Perez, MD[2], Scott Jacober, DO[3], Ronald Goldberg, MD[4], Meng Tan, MD[3], David Kendall, MD[5]; (1)Takeda Pharmaceuticals North America Inc., Lincolnshire, IL; (2)Takeda Global Research and Development Center, Lincolnshire, IL; (3)Eli Lilly and Company, Indianapolis, IN; (4)University of Miami School of Medicine, Miami, FL; (5)Park Nicollet Institute, Minneapolis, MN.

Patients with type 2 diabetes (T2D) often demonstrate metabolic abnormalities associated with insulin resistance, such as dyslipidemia. This cluster of abnormalities is associated with increased cardiovascular disease risk. The thiazolidinediones, pioglitazone (PIO) and rosiglitazone (ROSI), have glucose-lowering and potentially lipid-altering qualities. The effects of low-dose PIO (30-mg QD) and low-dose ROSI (4-mg QD) are reported here.
This randomized, double-blind, multicenter, head-to-head comparison of PIO and ROSI enrolled patients with T2D (WHO criteria) and dyslipidemia (fasting TG ≥150 and ≤600 mg/dL; fasting LDL-C ≤130 mg/dL). At randomization, patients discontinued prior oral antihyperglycemic medications and began a 4-week placebo washout. Active treatment started with 30-mg PIO QD or 4-mg ROSI QD for 12 weeks, increasing to 45 mg QD and 4 mg BID, respectively, for an additional 12 weeks. No other lipid-lowering therapies were allowed before or during the study.
LS Mean (SE) Change From Baseline to Week 12

	PIO 30 mg (n=369)	ROSI 4 mg (n=366)	P-Value Between Groups
HbA1c (%)	-0.46 ± 0.05*	-0.31 ± 0.05[U]	0.017
TG (mg/dL)	-50.83 ± 7.27*	26.97 ± 7.30*	<0.001
Total cholesterol (mg/dL)	5.87 ± 1.65*	20.74 ± 1.67*	<0.001
HDL-C (mg/dL)	4.71 ± 0.43*	1.11 ± 0.44	<0.001
LDL-C (mg/dL)	10.39 ± 1.30*	13.14 ± 1.32*	0.102*

P<0.001, [U]P<0.05 vs baseline.

Low-dose PIO significantly improved glucose levels, TGs, and HDL-C compared to low-dose ROSI. Additionally, total cholesterol increases were significantly higher with low-dose ROSI than with low-dose PIO, whereas quantitative changes in LDL-C did not differ between treatments. Overall, slight glycemic reduction and potentially beneficial lipid changes were achieved with low-dose PIO compared to low-dose ROSI at week 12.

97E. Effects of pioglitazone with stable statin and fenofibrate therapy on lipid changes in subjects with type 2 diabetes and dyslipidemia after treatment conversion from rosiglitazone. *Charles Kelly, PharmD*[1], Mehmood Khan, MD[1], Alfonso Perez, MD[2], Seleshi Demissie, MSc, DrPH[2], Penny Fleck, MT[2], Stuart Kupfer, MD[2]; (1)Takeda Pharmaceuticals North America Inc., Lincolnshire, IL; (2)Takeda Global Research and Development Center, Lincolnshire, IL.

The current open-label study, "COMPLEMENT," was designed to determine whether lipid differences observed in a head-to-head randomized controlled study in the absence of concomitant lipid-altering therapies would be similar when subjects are converted from rosiglitazone to pioglitazone while

maintaining existing, stable statin and other lipid-altering regimens. Although allowed, fenofibrate and/or niacin was used by only 10% of patients (only 8 used niacin). Results with and without fenofibrate use are presented for triglycerides, total cholesterol, LDL-C, and HDL-C.In this multicenter, open-label study, 305 patients with type 2 diabetes and dyslipidemia (18-70 years; 195 men, 110 women; triglycerides 200-1000 mg/dL) who had been taking stable rosiglitazone and statin doses (>90 days) were converted to pioglitazone 30 mg/day (titrated to 45 mg/day) at baseline and treated for 17 weeks while continuing existing statin and other lipid-altering regimens.

		Lipid, mg/dL Triglycerides	Total Cholesterol	LDL-C	HDL-C
Fenofibrate	Baseline	367.2	209.2	106.3	36.1
	(n=27)	(220.86)	(48.49)	(27.45)	(10.96)
	Week 17 Change	-83.8	-24.8	-1.8	1.8
	(n=26)	(192.92)	(38.31)	(27.39)	(6.15)
No fenofibrate	Baseline	297.1	197.5	103.3	43.1
	(n=277)	(149.07)	(41.02)	(33.24)	(9.86)
	Week 17 Change	-63.0	-20.1	-2.7	-0.2
	(n=254)	(117.49)	(31.16)	(26.14)	(6.33)

Baseline triglycerides, LDL-C, and total cholesterol were higher and HDL-C was lower in subjects using fenofibrate. After conversion, reductions in triglycerides, total cholesterol, and LDL-C were similar regardless of fenofibrate use, while HDL-C increased in the fenofibrate group only. Results (not shown) for niacin use were similar. In conclusion, switching subjects with type 2 diabetes from rosiglitazone to pioglitazone while maintaining concomitant statins resulted in decreases in triglycerides, total cholesterol, and LDL-C with or without fenofibrate use.
Published in Diabetes 2005;54(Suppl 1):A516.

98. Conivaptan, a novel arginine vasopressin antagonist, produced aquaresis and increased serum sodium concentration in patients with euvolemic and hypervolemic hyponatremia. *Joseph G. Verbalis, MD*[1], Jalal K. Ghali, MD[2], Peter Gross, MD[3], Walker A. Long, MD[4], Neila Smith, MD[5]; (1)Georgetown University Medical Center, Washington, DC; (2)Louisiana State University, Shreveport, LA; (3)Universitätsklinikum Carl Gustav Carus, Dresden, Germany; (4)Cato Research, Durham, NC; (5)Astellas Pharma US, Inc., Deerfield, IL.

PURPOSE: Hyponatremia serum sodium concentration ([Na^+]) <135 mEq/L is a common electrolyte disorder often associated with elevated arginine vasopressin (AVP). The effect of conivaptan (CNV), a novel AVP V_2/V_{1A}-receptor antagonist, on renal excretion of electrolyte-free water, determined by change in free water clearance (FWC), was evaluated in 3 randomized, double-blind, placebo (PBO)–controlled trials (1 intravenous [IV], 2 oral) in patients with euvolemic or hypervolemic hyponatremia ([Na^+] 115 to <130 mEq/L).
METHODS: Eighty-four patients were randomized to receive a PBO or CNV 20 mg IV loading dose, followed by continuous infusion of CNV 40 or 80 mg/d or PBO for 4 days. In the 2 oral trials, 83 and 74 patients, respectively, were randomized to oral CNV 40 or 80 mg/d or PBO in 2 divided doses for 5 days.
RESULTS: On day 1, IV CNV 40 and 80 mg/d increased FWC 1953 (P=0.0004) and 1670 mL (P=0.0007), respectively, from baseline while a decrease of 274 mL occurred in the PBO group. Consequently, serum [Na^+] increased 6.4 and 8.1 mEq/L with IV CNV 40 and 80 mg/d (P=0.0001 for both), vs 0.4 mEq/L with PBO. Oral CNV also produced aquaresis the electrolyte-sparing excretion of water. On day 1 in the first oral trial, FWC increased 957 and 1307 mL, respectively, from baseline with CNV 40 and 80 mg/d (P=0.0004 and P=0.0001), vs 48 mL with PBO. On day 1 in the second oral trial, FWC increased 669 and 1074 mL with CNV 40 and 80 mg/d (P=0.611 and P=0.021) but decreased 34 mL with PBO. Serum [Na^+] also increased from baseline with oral CNV. In each study, improvements in FWC with CNV were largest on day 1 and were maintained throughout the treatment period.
CONCLUSIONS: CNV produced significant aquaresis, as determined by increased FWC. The aquaresis was associated with significant increases in serum [Na^+].

99. Insulin glargine: clinical efficacy and predictors of twice daily dosing. *Amie D. McCord, Pharm.D., BCPS, CDE*, Patrick J. Kiel, Pharm.D. candidate, Dawn Deurloo, Pharm.D. candidate, David P. Zgarrick, PhD; Midwestern University–Chicago College of Pharmacy, Downers Grove, IL.

PURPOSE: Evaluate differences in clinical efficacy when using insulin glargine twice compared to once-daily. Determine if patient characteristics serve as predictors of twice-daily insulin glargine use.
METHODS: A retrospective review of 400 medical records was conducted. Thirty patients on twice-daily glargine and thirty age-matched controls on once-daily glargine were identified. Data collection included fasting blood glucose, A1c, cholesterol, weight, body mass index, creatinine clearance, total daily glargine dose, use of fast-acting insulin analogues, patient gender, duration of insulin and of glargine. All data were collected at baseline (time of glargine initiation) and follow-up (most recent as of April 2005).
RESULTS: Mean baseline age was 54 ± 9.6 years. There were no significant differences between the once and twice-daily groups in baseline values for fasting blood glucose, A1c, creatinine clearance, BMI, LDL or triglycerides. Patients in the once-daily group had a lower HDL at baseline (40.5 ± 9.16 vs. 45.13 ± 17.53; p=0.049). More patients in the twice-daily group were taking fast-acting insulin analogues at baseline (58% vs 26% p=0.02) and at follow-up (90% vs. 39% p<0.001). There were no significant between-group differences in mean change from baseline to follow-up for fasting blood glucose, A1c, HDL, triglycerides, or weight. All patients experienced significant reductions in fasting blood glucose, A1c, and triglycerides. Patients experienced weight gain over time regardless of the dosing schedule. There was a greater reduction in LDL for the twice-daily group (-9.25 ± 24.35 vs. −26.06 ± 42.8; p=0.039). Patients on twice-daily glargine had a significantly longer duration of insulin therapy and glargine therapy than control patients.
CONCLUSIONS: Twice-daily glargine use was as clinically effective as once-daily. A longer duration of insulin therapy and need for a higher insulin dose were the only significant predictors of twice-daily insulin glargine use.

100. Can a pamphlet incorporating American Diabetes Association educational standards for patients utilizing insulin pump therapy improve knowledge about managing diabetes? *Christopher S. Holaway, Pharm.D, BSPharm, B.S.*; University of Georgia College of Pharmacy, Albany, GA.

PURPOSE: The purpose of this project was to determine if a pamphlet incorporating American Diabetes Association (ADA) educational standards for patients utilizing insulin pump therapy would improve knowledge about managing diabetes. Study design: This was a prospective, randomized, single blind, controlled, parallel group study.
METHODS: Children and adolescents with Type I diabetes were randomly assigned to receive a pamphlet and a questionnaire (experimental group) or a questionnaire alone (control group) utilizing a permuted block randomization method. The pamphlet contained information regarding the complications and goals of managing diabetes. The questionnaire, incorporating ADA educational standards, was used to assess the patient and/or caregivers knowledge about managing diabetes utilizing insulin pump therapy. Participants were mailed a packet of material which included a self-addressed, stamped envelope, consent form, pamphlet (experimental group participants) and questionnaire. Participants were asked to complete and return the completed questionnaires. Control group participants were asked not to use additional resources to complete the questionnaire.
RESULTS: One hundred thirty six packets of information were mailed. Fifty percent received the pamphlet with the questionnaire and 50% received the questionnaire without the pamphlet. Forty-nine questionnaires (36%) were returned with 24 indicating that they had received the educational pamphlet with the questionnaire and 24 indicating that they had not. One questionnaire was returned blank. One questionnaire in the experimental group and one questionnaire in the control group were only partially completed. The mean (+ SD) questionnaire score in the experimental group was 96.9+ 3.6 compared with 95.6+ 6.9 in the control group (p=0.81).
CONCLUSION: An educational pamphlet mailed to participants that contained information about the management of diabetes in patients utilizing insulin pump therapy did not statistically improve questionnaire scores. Based on median questionnaire scores, a sample size of 232 is needed to reach statistical significance.

101. Relationship of patients' self-management knowledge of diabetes to attainment of ADA goals for lipids, systolic blood pressure and A_{1c}. *Sharm Steadman, PharmD, BCPS, CDE*, Tim Mullenix, PharmD, MS; USC Department of Family and Preventive Medicine, Columbia, SC.

PURPOSE: To determine the relationship between patients' self-management knowledge of diabetes and their current A_{1c}, lipid and systolic blood pressure values.
METHODS: Members of a health plan with a diagnosis of diabetes completed a health screening that included blood pressure, lipid profile, and hemoglobin A_{1c} measurements. Each participant's knowledge of diabetes self-management was evaluated by completing the Diabetes Knowledge Test from the Michigan Diabetes Research and Training Center. The relationship between test scores and achievement of ADA goals for A_{1c}, systolic blood pressure, and LDL-C were evaluated utilizing a Students *t*-test.
RESULTS: 43 participants completed both the health screening and Diabetes Knowledge Test. There were 34 females and 9 males with an average age of 54.8 years (31–80 years). The average A_{1c} was 7.2% (1.6) with 53% less than the ADA goal of 7%. The average LDL-C was 102.6 mg/dl (37.1) with 46% less than 100 mg/dl. The average systolic blood pressure was 131.5 mmHg (12.4) with 46% less than 130 mmHg. The average test score was found to be higher in those with a measured A_{1c} less than 7%. (p=0.0013) A difference was not found between test scores and either blood pressure (p=0.66) or LDL-

C (p=0.98) goal attainment.
CONCLUSIONS: There was a significant relationship found between diabetes knowledge of self-management and patients who had current A_{1c} values less than 7%. Less than 50% of participants had blood pressure and LDL-C measurements that met ADA goals. Patient knowledge appears to positively correlate with attainment of glycemic control. This data suggests that more emphasis needs to be placed on cardiovascular risk reduction in diabetes.

102. Control of vascular disease risk factors among adults with diabetes in Alabama. *Miranda R. Andrus, Pharm.D., BCPS*[1], Kristi W. Kelley, Pharm.D., BCPS, CDE[1], Renee M. DeHart, Pharm.D., BCPS[2], Katherine C. Herndon, Pharm.D., BCPS[3]; (1)Auburn University Harrison School of Pharmacy, Auburn, AL; (2)Samford University McWhorter School of Pharmacy, Birmingham, AL; (3)Pfizer Inc., Birmingham, AL.

PURPOSE: Alabama ranks among the top states in the nation for the prevalence of diabetes. This project was designed to evaluate the control of vascular disease risk factors (blood glucose, blood pressure, and cholesterol) among a cohort of adults with diabetes in Alabama.
METHODS: A retrospective medical record review was conducted at seven ambulatory care centers across Alabama to collect data regarding the control of glycosylated hemoglobin (HbA1c), blood pressure, and cholesterol in patients with diabetes aged 20 years and older with one or more clinic visits in the 12 months prior to the review (n = 755; 59.1% female). Goal attainment rates were based on current American Diabetes Association (ADA), JNC 7, and ATP III practice guidelines, and compared with data from the National Health and Nutrition Examination Survey (NHANES) 1999-2000.
RESULTS: HbA1c, blood pressure, and lipid profile results were documented in 93.5%, 99.3%, and 80% of patients, respectively. The goal HbA1c level of less than 7% was achieved in 44.2% of patients (mean HbA1c = 7.6 ± 2.0%; range = 4.4%–21.2%). Only 21.1% of patients achieved the goal blood pressure of <130/80 mm Hg (mean SBP = 137.4 ± 20.1 mm Hg; mean DBP = 79.8 mm Hg ± 11.4 mm Hg), and 48.1% had hypertensive blood pressure levels (SBP ≥140 or DBP ≥90 mm Hg). Total cholesterol (<200 mg/dL) and LDL cholesterol (<100 mg/dL) goals were achieved in 51.9% and 34% of patients, respectively. Control of HbA1c, blood pressure, and total cholesterol was achieved in only 8.8% of patients in Alabama compared with 7.3% of patients in the NHANES 1999-2000 report (p=0.417).
CONCLUSION: Poor control of risk factors for vascular disease in patients with diabetes may provide substantial opportunities for the development of clinical pharmacy services in Alabama.

103. Putative insulin mediator, D-chiro-inositol-containing inositolphosphoglycan (DCI-IPG) and insulin sensitivity in women with polycystic ovary syndrome. *Kai I. Cheang, Pharm.D.*[1], Jean-Patrice Baillargeon, MD[2], John E. Nestler, MD[1]; (1)Virginia Commonwealth University, Richmond, VA; (2)Ctr Hosp Univ de Sherbrooke, Univ de Sherbrooke, Sherbrooke, QC, Canada.

PURPOSE: Evidence suggests that some actions of insulin are mediated by putative inositolphosphoglycan (IPG) mediators, and a deficiency in a specific D-chiro-inositol-containing IPG (DCI-IPG) may contribute to insulin resistance in women with polycystic ovary syndrome (PCOS). Increased DCI-IPG release has been shown to be correlated with improved insulin sensitivity. The amount of DCI-IPG available for release, and thereby its insulin-mediating action, may be affected by dietary factors, DCI-IPG supplementation and insulin sensitizing drugs. In this study, we study whether DCI-IPG mediator release is correlated with insulin sensitivity in women with PCOS regardless of environmental and dietary changes.
METHODS: We analyzed DCI-IPG released during an OGTT in 11 PCOS women at two time points, separated by 8 weeks. There were no dietary restrictions during these 8 week period. The subjects were part of an ongoing randomized placebo-controlled trial of DCI supplementation in PCOS. Serum DCI-IPG released during the OGTT is calculated as the percentage of its bioactivity (measured by PDH bioassay) compared to 0 min. Insulin sensitivity was measured by Bergman's modified frequently-sampled intravenous glucose tolerance test (FSIVGTT).
RESULTS: There was a significant linear relationship between insulin sensitivity and AUC for DCI-IPG release (per unit of insulin release) during an OGTT both at baseline (p=0.0193) and at 8 weeks (p=0.0003), as well as when data for the two time points are combined (p<0.05). This was despite the fact that both insulin sensitivity and DCI-IPG release for most subjects did not remain constant throughout the 8 week periods.
CONCLUSIONS: In women with PCOS, increased DCI-IPG release is significantly correlated with improved insulin sensitivity, despite environmental and dietary factors that may alter DCI-IPG levels. The significant relationship between DCI-IPG release and insulin sensitivity suggest that the DCI-IPG insulin mediator may be a target for therapeutic interventions in PCOS and other insulin resistant states.

Gastroenterology

104. Online peer support groups for hepatitis C: An exploratory study of medication beliefs and management. *Richard H. Parrish II, PhD*, Sontheary Kem, PharmD, Jacqueline Pham, PharmD; Shenandoah University, Winchester, VA.

BACKGROUND: A lack of information and understanding exists regarding hepatitis C (HCV) online peer support groups (OPSG) and their beliefs about medications and management.
PURPOSE: to pilot test a validated belief and medication management instrument in a self-selected sample of HCV OPSG participants.
METHODS: an online survey of HCV OPSGs.
RESULTS: 417 participants transmitted a survey. Respondents were typically married or partnered, and evenly divided between male and female gender; 10% did not know their viral genotype. Almost 50% indicated that their regimen overwhelms them. Over 25% were uncertain that taking a prescribed medication would make them feel better. Belief sub-scale (r = 0.385) and medication management sub-scale (r = 0.393) were significant correlated with total summative score (p<0.0001). There was no correlation between the total summative score and any other demographic variables such as age, gender, marital status, annual income, and genotype. Cronbach a (0.8 and 0.923) values for the instrument's subscales were consistent with a prior study's results for beliefs and medication management in an elderly population.
CONCLUSION: An existing instrument for measuring medication use beliefs and management was reliable for application to HCV OPSG participants regardless of demographic characteristics.

105. Pharmacist survey on the use of intravenous proton pump inhibitors for the treatment of acute upper gastrointestinal bleeding. Erinn Kao, Pharm.D., *David R. Foster, Pharm.D.*; Purdue University, Department of Pharmacy Practice, Indianapolis, IN.

PURPOSE: The role of intravenous (IV) proton pump inhibitors (PPIs) following endoscopic treatment of acute non-variceal upper gastrointestinal bleeding (UGIB) is controversial. The purpose of this project was to determine clinician opinions and practice patterns regarding the use of IV PPIs in the therapy of UGIB.
METHODS: Members of the ACCP "Critical Care" and "Gastroenterology/Liver/Nutrition" Practice and Research Networks' list-serves were invited to participate in this web-based survey between 11/12/04 and 12/14/04. This 31-item survey queried respondents' opinions, institutional practices, and demographics. Responses were summarized with descriptive statistics.
RESULTS: 56 responses were received. Reported practice areas included critical care (62%), gastroenterology/nutrition (8.5%), trauma/surgery (8.5%), internal medicine (8.5%), general medicine (4%), drug information (4%), cardiology (2%), and pharmacokinetics (2%). 59% of respondents agreed that evidence supports IV PPIs as preferred therapy for UGIB following endoscopic hemostasis. 20% agreed IV PPIs are the best choice in this situation although specific supporting data are lacking, and 11% believed that a role for IV PPIs in acute UGIB may exist, however, data are insufficient to warrant their use in this situation. 12.5% considered oral PPIs to be preferred. The most prevalent regimen recommended for IV pantoprazole was 80mg IV bolus and 8mg/hr continuous infusion, and for IV lansoprazole was 60mg IV bolus and 6mg/hr continuous infusion. Recommended duration of therapy varied from 24–96 hours. 62% of respondents reported no difference in the use of acid-suppressive therapy at their institution between patients with UGIB following endoscopic hemostasis and patients without endoscopic treatment.
CONCLUSIONS: The majority of respondents believe that an IV PPI is preferred for the prevention of rebleeding in the treatment of most UGIB, although alternate opinions were also expressed. These data may assist clinicians in the use of IV PPIs for the treatment of UGIB until more prospective data are available.

106E. Older patients have no increased rate of adverse events (AEs) with sodium phosphate (NaP) tablets. *Martin Rose, M.D., J.D.*[1], Barbra T. Nagle, Ph.D.[1], Margaret M. Hannan, M.S.[1], William G. Kramer, Ph.D.[2], Kelli Walker, PharmD, MS[1]; (1)InKine Pharmaceutical Co., Inc., Blue Bell, PA; (2)Kramer Consulting LLC, North Potomac, MD.

Colonoscopy is a frequent procedure in persons over the age of 50. To determine whether age or other demographic factors affected the clinical safety of Visicol (NaP) tablets, data were analyzed from 2 randomized trials comparing Visicol 60g to NuLYTELY (PEG) 4L in 859 adults undergoing colonoscopy. The trials were designed to demonstrate equivalence in colon cleansing efficacy. The design and results of these trials have been reported previously. Stepwise logistic regression was used to examine the effects of age, gender, race, and weight on the incidence of the most common AEs. In the

Visicol group (N=427), the median age was 56.0 years (range, 19-84); 19.9% of patients were >65-75 and 8.0% were >75. About 51.3% of patients were women and 89.2% Caucasian. The median weight was 179.7lb (range, 92-336). The PEG group (N=432) was comparable in all these parameters. The common AEs occurring in more than 3.0% of patients overall were bloating, nausea, abdominal pain (pain), and vomiting. Visicol was associated with a significantly lower incidence of bloating (47.2% vs. 62.3%), nausea (35.8% vs. 54.2%), and vomiting (9.1% vs. 18.3%) than PEG; the incidence of pain was comparable (Visicol 31.1%, PEG 36.6%). In Visicol patients, increased age was a significant predictor of a lower incidence of all common AEs. Increased weight predicted a lower incidence of vomiting, bloating, and pain; male gender predicted a lower incidence of nausea. In PEG patients, increased age and male gender each significantly predicted a lower incidence of all common AEs; non-Caucasian race predicted a lower incidence of pain. In conclusion, Visicol was well tolerated by colonoscopy patients (age 19-84). In a stepwise logistic regression analysis, increased age was a predictor for a reduced incidence of all common AEs for Visicol and PEG. Other demographic variables also predicted the incidence of common AEs.
Published in Amer J Gastroenterol 2000;95(9):2549.

107. An in vitro comparison of different providers to deliver four proton pump inhibitor (PPI) products through a feeding tube. *Angie Bakshi, Pharm.D.*[1], Kathy Bungay, Pharm.D.[1], Keith M. Olsen, Pharm.D.[2], John W. Devlin, Pharm.D.[3]; (1)Tufts-New England Medical Center, Boston, MA; (2)University of Nebraska Medical Center, Omaha, NE; (3)Northeastern University, Boston, MA.

PURPOSE: It is unclear if newer liquid PPI formulations [e.g., esomeprazole in water (EW), lansoprazole oral disintegrating tablet (LODT) in water, or omeprazole/sodium bicarbonate power (OSB) in water] lead to improved delivery over older PPI formulations [e.g. simplified lansoprazole suspension (SLS)]. Using an in vitro model, we compared PPI delivery among 4 PPIs (EW, LODT, OSB, SLS) when administered through a narrow caliber (8F) feeding tube (FT) by either skilled [critical care nurses (CCRN)] or unskilled (lay) providers.
METHODS: Following standardized instructions, 16 college-educated subjects (8 CCRN, 8 lay; mean age 43.6 ± 11 years,75% female) were independently observed by two trained investigators delivering the 4 PPIs in a sequential but random fashion through a FT. The PPI content of the delivered fluid was quanitified using HPLC. All hypothesis testing was two-sided with a type I error rate of 0.05.
RESULTS: Delivery time (seconds) was faster with both LODT (115.5 ± 49.5; P=0.12) and SLS (124.9 ± 42.3, P = 0.03) than EW (189.2 ± 105.1) but not different than OSB (148.9 ± 50.7; P = 0.18). Delivery quality (predefined with a maximum score of 8) was higher with OSB (7.5 ± 1.0) than either EW (6.4 ± 1.2; P = 0.01) or SLS (6.4 ± 1.2; P = 0.01) but similar to LODT (7.1 ± 1.1; P =0.26). Much of the observed difference in delivery time between PPIs occurred during the preparation phase in the lay group. Differences in delivery quality occurred predominately during preparation and were similar between CCRN and lay groups. HPLC results are pending.
CONCLUSIONS: Significant variability in PPI delivery exists among PPI products when administered through a FT. Future studies need to elucidate the clinical and economic implications of these observed differences.

108E. Locust bean gum associated to sorbital has potential as an oral contrast media for magnetic resonance imaging. *Ana Sofia C. CAPACHO, Pharm.D.*, Miguel Ramalho, M.D., Armando Alcobia, Pharm.D.; Hospital Garcia de Orta, Almada, Portugal.

PURPOSE: Locust bean gum (LBG) associated to sorbitol has shown potential as an oral contrast media when followed by a gastric prokinetic–erythromycin (100 mg) for the investigation of inflammatory bowel disease by Magnetic Resonance Imaging (MRI). This study intends to establish a preparation method, characterize the suspension and observe its tolerability and quality of images.
METHODS: Bibliographic research as well as analysis and identity of raw materials suppliers were reviewed. We made a comparison with other contrast media used and full physical chemical characterization of the suspension. The choice of the osmotically active carbohydrate sorbitol is supported by recent literature (superior to mannitol) as well as its proportion to LBG, a thickener that permits low absorption of the suspension.
RESULTS: A LBG-Sorbitol production file was elaborated. Between April 2004 and May 2005, 98 litres of LBG-sorbitol were prepared leading to 49 MRI's, resulting in images of high signal intensity. The suspension was fully characterized being yellowish brown with vanilla odour, pH 5.62–FP VII (2.2.3) method–and osmolarity 120mOsm/kg–FP VII (2.2.35). Besides being a non invasive method, with better patient acceptability, we found a reduction of cost of 2.8 euros per exam compared with other contrast media (e.g. barium sulphate), with the same image quality.
CONCLUSIONS: Better patient acceptability, less time and consuming, lack of exposure to ionizing radiation and low cost lead us to the benefits of this contrast media showing high signal intensity. Nevertheless new alternatives for optimal bowel distension (similar to enteroclysis), ingesting a lower contrast volume are welcome in order to overcome the need for drinking two litres of this suspension for a good image quality.
Presented at the 5th National Congress of Portuguese Hospital Pharmacy Association, Lisbon, Portugal, November 24-27, 2004.

109E. Activation of P-glycoprotein during Listeria monocytogenes infection. *Brien L. Neudeck, Pharm., D.*, Terri D Alford, M.S., Teresa Liu, B.S; University of Tennesse College of Pharmacy, Memphis, TN.

PURPOSE: We have previously shown that expression and function of intestinal P-glycoprotein (P-gp)is important for innate defense against *Listeria monocytogenes*. We therefore sought to determine if *Listeria monocytogenes* attachment and invasion altered P-glycoprotein expression and function.
METHODS: Caco-2 cells were incubated for 0 (media), 15, 30, 45, 60, and 120 minutes with $1x10^7$ *L. monocytogenes* EGD (LM) or *L. innocua* (LI) (n=4 per condition). After the designated incubation, extracellular bacteria were killed with gentamicin and Caco-2 cells loaded with the P-gp substrate rhodamine 123 (Rh123) for 60 minutes. Intracellular Rh123 was measured after 1 hour. Expression levels of P-gp and the transcription factor PXR were measured using real-time RT-PCR.
RESULTS: No difference in Rh123 accumulation was detected at 15 minutes of LM infection of Caco-2 cells compared to control (Control: 781 ± 46; 15 min: 759 ± 43 arbitrary units). However, P-gp activity was significantly increased at 30, 45, and 60 minutes illustrated by decreased intracellular Rh123 [Control: 781 ± 46; 30 min :706 ± 31; 45 min: 697 ± 22; 60 min: 708 ± 30]. By 120 minutes P-gp activity in LM treated cells had returned to values similar to control (792 ± 84). After 45 minutes of LM infection, P-gp expression was increased 2.6 fold compared to control cells. At 60 min, P-gp expression was decreased 2 fold. By 120 minutes, expression levels were similar to baseline. There was no change in PXR expression. Infection of Caco-2 cells with LI did not alter P-gp function. No changes in PXR expression were detected in LI treated cells.
CONCLUSIONS: P-gp activity is significantly increased early into the infection process and returns to baseline functionality by 120 minutes. Thus it appears that epithelial cells are able to mount a brief innate immune response against *Listeria monocytogenes*.
Presented at the General Meeting of the American Society for Microbiology, Atlanta, GA, June 5-9, 2005.

110. Low dose recombinant factor VIIa improves the INR in patients with liver failure. *David J. Quan, Pharm.D.*[1], Nelson Chee, Pharm.D.[2], Nathan Bass, MD, PhD[2]; (1)University of California San Francisco Medical Center, San Francisco, CA; (2)University of California San Francisco, San Francisco, CA.

PURPOSE: Coagulopathy of liver disease is associated with significant morbidity and mortality. This coagulopathy can be transiently reversed with the administration of fresh frozen plasma (FFP), but is associated with a significant fluid and sodium load. Administration recombinant factor VIIa (rVIIa) can also reverse this coagulopathy, but the optimal dose remains unestablished. The purpose of this study is to evaluate the effect of 1200mcg of rVIIa on the international normalized ratio (INR) value in patients with a coagulopathy of liver failure.
METHODS: Medical records for patients admitted to the liver transplant service at UCSF Medical Center who received rVIIa between 10/2001 to 5/2004 were reviewed. Patients who received rVIIa intraoperatively for hemostasis were excluded. Patients were divided into two groups (1200 µg/dose and >1200 µg/dose). Comparisons were made for the MELD score, pre- and post-treatment INR using paired and unpaired student's *t*-test.
RESULTS: A total of 40 patients were included in the study. Baseline PT, INR, weight and MELD score was similar. Administration of 1200 µg of rVIIa decreased the INR value from a baseline of 2.9 ± 0.9 to 1.8 ± 0.6 ($p<0.05$). Administration of a mean of 4629 ± 2372mcg (>1200 µg/dose group) of rVIIa decreased the INR value from a baseline of 4.4 ± 3.5 to 2.3 ± 1.3 (p=0.004). The change in INR value of –1.1 ± 0.7 vs. –2.1 ± 2.9 for the 1200 µg and >1200 µg groups respectively were similar (p=0.154). In addition, there was no difference in the relative decrease as measured by the post:pre INR ratio of 0.64 ± 0.15 vs. 0.64 ± 0.26 for the 1200 and >1200 µg groups respectively (p=0.972).
CONCLUSIONS: Administration of 1200 µg of rVIIa results in a decrease of the INR value in patients with liver failure. Larger doses of rVIIa also decrease the INR value, but offer no additional benefit.

111E. Evaluation of efficacy and tolerance of Pegasys plus ribavirin therapy in Asian compared to non-Asian hepatitis C patients. *LanChi Bui, Pharm.D.*, Hoa N. Hoang, Pharm.D., Namgyal Kyulo, M.S., Ke-Qin Hu, M.D.; UCI Medical Center, Orange, CA.

PURPOSE: The clinical presentation and treatment response of chronic hepatitis C (CHC) could vary among ethnic groups, but little is known

whether these differences are also present in Asian Americans (AA). The purpose of this study was to compare the treatment response and tolerance of drug therapy in AA versus Non-Asian Americans (non-AA) of CHC.
METHODS: Medical records of 300 charts identified as HCV+ between January 1, 1998 and January 31, 2005 in UCIMC were reviewed. Patients' medical history, liver function tests, HCV PCR quantitative, HCV genotype, liver biopsy, Pegasys and ribavirin doses and duration of treatment were documented.
RESULTS: Asian patients presented with lower frequency of history of excessive alcohol use (20.8% vs. 60.0%, p<0.01) than non-Asian patients. HCV genotype-6 was more frequently seen in Asian patients than non-Asian patients (20.8% vs. 0.0%, p=0.002). The intent-to-treat (i.e. all patients who received HCV treatment) sustained virological response (75.0% vs. 41.0%, p=0.01), was significantly higher in Asian patients than non-Asian patients. Furthermore, the numbers of patients with good tolerance (i.e. patients were able to complete treatment without interventions for adverse effects) to the therapy was significant higher in Asian patients than non-Asian patients (95.8% vs. 64%, p=0.01)
CONCLUSIONS: Compared to non-Asian American patients, Asian American patients tolerated significantly better the combination therapy and had a significantly higher rate of sustained virological response.
Presented at the Western States Conference, Asilomar, CA, May 15–18, 2005.

Geriatrics

112. Assessment of potentially inappropriate medications using the Beers criteria in an ambulatory setting. *Holly M. Macfall, PharmD*, Nannette M. Berensen, PharmD, BCPS, Kelli L. Davis, PharmD, Sabrina W. Cole, PharmD, Stacy M. Prutting, PharmD, BCPS, Krystal L. Moorman, PharmD, Heather E. Whitley, PharmD, Jennifer B. Jastrzembski, PharmD, Sarah P. Shrader, PharmD; Medical University of South Carolina, Charleston, SC.

OBJECTIVE: To evaluate potentially inappropriate medication (PIM) use in patients 65 years and older and to assess clinically important drug interactions encountered in the ambulatory setting.
METHODS: To be included in the evaluation, patients had to be at least 65 years of age and receive care at the Adult Primary Care Center or the University Diagnostic Clinic, both of which are adult internal medicine facilities. Patients were assigned using a simple randomization scheme. Pharmacists used a standardized data collection form to gather information including patient demographics, number of medications, number of disease states, PIM usage based on the Beers criteria, and potentially clinically important drug interactions.
RESULTS: Of 200 patients evaluated, complete records were available for 192 patients (96%). Of these, 56 patients (28%) had 1 PIM in their medication profile, 9 patients (5%) had 2 PIMs, 2 patients (1%) had 3 PIMs, and 1 patient (0.5%) had 4 PIMs. Out of the 84 PIMs prescribed in this patient population, the most common included amitriptyline (n = 8, 10%), ferrous sulfate (n = 11, 13%), and propoxyphene-containing products (n = 21, 25%). Based on the potentially clinically important drug interactions encountered in the ambulatory setting, as defined by Malone and colleagues, none of the patients were prescribed these agents concomitantly.
CONCLUSION: PIMs are frequently prescribed to elderly patients receiving care in the Adult Primary Care Center and the University Diagnostic Clinic. Healthcare professionals should be educated about the Beers criteria and prescribers should be encouraged to use PIMs only when safer alternatives have been exhausted. Patients receiving PIMs should be regularly evaluated for untoward effects. It is favorable that patients evaluated were not receiving concomitant medications that have the potential to result in clinically important drug interactions.

113. Modifiable coronary heart disease risk factors: quality of care in an academic VA geriatrics clinic. *Nicole L. McMaster, Pharm.D., BCPS*, Sharon A. Jung Tschirhart, Pharm.D., BCPS, Thane C. Erwin, R.Ph., William D. Linn, Pharm.D.; South Texas Veterans Health Care System/University of Texas Health Science Center at San Antonio, San Antonio, TX.

PURPOSE: Elderly patients experience more coronary events than any other age group. Studies indicate that evidence-based therapies are being underutilized in this population when, in fact, the elderly experience a greater benefit from treatment compared to their younger counterparts. This study evaluates the quality of care currently provided to high-risk elderly patients followed at an academic VA geriatrics clinic.
METHODS: Eligible patients were ≥ 70 years old currently enrolled in the Geriatrics Evaluation and Management (GEM) Clinic with a diagnosis of coronary heart disease (CHD) and/or diabetes (DM). Subjects were evaluated for the following CHD risk factors: positive smoking status, hypertension, uncontrolled diabetes and hypercholesterolemia. Appropriate management of these risk factors was assessed according to goals from national guidelines for hypertension, diabetes, and hypercholesterolemia. The number of cardiovascular-related hospital admissions, urgent care visits, and acute care clinic visits within a six-month period were also documented.
RESULTS: One hundred eighty-eight patients met inclusion criteria. Fifty-six percent (105/188) of patients did not meet systolic BP goals for DM or CHD. Fifty-two percent (97/188) of patients did not meet total cholesterol goal, 28% (53/188) did not meet triglyceride goal, 31% (59/188) did not meet LDL goal and 45% (84/188) did not meet HDL goal. Of the 168 diabetic patients, 27% did not meet A1C goal. Four percent (7/188) of patients were current smokers. Twenty-four percent (9/37) of hospital admissions, 12% (12/115) of urgent care visits, and 16% (10/62) of acute care clinic visits were cardiovascular-related.
CONCLUSIONS: Greater than half of all high-risk patients identified in the GEM Clinic did not meet total cholesterol or blood pressure goals. Almost one-third of patients did not meet goals for triglyceride or LDL levels. A GEM Pharmacy Research Clinic has been created to assist in CHD risk reduction in these high-risk elderly patients.

114. Evaluation of real-world persistency with weekly oral bisphosphonates for osteoporosis. *M. A. Omar, PhD, R.Ph*, D. Gause, MS, DrPH; Novartis Pharmaceuticals Corporation, East Hanover, NJ.

PURPOSE: The oral bisphosphonates (OB) have been shown in clinical trials to reduce the risk of fractures by approximately half. In order to achieve similar fracture risk reduction in the non-clinical trial setting, patients need to be persistent with therapy. The objective of this study was to evaluate the persistency of osteoporosis patients on the weekly dosing regimen of OB in a non-clinical trial setting.
METHODS: This was a retrospective analysis of MarketScan, a secondary medical and pharmacy claims database. We studied female patients who met the following criteria: continuous medical and pharmacy coverage from 01/01/2001–12/31/2003; a diagnosis of osteoporosis and an index prescription for once weekly regimen of either alendronate or risedronate anytime in 07/01/2001–12/31/2002; and no prescription in the first six months of 2001, thus allowing for at least 6 months of drug-free pre-index period. Patients were considered persistent if they did not have a gap of more than 45 days from the end of drug supply of the previous refill. All patients were followed for 12 months from the date of the index prescription for assessment of persistence.
RESULTS: There were a total of 37,779 patients newly treated with the OB. Of these, the percent persisting at 3, 6, 9 and 12 months were as follows: 74%, 65%, 57% and 50%. Of those patients that discontinued within a year, the median and mean time to discontinuation was 87 days and 129 days.
CONCLUSION: Persistency of patients on the OB in the non-clinical trial setting is poor, and as a logical consequence, this might result in sub-optimal fracture risk reduction compared to that demonstrated in the clinical trials. Patient education and newer therapies that help promote longer exposure might improve fracture outcomes.

115. Clinically serious drug-disease interactions in the elderly: opinion of a consensus panel. *Catherine I. Lindblad, PharmD*[1], Joseph T. Hanlon, PharmD[2], Cynthia R. Gross, PhD[1], Richard J. Sloane, MPH[3], Carl F. Pieper, DrPH[3], Emily R. Hajjar, PharmD[4], Christine M. Ruby, PharmD[3], Kenneth E. Schmader, MD[3]; (1)University of Minnesota–College of Pharmacy, Minneapolis, MN; (2)Department of Medicine (Geriatrics)–School of Medicine, Pittsburgh, PA; (3)Duke University Medical Center, Durham, NC; (4)Philadelphia College of Pharmacy–University of the Sciences in Philadelphia, Philadelphia, PA.

PURPOSE: Elderly patients have decreased homeostatic reserve, multiple chronic diseases and often take multiple medications. Therefore, elders may be less likely to be able to compensate after receiving a drug that exacerbates a chronic disease. The objective of our study was to achieve consensus by an expert panel of health care professionals on a list of clinically important drug-disease interactions in the elderly.
METHODS: We first conducted a comprehensive literature review to identify possible drug-disease interactions. Second, we conducted a two-round, written survey, based on the Delphi process of providing feedback information on the responses of the group. Each expert panel member (n=9) rated each drug-disease interaction on a five point Likert scale (5=definitely clinically deleterious and 1=definitely not clinically deleterious). We calculated means and 95% confidence intervals (CI). A drug-disease interaction with a lower 95% CI greater than or equal to 4.0 was determined to have reached consensus.
RESULTS: Through our literature review and suggestions from our panel, we identified a total of 65 potential drug disease interactions. Our panel reached consensus on 28 individual drug-disease interactions. The diseases more commonly seen in older adults with a higher number of drugs associated with an interaction were dementia (anticholinergics, benzodiazepines, and barbiturates) and falls (benzodiazepines, sedative/hypnotics, typical antipsychotics, and tricyclic antidepressants).
CONCLUSIONS: Through a survey of experts, we have developed a consensus list of clinically important drug-disease interactions in the elderly.

Further research is needed to examine the impact of these drug-disease interactions on health outcomes in the elderly.

Health Services Research

116E. Initial revascularization is associated with lower long-term cost in managed care enrollees with acute coronary syndromes. *Patrick L. McCollam, PharmD*[1], Lida Etemad, PharmD, MS[2]; (1)Lilly Research Laboratories, Indianapolis, IN; (2)Ingenix, Eden Prairie, MN.

BACKGROUND: Previous studies indicate patients with acute coronary syndromes (ACS) treated with early invasive versus conservative strategies have better clinical outcomes. It was hypothesized that receiving revascularization as part of an initial episode of care would also be associated with lower long-term cost.
METHODS: A retrospective study was conducted utilizing data from a large U.S. managed care organization (MCO). ACS was defined as the unstable angina (UA) or acute myocardial infarction (AMI). Patients without claims for ACS in the prior 6 months were identified. Patients were followed up to 365 days or until death, or until disenrollment was noted in their medical claims. Two cost methods were utilized and included the initial episode and subsequent follow-up. Patients were dichotomized as high cost (top 20%) or low cost (bottom 80%) based on total costs incurred. Logistic regression was used to determine the association between revascularization during the initial episode and being classified as a high cost patient, while controlling for patient characteristics.
RESULTS: A total of 13,731 patients were included: 51.7% with UA and 48.3% with AMI. The mean age was 54.2 years and a majority were male. When including cost from initial episode through end of follow-up, patients receiving a revascularization during their initial ACS episode of care were less likely to be high cost patients (odds ratio [95% CI] of 0.615 [0.506–0.748]). Using Cost Measurement 2, the association was even more profound with an odds ratio of 0.081 [0.066–0.099].
CONCLUSION: After controlling for receipt of a revascularization procedure overall, ACS patients receiving revascularization during the initial care episode were less likely to be high cost patients during the first year of care. These data provide economic support for early revascularization when clinically indicated.
Published in J Man Care Pharm 2005;11(3):274.

117. Assessment of medication administration at Moi Teaching and Referral Hospital in Eldoret, Kenya. Amanda McPhearson, PharmD, *Ellen M. Schellhase, PharmD*, Julie A. Everett, PharmD; Purdue University, 1001 W. 10th St, Indianapolis, IN.

PURPOSE: Moi Teaching and Referral Hospital (MTRH) in Eldoret, Kenya, is a 350 bed facility where limited medication availability and lack of electronic records make the provision of care and documentation a challenge. Purdue University pharmacy students providing pharmaceutical care on the medical wards, recognized that medications were frequently not recorded on medication administration records (MARs). Due to poor documentation, it could not be determined if the medications were not given, out-of-stock, or given, but not recorded properly. The purpose of this study was to assess the significance of omitted doses and to identify reasons for omissions in medication administration at MTRH in order to improve the medication administration process.
METHODS: Data was collected for 21 days on both pediatric and adult medicine wards. Data collected included: medications scheduled for administration, medications missed, and reasons charted for missed medications. Intravenous fluids, insulin, and chemotherapy agents were not recorded on MARs and therefore were not included in the analysis. Methods used to determine reasons for omission included chart review, staff interviews, and verification of pharmacy out-of-stock status.
RESULTS: Poor MAR documentation was considered to be significant as 5% (110 of the 2194 doses ordered) of all ordered medications were not charted appropriately. Doses not given accounted for 53% of MAR omissions, 26% were doses given but not recorded on the MAR, and 21% were out-of-stock and therefore not given.
CONCLUSIONS: Further analysis, including trends in missed doses (i.e. time of day, types of medications, specific staff members), will be helpful in determining methods for improvement. Developing a program for reporting out-of-stock medications may reduce the number of omitted doses. Nursing education may improve the documentation of medication administration. After education and program implementation, data will be re-collected to assess the impact of the interventions.

118. Pharmacists as immunizers: assessing attitudes of pharmacists in the independent, community pharmacy setting. *Denise R. Sokos, PharmD*[1], Timothy J George, PharmD[1], Richard K. Zimmerman, MD, MPH[2]; (1)University of Pittsburgh School of Pharmacy, Pittsburgh, PA; (2)University of Pittsburgh School of Medicine and Graduate School of Public Health, Pittsburgh, PA.

PURPOSE: Nationally and in Pennsylvania (PA), adult vaccination rates are well below national goals. Recently, the PA Pharmacy Practice Act was revised granting pharmacists the authority to administer vaccines. This study was conducted to determine PA pharmacists' awareness of these regulations, interest and willingness to implement an immunization service, and attitudes regarding the influenza and pneumococcal vaccines.
METHODS: Between January and March 2005, a 19-question cross-sectional survey was distributed via postal mail to a stratified, random sample of 700 independent, community pharmacy owners or managers in PA. Initial non-respondents received one additional mailing. The questionnaire addressed sources of practice regulations, attitudes toward immunizations services, personal views of the influenza and pneumococcal vaccines, and demographic data.
RESULTS: Two mailings yield a response rate of 45%. Respondents were, on average, 80% male, 49 years of age, and practicing for 25 years. Fifty-three percent reported being aware of the legislative change and 26% indicated a strong likelihood of initiating a pharmacist-run vaccination program. Forty-six percent agreed that pharmacists should be providers of vaccinations with a large proportion (39%) neutral. The most important factors identified in pharmacists' decision to initiate vaccination programs were liability, training, and third party reimbursement. Approximately 13% of respondents agreed that the influenza and pneumococcal vaccines were ineffective and nearly 22% agreed that these vaccines frequently cause serious adverse reactions.
CONCLUSIONS: The awareness of the legislative change allowing PA pharmacists to provide immunizations is currently inadequate. Pharmacists practicing in the independent setting have not embraced the role of immunization provider and misconceptions exist regarding the efficacy and safety of the influenza and pneumococcal vaccines. We anticipate this pilot study will lead to future research into the development of interventions aimed towards increasing pharmacists' involvement in immunization services.

119. Use of time-stamped hospital data to examine care patterns of acute coronary syndrome patients undergoing percutaneous coronary intervention. *Cheng Wang, MD, PhD*[1], Jianming He, MS[1], Patrick L. McCollam, PharmD[2], Jay P. Bae, PhD[2], Brian T. Griffin, MBA[1]; (1)Solucient Inc, Berkeley Heights, NJ; (2)Eli Lilly & Company, Indianapolis, IN.

PURPOSE: Quality improvement initiatives in acute coronary syndrome (ACS) such as CRUSADE have found marked increase in treatment guideline adherence during the past several years. This descriptive study used time-stamped data to examine pharmacologic treatment and laboratory biomarker utilization patterns in ACS patients who underwent percutaneous coronary intervention (PCI).
METHODS: The data source consisted of 19 hospitals throughout the U.S. that used time-stamp data from 1/2003-9/2004. ACS was identified in the dataset using ICD-9 diagnosis codes for unstable angina and/or myocardial infarction (MI). The time-stamp allowed more precise measurement of drug administration and biomarker sampling. Biomarker definition of MI was CK-MB >3 times upper limit of normal, troponin I and myoglobin > 1 times upper limit of normal.
RESULTS: A total of 6,282 ACS patients who had been given clopidogrel were identified with adequate time-stamp information. The most common recorded comorbid diagnoses were ischemic heart disease 91.2%, hypertension 54.4%, lipid disorder 57.9%, and diabetes 21.7%. Aspirin (ASA) plus clopidogrel was received by 75.9% of patients and initiated on the day of PCI in 88.3% of patients. The majority of initial ASA plus clopidogrel administration was minus (-)10 to plus (+)14 hours from PCI. GPIIb/IIIa inhibitors were received by 68.6% and statins by 73% of patients, respectively during hospitalization. Post-procedure (> 8 hours after PCI) biomarker monitoring (CK-MB, troponin I or myoglobin) was performed in 67.9% of patients. The majority of testing was CK-MB or troponin I. Results suggestive of MI were found in up to 67% of patients.
CONCLUSIONS: This novel examination of ACS treatment using time-stamped data found ASA, clopidogrel, GPIIb/IIIa inhibitors and statins were often used in this cohort. A wide range of initial administration time for ASA plus clopidogrel around PCI was found. Post-procedure biomarker monitoring occurred frequently and was often positive.

120. Evaluating the usefulness of telemedicine cancer kiosks in community pharmacies. *Christopher L. Cook, Pharm.D., Ph.D.*[1], Lorilee Sandmann, Ph.D.[2], Jeff Springston, Ph.D.[3], Robert Galen, M.D., M.P.H.[4]; (1)University of Georgia College of Pharmacy, Athens, GA; (2)University of Georgia College of Education, Athens, GA; (3)University of Georgia College of Journalism & Mass Communication, Athens, GA; (4)University of Georgia College of Public Health, Athens, GA.

PURPOSE: To evaluate an internet-enabled telemedicine kiosk to provide cancer education, screening, and local resource information in the community

pharmacy setting.
METHODS: A user-friendly, touch-screen, web-enabled telemedicine kiosk has been developed to provide general cancer information, screening guidelines and access information to local cancer care resources. Educational topics accessible through the web portal include about caregiving, about cancer, screening, treatment, and after treatment. Local resource topics include healthcare providers, screening locations, treatment centers, support groups, equipment and medicine, end of life care, and transportation. Additional key features of the kiosk include: a 24-hour hotline phone connection to the American Cancer Society, blood pressure, weight, and BMI measures, as well as printing capabilities. Kiosks were installed in two community pharmacy sites in the Athens, GA area. A 34-day evaluation phase within the 3 month pilot trial includes data from a site-monitoring program, site observation, face-to-face interviews and on-screen questionnaires. Analysis of the data is focused on examining kiosk usage patterns, content, functionality, and outcomes.
RESULTS: Reports indicate 370 patients have used the kiosks during the evaluation phase of the 3 month pilot trial. The most commonly accessed educational information includes: about cancer, screening, and about caregiving. The most frequently utilized local resource information accessed includes support groups, healthcare providers, screening locations, and transportation. The average user spent 3 minutes 30 seconds per visit and explored 2.74 screens. The printing feature was used 53 times for cancer information. Concerns regarding stability of the technology, improved user friendliness, and user comfort regarding privacy are needs identified to be addressed.
CONCLUSION: Evaluation phase results demonstrate community acceptance of the health portal kiosk concept. Final pilot trial results will be presented at the meeting.

121E. Influenza vaccination rates in high-risk cardiovascular patients before and after a pharmacist vaccination program. *Susan M. Loughlin, Pharm.D.*[1], Ali Mortazavi, M.D.[1], Kevin W. Garey, Pharm.D.[2], Gary K. Rice, M.S.[1], Kim K. Birtcher, M.S., Pharm.D.[2]; (1)Kelsey-Seybold Clinic, Houston, TX; (2)University of Houston College of Pharmacy, Houston, TX.

PURPOSE: Influenza is responsible for approximately 36,000 deaths annually in the United States. Vaccination against influenza can reduce secondary complications, hospitalizations, and exacerbations of underlying chronic disease. Pharmacists are supported by the American College of Physicians-American Society of Internal Medicine in the role of immunization providers. Pharmacist immunization programs have increased rates of influenza vaccinations in hospitals and rural primary care clinics. The objectives of this study are to compare influenza vaccination rates before and after implementation of a pharmacist immunization program at a secondary prevention lipid clinic (SPLC) and to determine if age or gender disparity exists among those vaccinated.
METHODS: A Kelsey-Seybold clinical tracking database was used to gather immunization dates, age, and gender for SPLC patients during the 2003–4 and 2004–5 influenza seasons. Immunization rates were determined by dividing the number of immunized patients by the total number of patients seen in the SPLC during the time periods. Chi square analysis was used for all statistical inferences. A $p<0.05$ was considered significant.
RESULTS: Influenza vaccination rates in the high risk population increased significantly from 39% to 76% ($p<0.0001$) after the pharmacist vaccination program. Increased vaccination rates were apparent in all gender and age categories. Vaccination rates in patients ≥65 were twice as high as those <65 years of age (58% vs 29%, $p<0.0001$) for the 2003–4 season. Age disparity was overcome for the 2004–5 season (77% vs 76%, $p>0.8$). No gender disparity existed in those vaccinated for both seasons.
CONCLUSIONS: The pharmacist vaccination program increased influenza vaccination rates in high-risk cardiovascular patients. Age disparity in vaccination rates that existed in the 2003-04 season was overcome in the 2004-5 season with the implementation of the vaccination program. No gender disparity existed in those vaccinated for both seasons.
Presented at the 39th Midyear Clinical Meeting of the American Society of Health-System Pharmacists, Orlando, FL, December 5-9, 2004.

Hematology/Anticoagulation

122. Economic analysis of a hospital-based anticoagulation clinic. *Peter Dumo, Pharm.D.*, Greg Polk, RPh; Harper University Hospital, Detroit, MI.

BACKGROUND: Financial justification for clinical services has become increasingly important in today's health care environment. Cost-avoidance and facilitating shorter length of stay have traditionally been the primary justification for anticoagulation clinics (AC). However, revenue generation is more tangible and of more value to most health care centers. We recently implemented several technology improvements in our AC, which includes billing for clinical services. We report on the initial financial results since implementing billing.
METHODS: After confirming with Medicare, our hospital billing experts and other centers currently billing, it was determined that billing was feasible and legal. A platform was created using existing technologies (Cerner) for both clinical documentation and billing for AC visits. Revenue was determined by multiplying the current charges by calculated charge: cost ratio. This cost: charge ratio was confirmed through revenue: charge analysis. Expenses were based on the known costs for pharmacist and technician salaries and supplies.
RESULTS: There were a total of 590 anticoagulation clinic visits during the first 2 months (April/May) of billing. This resulted in a total $22,696.00 in charges to patients' insurance. Adjusted for a charge-to-cost ratio of 0.63, estimated revenue was $14,298.48. Total expenses for the first 2 months were determined to be $16,997.20, with pharmacist salaries making up 70% of the expenses. There was an estimated net loss of $1,349.36 per month since implementation of billing. Expenses in the pre-billing era were calculated to be $8,500/month.
CONCLUSIONS: Billing in our AC has resulted in significant revenues; however, the clinic continues to operate at a loss. Nevertheless, the small monthly loss of $1,350 is a significant improvement over the estimated pre-billing losses of $8,500 per month. We will focus on improving efficiency and increasing patient visits in order to achieve a cost-neutral anticoagulation clinic.

123. The effect of pharmacist intervention and education on venothromboembolism prophylaxis and secondary ventothromboembolism in hospitalized patients. *Patrick J. McDonnell Jr., PharmD*[1], Dennis K. Constan, PharmD[1], George B. Miller, RPh[2], John P Woodward, MD[2], Cynthia Oliva, PharmD[1]; (1)Temple University School of Pharmacy, Philadelphia, PA; (2)Jeanes Hospital, Philadelphia, PA.

PURPOSE: This project evaluated the impact that pharmacists would have on physician responsiveness to the issue of venothromboembolism (VTE) prophylaxis and the overall development of VTE in hospitalized patients
METHODS: This evaluation was conducted in a 202-bed community hospital. A VTE risk factor assessment evaluation form was developed by pharmacists based on guidelines from the American College of Chest Physicians. Pharmacists and pharmacy clinical interns evaluated random patients identifying whether VTE prophylaxis was appropriate. Recommendations were made regarding appropriate prophylaxis. Physicians were given 48 hours to respond to the recommendations which were evaluated for "acceptance." The study occurred in two phases. Phase I occurred per the above protocol in March 2004 in 98 patients. After this phase ended, the pharmacy department initiated a two-month VTE awareness program to educate physicians about this issue through inservices and newsletter publications. After 2 months of education, Phase II of the study was repeated in 124 patients. Prophylaxis rates and responsiveness to pharmacist recommendations were analyzed to determine whether intervention had an impact on physician practice. Outcome evaluation of secondary VTE rates during this year was also evaluated.
RESULTS: After the end of Phase II of the study, results were: (1)Baseline prophylaxis increased from 42% to 58.3% ($p=0.017$); (2) physician acceptance rate of pharmacist-initiated prophylaxis recommendations increased from 4.5% to 31.3% ($p=0.017$). Overall (physician/pharmacist recommendation) prophylaxis rates increased from 43.5% to 69.3% ($p<0.001$). (3) Secondary VTE rates were then compared from January to June 2004 versus July 2004-December 2004. From Jan-Jun 2004 there were 5613 admissions with 162 secondary VTEs (2.9%) compared to the Jul-Dec 2004 with 5572 admissions with 108 secondary VTEs (1.9%) [$p<0.001$].
CONCLUSION: Pharmacists can play a significant role improving appropriateness of patient VTE prophylaxis and decreasing the incidence of venothromboembolic disease.

124. Evaluation of bleeding incidence and prescribing pattern of enoxaparin in patients with renal insufficiency. *Eunice P. Chung, Pharm.D.*[1], Helen Achio, Pharm.D.[1], Levita K. Hidayat, Pharm.D.[2]; (1)Western University of Health Sciences, College of Pharmacy, Pomona, CA; (2)Huntington Memorial Hospital, Pasadena, CA.

PURPOSE: Prior to 2004, there was no guideline for dosing enoxaparin in patients with renal impairment and usage in this population required precaution due to concerns of increased risk of bleeding. The objective is to evaluate the appropriateness of randomly adjusted enoxaparin doses and the rate of bleeding in this population at a community hospital.
METHOD: Retrospective chart review was conducted for patients with renal insufficiency (Scr>1.5 mg/dL), receiving enoxaparin therapy for > 2 days during acute hospitalization between March 2003 and January 2004. The appropriateness of the randomly adjusted renal doses was determined by comparing to the renal dosage recommendations in the current enoxaparin prescribing information. The incidence of bleeding was compared within these groups as well as with patients with normal renal function, using the rates documented in major clinical trials.

RESULTS: Of the 107 patients evaluated, the dose was determined to be appropriate, too low and excessive in 29%, 16% and 55%, respectively. There was no difference (p=0.921) in the rate of bleeding between the patients who received excessive and appropriate doses of enoxaparin. The overall incidence of bleeding was 8.4%, and all were determined to be minor bleeding. All bleeding incidences occurred in patients >65 years old, with the highest (55.6%) rate among patients with CrCl<30 mL/min. Compared to the incidence of bleeding in patients with normal renal function, documented in clinical trials, the bleeding incidence was higher in our study patients for all indications except when used as prophylaxis for venous thromboembolism.
CONCLUSION: Random renal adjustment of enoxaparin by the prescriber resulted predominantly in administration of doses higher than the current recommendation. However, this did not translate to higher incidence of bleeding. The bleeding incidence appears to be higher in patients with renal insufficiency, with close correlation to age and degree of renal insufficiency.

125E. Low molecular weight heparin (LMWH) bridging in patients receiving warfarin: a retrospective evaluation. *Nancy L. Shapiro, PharmD, BCPS*, Edith A. Nutescu, PharmD; University of Illinois at Chicago, Chicago, IL.

A retrospective cohort study was conducted from January 1997 to December 2003 of patients who received LMWH bridging from the UIC Antithrombosis Clinic. Reasons for bridging and number of cases included the following: initiation of warfarin (143), peri-procedure cases (106), and subtherapeutic INR (99). A total of 348 cases of LMWH in 265 patients were evaluated: 213 female cases (in 181 females) and 135 male cases (in 84 males), average age (mean + SD) 55.8 + 15.0 years (range 21 to 94 years), and weight (mean + SD) 87.0 kg + 23.5 kg (range 43.2 to 171.4 kg). Indications for warfarin included previous cerebral vascular accident (153), deep vein thrombosis (126), peripheral vascular disease (62), pulmonary embolism (36), atrial fibrillation (13), mechanical heart valve (6), and other indication (4). Hypercoagulable states were documented in 124 patients. Full treatment doses of LMWH were used in 326 cases and prophylactic doses in 22 cases. In the warfarin initiation cases, LMWH was used for 9.27 + 6.02 days, with 7.93 + 5.40 days of treatment as an outpatient. In the peri-procedure cases, warfarin was held for 4.48 + 2.43 days before the procedure, with LMWH given for 3.38 + 2.56 days prior to, and 7.51 + 4.36 days after the procedure. Total number of hospital days saved by giving LMWH as an outpatient during peri-procedure bridging was 7.29 + 4.38. No cases of thromboembolism occurred within 30 days of LMWH use. There were 3 (0.86% of cases) major bleeds identified: 2 patients on tinzaparin had a GI bleed and needed a transfusion after having an EGD, and 1 patient on dalteparin was hospitalized to control bleeding from a venous stasis ulcer. Our experience suggests that LMWH bridge therapy appears to be a safe, feasible, and practical alternative to traditional methods of anticoagulation.
Presented at the Anticoagulation Forum 8th National Conference on Anticoagulant Therapy, Orlando, FL, May 7, 2005.

126E. Impact of human immunodeficiency virus (HIV) and hepatitis C virus (HCV) coinfection on hospitalization and resource use among hemophilia enrollees in a managed care population. *Wing Chan, MS*[1], Howard Friedman, PhD[2], Josephine Li-McLeod, RPh, PhD[1]; (1)Baxter Bioscience, Westlake Village, CA; (2)Friedman Analytic Consulting, Inc., Staten Island, NY.

PURPOSE: Previous research has shown hemophilia (H) patients infected in the 1980's with HIV and/or HCV from the blood supply have increased morbidity and mortality. This study examined how HIV and HCV co-infection impact hospitalization and resource use among hemophilia enrollees in a managed care population.
METHODS: This was a retrospective claims analysis of a nationwide managed care database from 1/97 to 4/04. Patients continuously enrolled for at least 6 months were included in the study. Hemophilia patients were identified using ICD-9CM, HCPCS, and NDC codes. Cases were >18 years of age and had HIV or HCV infection. Controls were hemophilia patients without HIV or HCV with matched age restrictions. Four categories were established: Controls (H only); H+HIV; H+HCV; H+HIV+HCV.
RESULTS: H+HIV+HCV conferred the greatest increase in hospitalization, followed by H+HCV. Most hospitalizations were related to an ICD-9CM diagnosis of coagulation defects (286.x). Number of distinct patients and (%) of select primary diagnoses of interest, HIV infection (042), Abdominal (789.x), and Pneumonia (486) are presented below. Annualized total charges were higher for hemophilia patients infected with HIV+HCV, HCV, and HIV compared to controls ($139,521, $114,415, $89,429, and $87,922, respectively).

	H only (N=115)	H+HIV (N=14)	H+HCV (N=52)	H+HIV+HCV (N=39)
Age–Mean	33.0	38.1	37.4	35.1
# (%) Hospitalized	27 (23%)	1 (7%)	18 (35%)	16 (41%)
Primary Diagnosis				
- Coagulation Defects	20 (74%)	1 (100%)	13 (72%)	10 (63%)
- HIV Infection	0 (0%)	1 (100%)	0 (0%)	8 (50%)
- Abdominal	2 (7%)	0 (0%)	6 (33%)	2 (13%)
- Pneumonia	0 (0%)	0 (0%)	1 (6%)	3 (19%)

CONCLUSIONS: Hemophilia patients with HIV and HCV may be more likely to be hospitalized than hemophiliacs without similar infection. Disease management resulting from pathogen transmission through hemophilia treatments can result in long-term additional health resource use.
Presented at the 45th Interscience Conference on Antimicrobial Agents and Chemotherapy, New Orleans, LA, September 21-24, 2005.

127. Evaluation of fondaparinux use for patients with confirmed or suspected heparin induced thrombocytopenia. *Melissa R. Pleva, Pharm.D.*, Jay M. Mirtallo, M.S., RPh, BCNSP, FASHP, Crystal Tubbs, Pharm.D., Anthony T. Gerlach, Pharm.D., BCPS; The Ohio State University Medical Center, Columbus, OH.

PURPOSE: To evaluate the efficacy and complications of fondaparinux in patients with suspected or confirmed heparin-induced thrombocytopenia (HIT).
METHODS: Data was retrospectively collected for all patients who received fondaparinux for HIT between July 1, 2003 and June 30, 2004. Data collected include demographics, indication, dose, duration of therapy, laboratory data including platelet aggregation assay (PAA), and presence of confirmed or suspected thromboembolism after start of fondaparinux. Platelet recovery was defined as 1.5 times nadir or return to >100x10^9/L if below this level at nadir. Major bleeding was defined as intracranial, retroperitoneal, into a prosthetic joint, or associated with hemoglobin decrease ≥2 g/dL with transfusion of ≥2 units of packed red blood cells (PRBC). Minor bleeding included all bleeding not meeting criteria for major bleeding, including any PRBC transfusion.
RESULTS: Forty-six patients received fondaparinux, 11 for history of HIT and 35 on suspicion of current HIT. Thirty patients received fondaparinux for thromboprophylaxis and 16 for treatment of thromboembolism. No patient developed a clinically evident new thrombosis during the observed period. Bleeding occurred in 18 patients including 4 patients who developed a major bleed.

	All patients with thrombocytopenia (N=35)	Positive PAA (N=12)	Negative PAA (N=15)	P-value (positive vs. negative PAA)
Mean Age	57	62	59	0.5823[1]
Male:Female	12:23	2:10	7:8	0.2172[2]
Platelet Recovery [Patients (%)]	24 (68.6%)	9 (75%)	10 (66.7%)	0.6957[2]

[1]Student's T-test
[2]Fisher's Exact Test

	Mean Platelet Count (x10^9/L) All patients with		
Day of fondaparinux	thrombocytopenia	Positive PAA	Negative PAA
0	110 (n=34)	134 (n=12)	96 (n=15)
7	262 (n=15)	299 (n=4)	188 (n=6)
P-value[1]	0.0019	0.0801	0.0537

[1]Paired T-test

CONCLUSIONS: Fondaparinux may be an effective anticoagulant for patients with HIT. PAA results may not reliably predict platelet recovery with fondaparinux therapy. Larger, prospective studies are needed to confirm these results and elucidate outcomes in relation to efficacy and complications.

128. Establishment of heparin-induced thrombocytopenia (HIT) treatment guidelines within a large teaching institution. *Katherine P. Holloway, Pharm.D.*, Jennifer L Frederick, PharmD, BCPS, Irene G Bemis, PharmD, BCPS; Grady Health System, Atlanta, GA.

PURPOSE: Direct thrombin inhibitors (DTI), argatroban and lepirudin, have been shown to reduce thromboembolic complications (TECs) and death from HIT. GHS not only had no DTI on formulary, but also had no guidelines for treatment of HIT. The objectives of this 3-phase study were to evaluate past usage of DTIs in treatment of HIT, establish HIT treatment guidelines, and evaluate improvements on management of suspected HIT within GHS.

METHODS: Phase 1 consisted of a retrospective review of all patients with a positive HIT antibody or receipt of lepirudin or argatroban within the past year. Phase 2 consisted of guideline development by an Expert Panel, addition of lepirudin and argatroban to hospital formulary, and education of guidelines to house staff. Phase 3 consisted of prospective assessment of compliance to new guidelines and outcome measures of study. Retrospective and prospective outcome measures were analyzed to assess benefit of established guidelines. Outcome measures included incidence of 14-day platelet restoration, new TECs, all-cause amputation, all-cause mortality, and major and minor bleeding rates.
RESULTS: A total of 35 patients were included in phase 1. Of those, 10 patients received DTIs. Retrospective outcome measures in non-DTI recipients and DTI recipients, respectively, were as follows: 60 and 80% incidence of 14-day platelet restoration, 16 and 20% development of new TECs, and 40 and 20% incidence of all-cause mortality. To date, 4 DTI recipients have been included in phase 3. Fourteen-day platelet restoration was achieved in 100% of patients, followed by 25% and 0% incidence of TECs and all-cause mortality, respectively. Incidence of amputation and major bleeding was 0% in both groups, and overall minor bleeding rates were minimal.
CONCLUSIONS: There were no significant differences in outcome measures between treatment groups. Phase 3 of the study is ongoing, and results from the ongoing review will be presented.

129. Evaluation of the use of direct thrombin inhibitors for anticoagulation. *Cathyyen H. Dang, PharmD*, Jean M. Nappi, PharmD, BCPS; Medical University of South Carolina, Charleston, SC.

PURPOSE: To evaluate the efficacy, safety, and associated costs of the use of argatroban, bivalirudin, and lepirudin in patients with heparin-induced thrombocytopenia (HIT) or presumed HIT.
METHODS: Medical records of patients hospitalized in 2004 who were treated with argatroban, bivalirudin, or lepirudin for a minimum of 24 hours were reviewed. The primary outcome measures were the number of aPTT measurements within the therapeutic range and the time to reach the desired goal. Secondary outcomes included cost, treatment duration, clinical outcomes, and adverse effects.
RESULTS: Of 52 patients who received a direct thrombin inhibitor in this time period, 42 patients met the inclusion criteria (13 argatroban, 24 bivalirudin, and 5 lepirudin). There was a significantly greater percentage of therapeutic aPTT levels in the bivalirudin group than in the argatroban or lepirudin groups (69.9% vs. 59.3% and 45.1%, respectively; p<0.001). However, when adjusted for clustering, the difference was not significant (p=0.167). Patients who received bivalirudin reached therapeutic aPTT levels earlier than either argatroban or lepirudin patients (9.2 hours vs. 14 hours and 27 hours, respectively; p=0.052). The average medication cost/day per patient was less in the bivairudin group compared to the other groups, while the average laboratory costs were similar. Patients in the argatroban group were treated for a longer duration than patients in the bivalirudin or lepirudin group. Bleeding rates were similar between argatroban and bivalirudin groups, but were higher than patients receiving lepirudin. A composite of clinical outcomes (DVT, non-fatal MI and stroke, limb amputation, all-cause mortality) were similar among all groups.
CONCLUSIONS: Anticoagulation therapy with bivalirudin reached a therapeutic aPTT level in less time than either argatroban or lepirudin. Bivalirudin produced more aPTT levels that were within the therapeutic range; however, when adjusted for clustering, the difference among the three drugs did not reach statistical significance.

130. A comparison of postoperative stroke rates among mechanical circulatory assist devices approved as bridges to cardiac transplantation. *Paul E. Nolan Jr., Pharm.D.*[1], Francisco A. Arabia, MD[2], Richard G. Smith, MSEE, CCE[3], Gulshan K. Sethi, MD[2], Raj K. Bose, MD[2], Pei H. Tsau, MD[2], Diane Covington, RN, CCRN[3], Marvin J. Slepian, MD[2], Jack G. Copeland, MD[2]; (1)University of Arizona College of Pharmacy, Tucson, AZ; (2)University of Arizona Sarver Heart Center, Tucson, AZ; (3)Artificial Heart Department, University Medical Center, Tucson, AZ.

PURPOSE: Thromboembolism particularly stroke (CVA) constitutes a serious postoperative complication following implantation of a mechanical circulatory assist devices (MCADs). Four MCADs have been approved for bridge to cardiac transplantation: the CardioWest total artificial heart (CWTAH) and the Heartmate (HM), Novacor (NOV) and Thoratec (THOR) ventricular assist devices (VADs). The purpose of this study was to compare the post-implantation CVA rates among these 4 MCADs.
METHODS: The number of implants, mean age, total support time and number of reported CVAs were extracted from published bridge-to-heart transplant studies for each MCAD. A linearized CVA rate was then calculated (Table). Chi-Square analysis also was performed based upon the total number of CVAs collectively observed for the 4 MCADs (n=34).

MCAD	No. Pts	Mean Age (years)	Total Support Time (months)	No. CVA's (%)	Linearized CVA Rate (CVA/pt-month)
CWTAH	67	51	195.2	2 (3%)	0.01
HM	191	49.4	454.6	9 (4.7%)	0.02
NOV	88	51	354	7 (8%)	0.025
THOR	84	46	140	16 (19%)	0.11

RESULTS: The CWTAH had the lowest calculated linearized CVA rate although it was only significantly different from the THOR (p=0.033). The observed vs. expected CVAs for the CWTAH, HM, NOV and THOR were, respectively, 2 vs. 5.3; 9 vs. 15.1; 7 vs. 7; and 16 vs. 6.6 (p=0.0002).
CONCLUSIONS: These findings suggest that the CWTAH has the lowest risk for post-implant CVA among MCADs currently FDA-approved as a bridge to heart transplantation.

131. Anticoagulation management in patients with antiphospholipid antibody syndrome. *Kathleen E. Horner, Pharm.D.*, Beth B. Phillips, Pharm.D., Erin N. Newkirk, Pharm.D., Deanna L. McDanel, Pharm.D., Peter J. Kaboli, MD; University of Iowa Hospitals and Clinics, Iowa City, IA.

PURPOSE: The purpose of this project was to optimize the care of patients with antiphospholipid antibody syndrome (APL) by 1) confirming the diagnosis of APL using Sapporo criteria, and 2) determining optimal anticoagulation therapy and appropriate target INR range.
METHODS: Data were collected and evaluated against Sapporo criteria, indication for anticoagulation, thromboembolic events and target INR range. Recommendations were made to the patients' physicians to confirm the diagnosis of APL with repeat testing and to optimize anticoagulation therapy.
RESULTS: From the University of Iowa Hospitals and Clinics Internal Medicine and Family Medicine Anticoagulation Clinics (n=384), 23 (6%) APL patients (mean age 45.2 ± 16 years) were identified. Seventy percent were female. Target INR ranges were 2.0-3.0 (57%), 2.5-3.5 (39%), and other (4%). Only six patients (26%) met Sapporo criteria for APL. Of the 74% (n=17) not meeting criteria, 47% (n=8) had another indication for life-long anticoagulation [(recurrent thromboembolism (TE), (n=5); peripheral vascular disease with graft occlusion, (n=1); atrial fibrillation and recurrent TE, (n=1); other thrombophilia and recurrent TE, (n=1)]. Seven patients underwent repeat testing for APL and five additional patients were found to meet Sapporo criteria upon retesting. A lower target INR range of 2.0–3.0 was determined appropriate for six patients previously managed at a higher range.
CONCLUSION: A majority of patients did not meet Sapporo criteria for APL. Of those, half had another indication for long-term anticoagulation. Over one-third of patients had a higher target INR range of 2.5–3.5. All patients receiving anticoagulation for APL should have confirmatory testing and be evaluated for the appropriate target INR range.

132. Effects of a computerized adverse event alerting system on patients at high risk for heparin induced thrombocytopenia (HIT). *Neal J. Benedict, PharmD*, Amy L. Seybert, PharmD, Rhonda Rea, PharmD, Melissa Saul, MSc, Sandra L. Kane-Gill, PharmD, MSc; University of Pittsburgh Medical Center, Pittsburgh, PA.

BACKGROUND: A computerized adverse event alerting system was developed and implemented in May 2004 to prompt early detection of HIT in patients admitted to a tertiary care hospital. Computer alerts signal when a patient has an active heparin order and following: 50% decrease in platelet count and/or platelet count < 100,000/mm3. Patients having an alert generated were considered high risk for HIT. Alerts were delivered via e-mail to the attending physician and clinical pharmacist.
PURPOSE: To describe the effects of a HIT alert system.
METHODS: Patients at high risk for HIT were identified retrospectively from May 2004 to December 2004. Effects of the detection system were measured by frequency of interventions and identification of HIT cases. Interventions evaluated were discontinuation of heparin, ordering of HIT diagnostic tests, or ordering hematology consults. Additional information obtained included heparin use (start/stop dates), platelet counts (PLC) over time, and other potential drug and non-drug causes. HIT confirmation occurred using the Warkentin scale and consensus between pharmacist and hematologist.
RESULTS: 501 alerts were generated for 471 patients (55% male) with an average age of 63 ± 15 years. The frequency of interventions were as follows: discontinuation of heparin 61 (12%), hematology consult 11 (2%), and HIT diagnostic tests 36 (7%). Eleven patients were diagnosed HIT and had minimum PLC ranging from 21–144 x 109/L, average nadir of 64 and maximum PLC ranging from 107–1068 x 109/L, average of 414. One HIT patient had positive diagnostic tests. Two patients suffered thromboembolic complications as a result of HIT. No deaths were reported.
CONCLUSION: Computer generated HIT alert system allows clinicians to make frequent interventions and provides early detection of HIT. Specificity of alerts could be improved. Evaluation of interventions on patient outcomes would be useful but logically, early identification of HIT should improve patient safety.

133. Patient controlled analgesia versus intermittent bolus dosing of morphine sulfate for the treatment of sickle cell pain crisis. *Amy Knauss, Pharm.D., BCPS*, Tara Hill, Pharm.D., Melanie Cooper, M.D., Michael D Knauss, Pharm.D., BCPS; Grady Health System, Atlanta, GA.

PURPOSE: Despite several therapeutic advantages, use of Patient Controlled Analgesia Pumps (PCA) is underutilized in Acute Sickle Cell Pain Crisis. The study was conducted to (1) determine if intravenous morphine sulfate administered by PCA leads to improved pain management compared to intermittent bolus dosing, the current institution's standard of care and to (2) compare safety and tolerability between PCA and intermittent dosing.
METHODS: The study is a prospective, randomized trial that included adult patients admitted to the hospital after evaluation in the Georgia Comprehensive Sickle Cell Center. Patients were randomized to receive intravenous morphine by either PCA or intermittent bolus dosing. Pain scores, adverse reactions and tolerability data were collected daily. Outcome measures included percentage of patients achieving a reduction in the average pain score of two points by hospital day three, time to achieve goal reduction in pain score, adverse reactions and length of stay. Additional secondary outcome measures were assessed.
RESULTS: Twelve patients were enrolled into each study arm. There was no difference between the PCA and intermittent bolus arms in the percentage of patients that achieved a goal reduction in the average pain score by day three(67% vs 67%, p=1.00). There was no difference between groups in the mean time to achieve the goal reduction in average pain scores (2.4 ± 1.6 vs 2.2 ± 1.3 days, p=0.67). Eight patients (67%) in the PCA arm versus ten patients (83%) in the intermittent bolus arm experienced adverse reactions to morphine (p=0.64). The most common adverse effects were gastrointestinal disturbances. Mean lengths of hospitalization for the PCA arm and the intermittent arm were similar (7.2 ± 3.5 vs 6.5 ± 3.7 days, p=0.66).
CONCLUSION: Administration of morphine via PCA is equally safe and effective as intermittent bolus dosing in Sickle Cell Pain Crisis at the Grady Health System.

134. Are extreme weights used in weight based dosing of unfractionated heparin a risk for bleeds or out of goal activated partial thromboplastin times? *Lance J. Oyen, PharmD, BCPS*, Narith N. Ou, PharmD, BCPS, Seth R. Bauer, PharmD, Jeffrey J. Armon, PharmD, Stephen Cha, MS; Mayo Clinic Rochester–Mayo Foundation, Rochester MN, Rochester, MN.

PURPOSE: To assess the results of weight-based dosing of unfractionated heparin in patients in four weight groups for 1) differences in bleeding frequency and 2) activated partial thromboplastin time (APTT) results within goal range.
METHODS: A retrospective chart review was performed for 1054 cardiac patients strictly treated with a UFH nomogram initiated with a 60 units/kg bolus followed by 12 units/kg/hr. Consecutive patients from 2/02 to 11/03 were included. All dosing data and APTT values were electronically collected concurrent to therapy, but patients were identified, screened, and bleeding frequency assessed retrospectively. Excluded patients were those treated with any other IV anticoagulation. The patient groups were equally divided into quartiles by Body Mass Index (BMI) as thin (15.9-25.9), normal (26.0-29.3), overweight (29.4-34.2), and obese (>34.3). Bleeding was prospectively defined as non-surgical transfusions, chart documented bleeding, radiographically identified bleeds, or at least 2 gm/dL drop in hemoglobin over 24 hours. Goal APTT range of 60-90 seconds was used for thromboplastin adjusted target heparin levels of 0.3-0.7 anti-Xa units.
RESULTS: No differences were noted in demographics besides weight and BMI between groups. Bleeding trended higher in the thin group compared to other groups but was not statistically relevant (p=0.12, Mantel-Hanzel). The first (6 hour) APTT mean was higher with increasing BMI group (p=0.0002), and mean goal APTT value was more common in the normal group than in either the thin or obese groups (49%, 41.6%, 40.9% respectively, p<0.05, pairwise analysis).

Group	Mean First 6 hour aPTT, secs	Mean % of aPTTs in Goal	Bleed (%)
thin	85.8	41.6	16 (6.1)
normal	94.5	49.0	14 (5.3)
overweight	97.1	44.1	15 (5.7)
obese	104.6	40.9	9 (3.4)

CONCLUSIONS: Our data suggest that weight-based dosing of UFH achieves goal APTTs most reliably in normal weight patients, with initial 6 hour APTT values directly proportional to body weight.

Herbal/Complementary Medicine

136. Preference of adults for an herbal or natural product over prescription medication to treat chronic illness. *Katina R. Rue, D.O.*[1], Gautam J. Desai, D.O.[1], Jacqueline S. Marinac, PharmD[2]; (1)Kansas City University of Medicine and Biosciences-College of Osteopathic Medicine, Kansas City, MO; (2)Pfizer Global Pharmaceuticals, Shawnee Mission, KS.

PURPOSE: Herbal products are a multi-billion dollar industry in the United States. Consumers' preferences were unknown, given the choice between natural or herbal products over traditional prescription medications to treat chronic illness. The survey's purpose was to determine the level of interest for using a natural or herbal product over a prescription medication.
METHODS: English-speaking adults who were started on a new chronic prescription medication for no more than six months' duration were eligible to complete the survey. The query asked, "To what extent do you prefer using an herbal or natural product over a prescription medication to treat your condition?" Data were stratified by demographic variables and compared using χ^2 analysis.
RESULTS: Three hundred twenty six (n=326) adults completed the survey. Nearly 70% were female; 47% between the ages of 45–64 years; 35% were employed full-time; 34% had completed some college. Results of the query were: 29.4% responded 'not at all'; 19.9% 'somewhat'; 18.1% 'minimally'; 15.3% 'great deal'; 12.9% 'quite a bit'; and 4.3% left the item blank. There was no significant difference in response based upon gender, education, or employment, although there was a significant difference between African American respondants and Caucasian respondants (p-value: 0.043).
CONCLUSION: Overall, if given the choice, 48.1% of surveyed adults would prefer a natural or herbal product over a prescription medication to treat their chronic condition. These findings suggest there is a high level of interest among American adults in finding non-legend products to treat chronic illness.

137. Analysis of ephedra-free labeled dietary supplements sold in the San Francisco Bay area. *Candy Tsourounis, Pharm., D.*[1], Cathi E. Dennehy, Pharm.D.[1], Jennifer W. Tam, Pharm.D.[2], Richard Ko, PharmD, PhD[3]; (1)University of California, San Francisco, School of Pharmacy, San Francisco, CA; (2)University of California, San Francisco, Medical Center, San Francisco, CA; (3)California Department of Health Services, Sacramento, CA.

PURPOSE: Ephedra-free dietary supplements are commonly marketed to consumers for weight loss as a safe alternative to ephedra containing products. The objective of this study was to sample dietary supplements (DS) labeled as ephedra-free to evaluate whether products met their labeling claim.
METHODS: One control DS product containing ephedra alkaloids and 29 DS labeled as ephedra-free were purchased from various retail locations in San Francisco. All products were sent to the California Department of Health Services (CDHS), Food and Drug Laboratory for content and quantity analysis. All laboratory personnel were blinded to product names and labeled contents. All DS products were screened for the presence of undeclared drugs, ephedra alkaloids, and heavy metals including lead, arsenic, cadmium and mercury. All products were also evaluated for compliance with the labeling requirements of the Dietary Supplement Health and Education Act [DSHEA] of 1994.
RESULTS: None of the DS labeled as ephedra-free tested positive for the presence of ephedra alkaloids; as expected, the control product did test positive. Heavy metals were detected in three ephedra-free DS products. Twenty-three of 29 products tested positive for caffeine, which was indicated on product labels. All but two products were in compliance with DS labeling as required by DSHEA.
CONCLUSIONS: This study demonstrates that manufacturers met their labeling claims for ephedra-free products. Special attention should be given to the presence of heavy metals and other drugs like caffeine, synephrine and botanical sources of caffeine as these ingredients have replaced ephedra.

138E. Complementary and alternative medicine in an urban family medicine clinic. *Andrea S. Franks, Pharm.D., BCPS*, Elizabeth B. Byrd, MSSW, MEd, BSN, Emily B. Hak, Pharm.D., FCCP, BCPS, BCNSP, Amanda Kizzee, student, Kristy Flowers, student; University of Tennessee Health Science Center, Memphis, TN.

PURPOSE: Our purpose was to characterize complementary and alternative medicine (CAM) use in a low income, urban population, and to assess patients' perceptions and attitudes about CAM.
METHODS: Two hundred patients were surveyed for demographic data, CAM use, attitudes about safety and efficacy, information sources, perceptions about health care providers' CAM expertise, and patient-provider communication about CAM.
RESULTS: Eighty-six (43%) reported CAM use, 61% had an annual income below $20,000, and 84% had Medicaid or Medicare. Sex, age, and income were not different between CAM users and non-users. Users were more likely to be Caucasian than African American (p=0.03) and to have pursued education after high school (p=0.05). Of those with an opinion, users were more likely to think that dietary supplements are as effective and safe as drugs than non-users (52% vs 27%; p=0.01 and 41% vs 21%, p=0.03, respectively). Of those with an opinion, both users and non-users thought there was a

potential for drug interactions (86% vs 75%, p=NS). Herbal products most often used were aloe vera, ginseng, garlic, ginkgo, and St. John's wort. CAM information was obtained from magazines (34%), TV/radio (33%), and relatives (26%). Only 22% of patients obtained CAM information from health care providers. Of those who used CAM, only 22% had disclosed their CAM use to their health care provider. Most respondents (74%) felt health care providers should know more about CAM.
CONCLUSIONS: A significant percentage of patients in this urban, low socioeconomic group use CAM and are more likely to be Caucasian and educated. Herbal products commonly used have a known potential for interaction and adverse effects. Most who use CAM do not discuss it with their health care providers and believe their providers should know more about CAM.
Presented at the Annual Meeting of the Society for Teachers of Family Medicine, Toronto, ON, Canada, May 12-16, 2004.

139. Development of an optimal sampling strategy for the green tea polyphenol, epigallocatechin gallate, in fasting and fed conditions. *Brian R. Overholser, Pharm.D.*[1], David R. Foster, Pharm.D.[1], Kevin M. Sowinski, Pharm.D.[1], H.H. Sherry Chow, Ph.D.[2]; (1)Department of Pharmacy Practice, Purdue University School of Pharmacy and Pharmaceutical Sciences, Indianapolis, IN; (2)Arizona Cancer Center, The University of Arizona, Tuscon, AZ.

BACKGROUND: Epigallocatechin gallate (EGCG) is a naturally occurring polyphenol derived from green tea with potent antioxidant and anti-inflammatory properties. The objective of this study was to develop and validate an efficient sampling strategy that optimally predicts EGCG pharmacokinetics following green tea administration.
METHODS: Ten healthy subjects received a single 800 mg oral dose of EGCG administered as Polyphenon E under both fasting and fed conditions in a crossover design. Serum samples were serially collected over 24 hr and EGCG concentrations were determined by HPLC. A 1-compartment model with a lag time for absorption best fit the concentration-time data. Maximum A Posteriori Bayesian (MAPB) priors were developed by a modified 2-stage approach by simultaneously fitting pharmacokinetic parameters from both study phases with ADAPT II. The D-optimal sampling designs were determined and Monte Carlo simulations were performed using the MAPB estimators. The original model with the estimators was used to fit the simulated data with the optimized sampling schemes.
RESULTS: The median 3 optimal sampling times were 0.7, 1.4, and 7.0h under fasting conditions; and 1.4, 3.62, and 8.7h under fed conditions. The median error (ME) and median absolute error (MAE) from the fitted simulations are presented in the table to demonstrate the predictive performance of the optimal sampling schemes.
CONCLUSIONS: The sampling schemes were accurate and precise in predicting EGCG pharmacokinetics under both fasting and fed conditions. The increased predictive performance for estimating pharmacokinetic parameters under fasting conditions was due to a decreased variability in absorption.

	$t_{1/2}$		V_D/F	
	%ME	%MAE	%ME	%MAE
Fasting	-0.4 (-1.8, 0.7)	1.3 (0.5, 3.1)*	0.48 (-0.8, 1.7)*	1.4 (0.6, 2.9)*
Fed	-3.4 (-13.2, 6.8)	10.5 (4.6, 19.1)	3.6 (-6.4, 12.0)	9.9 (4.6, 19.4)

Data presented as median (IQ range)
*p<0.05, compared to fed condition by nonparmametric ANOVA and Dunn's Multiple Comparison Test

HIV/AIDS

140. Adherence to efavirenz therapy and maintenance of HIV viral suppression. *Parya Saberi, Pharm.D.*[1], Nikolai Caswell, M.A.[2], Maria Amodio-Groton, Pharm.D.[1], Keith Veltri, Pharm.D.[1], Peter Alpert, M.D.[1]; (1)Montefiore Medical Center, Bronx, NY; (2)Independent, New York, NY.

PURPOSE: The objective of this study is to determine whether a lower rate of adherence (<95%) is sufficient to maintain HIV viral suppression on an efavirenz-based regimen. Previous research demonstrated that >95% adherence to protease inhibitors was required to maintain an undetectable viral load. Efavirenz has the benefits of once daily therapy, a long half-life (50-70 hours) and high serum levels much greater than the IC50 of HIV.
METHODS: Retrospective review of pharmacy refill records of HIV positive patients who had achieved at least one undetectable viral load (VL<400 copies/mL) while on efavirenz from December 2003 through March 2005. Adherence was determined via pharmacy refill records at the Montefiore Medical Center's HIV Pharmacy. Percent adherence was calculated based on the formula: [(pills dispensed/days between refills) x 100%].
RESULTS: Of 151 patients, viral suppression was maintained in greater than 80% of time periods for adherence rates down to 85–90%. The periods with 75-80% adherence also had higher than 85% suppression. Rates of suppression began to fall off below 75% adherence.
CONCLUSION: Lower adherence rates (<95%) on an efavirenz-based regimen were successful in maintaining viral suppression than previously found on "unboosted" (without ritonavir) protease inhibitor-based regimens. Although further prospective clinical trials are necessary to confirm our results, these outcomes may be applicable to other antiretroviral medications with similar pharmacokinetic parameters.

141E. Efficacy of epoetin alfa 40,000 U SC every two weeks to maintain hemoglobin levels in anemic HIV-infected patients. Alexandra M. Levine, MD[1], *Gerhard Leitz, MD, PhD*[2]; (1)University of Southern California, Keck School of Medicine, Los Angeles, CA; (2)Ortho Biotech Clinical Affairs, LLC, Bridgewater, NJ.

PURPOSE: This study was conducted to investigate the effectiveness of epoetin alfa Q2W on maintaining Hb in anemic HIV+ pts.
METHODS: In a 24-week, multicenter, open-label study, HIV-infected pts with Hb<=12 g/dL were given epoetin alfa 40,000 U SC QW until a target Hb of 13 g/dL was achieved. Pts were then switched to a maintenance phase (MP) during which epoetin alfa was given at a dosage of 40,000 U SC Q2W. If, during Q2W dosing, Hb measured <=11 g/dL, pts were switched back to QW dosing; if Hb was >= 14 g/dL, dosing was temporarily withheld until Hb reached < 14 g/dL when previous maintenance dose resumed. Due to this possible dose titration in the MP, epoetin alfa may have been administered more or less frequently than Q2W.
RESULTS: At the time of this interim analysis, 261 pts have been enrolled. Baseline characteristics are as follows: median age, 43 y (range, 20–74 y); 61% men; 71% on highly active antiretroviral therapy (HAART); median CD4+, 232 cells/μL(range, 1–1461); median HIV-RNA, 960 copies/mL (range, 2–750,001); median Hb, 11.1 g/dL (range, 7.2–12.8 g/dL). 208 pts entered MP with a median Hb of 13.3 g/dL in a median of 3.3 wks (range, 1–21 wk). Median Hb at end of study was 13.0 g/dL. Based on calculated dosing interval, Hb was maintained in 3 pts (1.5%) w/QW dosing, 91 (47%) w/Q2W, 56 (29%) w/Q3W, 15 (7.7%) w/Q4W, and 29 (14.9%) w/>Q4W. In 14 pts, dosing interval data was missing. During MP, median dosing interval of epoetin alfa 40,000 U SC was Q3.4 wk (range, 1.1–24.3 wk). No related SAEs were reported.
CONCLUSIONS: These data suggest that the majority of anemic, HIV+ pts can effectively maintain a target Hb level of approximately 13 g/dL with Q2W or Q3W dosing regimens of 40,000 U epoetin alfa.
Presented at the Annual Meeting of the Infectious Diseases Society of America, Boston, MA, October 2, 2004.

142E. Epoetin alfa once every two weeks maintains quality of life in anemic HIV-infected patients. Patricia Salvato, MD[1], *Gerhard Leitz, MD, PhD*[2], Alexandra M. Levine, MD[3]; (1)Diversified Medical Practices, Houston, TX; (2)Ortho Biotech Clinical Affairs, LLC, Bridgewater, NJ; (3)University of Southern California, Keck School of Medicine, Los Angeles, CA.

PURPOSE: Anemia can cause symptoms that decrease day-to-day functioning and quality of life(QOL). Hemoglobin(Hb) increases have been associated with improved QOL. This study investigates the effect of epoetin alfa Q2W on QOL.
METHODS: In a 24-week, multicenter, open-label study, HIV-infected patients with Hb<=12 g/dL were administered epoetin alfa 40,000 U SC QW until a target Hb of 13 g/dL was achieved. Patients were then switched to a maintenance phase(MP) during which epoetin alfa was given at a dosage of 40,000 U SC Q2W. If, during Q2W dosing, Hb measured <=11 g/dL, pts were switched back to QW dosing;if Hb increased to >= 14 g/dL, dosing was temporarily withheld until Hb reached <14 g/dL, when previous maintenance dose resumed. QOL was measured by LASA (at baseline and Q2W thereafter) and by MOS-HIV (at baseline, the week the pt converted to MP, and Weeks 16 and 24).
RESULTS: For this interim analysis, 208 patients were evaluated. Mean Hb increase was 2.6 g/dL from baseline to start of MP. Mean changes in LASA Energy, Activity, and Overall QOL were 22mm, 18mm, and 16mm, respectively (P<.001). Of the 10 MOS-HIV domains, those with the greatest increase were health transition (18 points), energy/fatigue (17 points) and health distress (11 points).The MOS-HIV Physical Health Summary score improved by 4.7 points and the Mental Health Summary Scores increased by 5.3 points (P<.001). From the start of MP to the end of study, QOL was maintained in all 10 domains of the MOS-HIV. Also, the LASA Energy, Activity and overall QOL scales showed improvements of 7 mm, 5 mm and 5 mm (P<=.001), respectively. Epoetin alfa was well tolerated. No related serious adverse events (SAEs) were reported.
CONCLUSIONS: These data suggest QOL can be maintained effectively with a Q2W dosing regimen of epoetin alfa.
Presented at the 44th Interscience Conference on Antimicrobial Agents and Chemotherapy, Washington, DC, October 30–November 2, 2004.

143. Quality of life (QOL) improvement in human immunodeficiency virus (HIV)-infected population treated with epoetin alfa (EPO) and its association with gender. Rym Ben-Hamadi, MS[1], Dominic Mitchell, MA[1], Mei Sheng Duh, MPH, ScD[1], *Marya Zilberberg, MD*[2]; (1)Analysis Group, Inc, Boston, MA; (2)Ortho Biotech Clinical Affairs, LLC, Bridgewater, NJ.

PURPOSE: Treatment of anemia with EPO in HIV patients improves QOL in association with hemoglobin (Hb) rise. Since it is not known whether gender may impact this change, we examined whether the association between improvements in Hb and QOL varies by gender.
METHODS: A secondary analysis of the Community HIV Anemia Management Protocol Site (CHAMPS) study was conducted. Anemic (Hb <=11 g/dL) HIV patients receiving antiretroviral therapy were treated with epoetin alfa 40,000 U SC in this open-label, multicenter, 16-week study. QOL was measured by Linear Analog Score Assessment (LASA) and Medical Outcomes Study HIV (MOS-HIV). Ordinary least squares linear regression analysis stratified by gender examined the association between Hb change and LASA energy, LASA activity and MOS-HIV energy/fatigue scores.
RESULTS: Of the 650 patients evaluated for efficacy, 219 (34%) were female (F). For the following baseline characteristics the difference between males (M) and females, respectively was: mean age (44.0±8.7 vs. 42.3±9.5), baseline CD4+ cell count (157±195 vs. 247±235), and baseline viral load (92,068±162,923 vs. 66,318±145,062) (all P<=.05), with no difference in the baseline Hb (9.7±1.1 g/dL each). Multivariate analyses demonstrated that Hb changes were independently associated with improvements in LASA Energy (P=.023 [F], P<=.0001 [M]), LASA Activity (P=.0315 [F], P=.0009 [M], and MOS-HIV Energy/Fatigue (P<=.0151 [F], P<.0001 [M]).
CONCLUSIONS: Despite differences in baseline age and disease characteristics between genders, Hb change was a significant independent determinant of QOL improvement in HIV patients treated with EPO regardless of gender. Significant gains in QOL may be achieved in anemic HIV patients of either gender through identification and correction of anemia.

144E. Abacavir + lamivudine fixed dose combination tablet once daily (QD) compared with abacavir (ABC) and lamivudine (3TC) twice daily (BID) in HIV-1 infected subjects (ESS30008). *Christina E. Hill-Zabala, PharmD*[1], Nestor Sosa, MD[2], Edwin DeJesus, MD[3], Gisella Herrera, MD[4], Allison M. Florance, MS[1], Maria E. Watson, PhD[1], Mark S. Shaefer, PharmD[1]; (1)GlaxoSmithKline, Research Triangle Park, NC; (2)Social Security Hospital, Panama City, Panama; (3)Orlando Immunology Center, Orlando, FL; (4)CIMA, San Jose, Costa Rica.

PURPOSE: ESS30008 compared ABC BID and 3TC BID to ABC+3TC fixed dose combination (Epzicom, EZC) QD, both in combination with a protease inhibitor (PI) or non-nucleoside reverse transcriptase inhibitor (NNRTI).
METHODS: 260 HIV-infected subjects who received >6 months ABC+3TC BID and a PI or NNRTI as initial antiretroviral therapy (ART), had HIV-1 RNA <400 c/mL for >3 months were enrolled. Subjects were randomized to continue ABC+3TC BID (n=130) or switch to EZC QD (n=130) for 48 weeks. Randomization was stratified by background ART (PI or NNRTI). Adherence was assessed by pill count.
RESULTS: At baseline median time on ABC+3TC BID was 22 months, median CD4 was 554 cells/mm3, and median HIV RNA was <50 c/mL. Most common 3rd agent was efavirenz (62%), fosamprenavir + ritonavir (17%), and nelfinavir (14%). Non-inferiority of EZC QD to ABC+3TC BID was established based on the primary endpoint of proportion of subjects who did not meet virologic failure criteria (confirmed HIV RNA ∞›1265 c/mL) (90% CI: -3.3,6.5) (ITT M=F). Proportions with HIV RNA <50 at Week 48 (ITT M=F) were 81% and 82% for EZC QD and ABC+3TC BID, respectively. Virologic failure was rare (2% QD, 3% BID). CD4 counts were stable through Week 48. The most common Grade 2–4 AEs were similar across groups. No drug-related SAEs or hypersensitivity reactions were reported. Over 48 weeks, median adherence was 93% in both groups; however, a higher proportion of the EZC QD group (38.6%) than the ABC+3TC BID (31.0%) had ∞›95% adherence to randomized treatment.
CONCLUSIONS: EZC QD was established as noninferior to ABC+3TC BID in a regimen containing either a NNRTI or PI over 48 weeks. A dual nucleoside backbone of ABC and 3TC administered QD or BID is effective, durable, and well-tolerated.
Presented at the 12th Conference on Retroviruses and Opportunistic Infections, Boston, MA, February 22-25, 2005.

145E. Patient satisfaction with abacavir (ABC)-lamivudine (3TC) fixed dose combination (FDC) tablet once daily (QD) compared with ABC and 3TC twice daily (BID) in HIV-1 infected patients (ESS30008). *Christina E. Hill-Zabala, PharmD*[1], Maria E. Watson, PhD[1], Nestor Sosa, MD[2], Edwin DeJesus, MD[3], Allison M. Florance, MS[1]; (1)GlaxoSmithKline, Research Triangle Park, NC; (2)Social Security Hospital, Panama City, Panama; (3)Orlando Immunology Center, Orlando, FL.

PURPOSE: Patient satisfaction was evaluated, and the effect of dosing symmetry explored, as part of a randomized open-label study (ESS30008) comparing ABC/3TC FDC QD and ABC BID+3TC BID plus a third agent. Results are from the final 48-week analysis.
METHODS: HIV-1 infected patients on initial treatment with ABC+3TC BID plus a protease inhibitor or non-nucleoside reverse transcriptase inhibitor for Ñd6 months with HIV-1 RNA <400 c/mL for Ñd3 months, were randomized to remain on ABC+3TC BID (n=130) or switch to QD (n=130). Baseline satisfaction was evaluated using the total score of a validated 10-item patient-completed questionnaire (HIVTSQ). At Week 48, the HIVTSQ change version (HIVTSQc) assessed treatment satisfaction relative to baseline. HIVTSQc item scores were compared between treatment groups, with Bonferroni adjustment for multiplicity (p <0.005). Additional exploratory analyses compared HIVTSQc item scores for patients on symmetrical HIV treatment regimens (pure QD, pure BID) versus asymmetrical regimens (mixed dosing frequencies).
RESULTS: Baseline satisfaction was high and comparable in both treatment groups (p=0.49). At Week 48, there were trends towards greater improvement in satisfaction with treatment convenience (p= 0.041) and treatment flexibility (p=0.074) in the FDC group. The effect of dosing symmetry was statistically significant for 6 HIVTSQc items (satisfied with current treatment, treatment demands, treatment convenience, treatment flexibility, treatment fits lifestyle and satisfied to continue treatment; p<0.05 for each). Patients on a pure QD regimen showed markedly greater improvements in satisfaction versus those on a mixed regimen.
CONCLUSIONS: Satisfaction with treatment convenience and flexibility were enhanced by switching patients from ABC BID+3TC BID to ABC/3TC FDC QD. Symmetrical dosing regimens appear to increase patient satisfac-tion.
Presented at the 3rd Conference on HIV Pathogenesis and Treatment of the International AIDS Society, Rio de Janeiro, Brazil, July 24-27, 2005.

146E. Quadruple nucleoside/tide regimen of Trizivir (TZV) + Tenofovir (TDF) is effective following early virologic failure on an initial regimen containing a thymidine analog + lamivudine in combination with a protease inhibitor (PI) or non-nucleoside reverse t *Christina E. Hill-Zabala, PharmD*[1], Allan Rodriguez, MD[2], Louis Sloan, MD[3], Thomas T. Jefferson, MD[4], Linda H. Yau, PhD[1], Maria E. Watson, PhD[1], David M. Irlbeck, BS[1], Mark S. Shaefer, PharmD[1]; (1)GlaxoSmithKline, Research Triangle Park, NC; (2)University of Miami, Miami, FL; (3)North Texas IDC, Dallas, TX; (4)Health for Life, Little Rock, AR.

PURPOSE: Commonly HIV-infected patients start treatment with a thymidine analog (zidovudine [ZDV] or stavudine [d4T]) + lamivudine (3TC) + PI or NNRTI. However, over time most regimens begin to fail (HIV RNA rises and CD4 cell count declines). This study investigated the effectiveness of TZV+TDF in patients experiencing early virologic failure.
METHODS: 51 HIV-infected subjects on an initial regimen of ZDV or d4T + 3TC + PI or NNRTI with HIV RNA between 400 and 10,000 c/mL and CD4 >100 cells/mm^3 were enrolled. Subjects with >2 NRTI-associated mutations or K65R on genotype were excluded. Subjects were treated with TZV twice daily (BID) + TDF once daily (QD) for 48 weeks.
RESULTS: Subjects were 78% male, 51% black, 39% white. Baseline median HIV RNA and CD4 were 1972 c/mL and 436 cells/mm^3. 75% of subjects completed the 48-week study. Reasons for discontinuation were adverse events (AE), lost to follow up, protocol violation, virologic failure, and site closure. At Week 48, 87% had HIV RNA <400 c/mL (ITT Obs; primary endpoint) and 59% (ITT M=F) and 77% (ITT Obs) had HIV RNA <50 c/mL. Median CD4 change from baseline was 71 cells/mm3 at Week 48. Two subjects met virologic failure criteria (confirmed HIV RNA Ñd1265 c/mL); treatment-emergent resistance mutations were detected in 1 subject (M184V and TAMs [D67N+ K70R+K219Q]). No abacavir hypersensitivity reactions were reported. AEs leading to discontinuation were nausea, fatigue, and cancer. Median adherence to TZV was 76% as measured by Medication Event Monitoring System (MEMS) Smartcaps.
CONCLUSIONS: TZV BID + TDF QD was an effective and well-tolerated regimen in subjects experiencing early failure on ZDV or d4T + 3TC + PI or NNRTI. Using a quad nucleoside/tide regimen following failure on a PI or NNRTI-based regimen may preserve future treatment options with other classes of antiretrovirals.
Presented at the 3rd Conference on HIV Pathogenesis and Treatment of the International AIDS Society, Rio de Janeiro, Brazil, July 24-27, 2005.

147E. Maintenance with trizivir (TZV) or TZV + efavirenz (EFV) for 48 weeks following a 48-week induction with TZV + EFV in antiretroviral-naive HIV-1 infected subjects (ESS40013). *Christina E. Hill-Zabala, PharmD*[1], Martin Markowitz, MD[2], Joseph Lang, MD[3], Edwin DeJesus, MD[4], Leonard N. Slater, MD[5], Qiming M. Liao, PhD[1], E. Randall Lanier, PhD[1], Mark S. Shaefer, PharmD[1]; (1)GlaxoSmithKline, Research Triangle Park, NC; (2)Aaron Diamond AIDS Research Center, New York, NY; (3)ID Consultants, Charlotte, NC; (4)Orlando Immunology Center, Orlando, FL; (5)University of Oklahoma, Oklahoma City, OK.

BACKGROUND: ESS40013 was designed to test a 4-drug induction (I)

followed by a 3-drug maintenance (M) approach to initial antiretroviral therapy (ART) using highly potent ART to rapidly reduce HIV-1 RNA (vRNA) followed by simplification to a more convenient and tolerable regimen.
METHODS: 448 ART-naive subjects with vRNA >5,000 c/mL had 48-week I with TZV+EFV. 282 subjects who met criteria for M including vRNA <50 c/mL at Weeks 36 and 44 were randomized to continue TZV+EFV (n=141) or simplify to TZV alone (n=141) for 48-week M. Genotypes were done at baseline (BL) and virologic failure (VF). Adherence was measured by the self-reported Patient Medication Adherence Questionnaire.
RESULTS: Proportions with vRNA <50 c/mL (ITT M=F) were 79% for TZV+EFV and 77% for TZV at Week 96 (p=0.697). Noninferiority of TZV to TZV+EFV was established (95% CI: –8.6%, -5.7%). Median CD4 change from BL was 179 cells/mm3 at Week 48 and was stable through Week 96. Proportions completing 48 week M were 85% for TZV+EFV and 89% for TZV. Drug-related AEs were more commonly reported for TZV+EFV compared to TZV (15% vs. 6%). Median change from BL in fasting total cholesterol was +30mg/dL at Week 48; changes from Week 48 to Week 96 were +3mg/dL for TZV+EFV and –22mg/dL for TZV. VF occurred in 16 TZV and 8 TZV+EFV subjects during M (p=0.134). There was no difference (p=0.85) in time to treatment failure. The most common treatment-emergent viral mutations during M were K103N and M184V in both arms. There was a trend for a greater proportion of subjects reporting perfect adherence to TZV compared to TZV+EFV at Week 96 (88.8% vs. 79.6%; p=0.057).
CONCLUSIONS: Simplification to TZV alone following induction with TZV+EFV maintains virologic control and immunologic response. Simplification to TZV reduces fasting lipids, reduces ART-associated AEs, and may improve adherence.
Presented at the 14th International AIDS Conference, Bangkok, Thailand, July 11-16, 2004.

148E. Comparison of darbepoetin versus erythropoietin for the treatment of HIV-related anemia in hospitalized patients. *Elizabeth Gonzalez, Pharm.D.*[1], Keith A. Hecht, Pharm.D., BCOP[2], Jingyang Fan, Pharm.D., BCPS[2], Dennis K. Fuller, Pharm.D.[1]; (1)University Medical Center of Southern Nevada, Las Vegas, NV; (2)University of Southern Nevada College of Pharmacy, Henderson, NV.

PURPOSE: Anemia is frequently seen in HIV-infected patients and is associated with increased mortality. Studies have demonstrated the safety and efficacy of erythropoietin (EPO) for the treatment of HIV-related anemia. There are currently no published trials evaluating darbepoetin (DARBE), a novel erythropoiesis stimulating protein, in this patient population. The purpose of this evaluation was to compare the efficacy and safety of DARBE versus EPO in hospitalized patients with HIV-related anemia.
METHODS: We conducted a prospective observational evaluation over 1 year of DARBE in hospitalized patients with HIV-related anemia compared to a retrospective control group previously treated with EPO. The study population included adult patients with HIV-related anemia (Hgb <12 g/dL) initiated on therapy with either DARBE or EPO. Patients with active bleeding or uncontrolled hypertension were excluded. The primary outcomes for efficacy were change in Hgb and number of patients that received blood transfusions. Safety was evaluated by blood pressure readings and reports of thromboembolic events.
RESULTS: 47 patients with HIV-related anemia were identified (DARBE, n=22; EPO, n=25). 7 DARBE and 3 EPO patients were excluded. Baseline characteristics were similar, except more patients in the EPO group had ESRD (3 vs. 0). The mean Hgb increase for the DARBE group was 0.99 ± 1.98 g/dL and for the EPO group was 1.53 ± 1.70 g/dL (p=0.39). The percentage of patients transfused in the DARBE group was 20% and 41% for the EPO group (p=0.29). No thromboembolic events were reported in either group. There were 3 cases of uncontrolled hypertension in the DARBE group and 4 cases in the EPO group.
CONCLUSION: This small, retrospectively controlled study supports the use of DARBE in the treatment of HIV-related anemia in hospitalized patients. DARBE appears to be as safe and efficacious as EPO in this setting.
Presented at the 43rd Annual Meeting of the Infectious Diseases Society of America, San Francisco, CA, October 6-9, 2005.

149. Maternal and newborn outcomes in a multidisciplinary HIV pregnancy program. Albert Franco, MD[1], Saju D. Joy, MD[1], Sheila Kang, Pharm.D.[2], Ming Poi, Pharm.D., Ph.D.[3], Jane Hunkler, RN[4], Michael T. Brady, MD[4], Susan L. Koletar, MD[1], Michael F. Para, MD[1], *Patty Fan-Havard, Pharm.D.*[3]; (1)The Ohio State University, College of Medicine and School of Public Health, Columbus, OH; (2)Thomas Jefferson University Hospital, Philadephia, PA; (3)The Ohio State University, College of Pharmacy, Columbus, OH; (4)Columbus Children's Hospital, Columbus, OH.

PURPOSE: An HIV High-Risk Pregnancy Program (HHRPP) was established in July, 2001 at the Ohio State University Medical Center to manage obstetrical and medical needs of HIV-infected women. We report maternal and newborn complications and outcomes four years following the implementation of the service.
METHODS: Patient demographics, virologic, immunologic and clinical outcome data were prospectively collected and reviewed from July 2001 to June 2005. Maternal and newborn complications and outcomes following antepartum antiretroviral therapy (ART) exposure were evaluated.
RESULTS: Of the 50 delivered patients, the median maternal age was 26.5 years, and 76% were African American. The median viral load (VL) was 9,274 copies/ml (range: undetectable to 134,644 copies/ml), and the median CD4+ cell count was 494/mm3 (range: 31 to 1,060/mm3) at the start of pregnancy. Antepartum ART therapies of the 50 delivered patients were refusal of drug therapy in two (4.0%); zidovudine (ZDV) monotherapy in one (2.0%); ZDV-lamivudine in six (12%); a nevirapine (NVP)-containing regimen in 24 (48%); and, a protease inhibitor (PI)-containing regimen in twelve (24.0%). Forty-three (86.0%) of 50 patients achieved undetectable VL prior to delivery. Serious adverse events occurred in four women: drug rash, eosinophilia and systemic syndrome (DRESS) [n=2]; asymptomatic hepatotoxicity [n=1]; and fatal postpartum cardiomyopathy [n=1]. Of the 50 delivered infants, rates of premature delivery (<37 weeks) and very premature delivery (< 32 weeks) were 24.0% and 2.0%, respectively, and correlated with the rates of low birth weight and very low birth weight among infants. Thirty infants delivered are confirmed HIV-negative and the remaining 20 are HIV-negative to date by HIV DNA PCR.
CONCLUSIONS: The multidisciplinary HHRPP provides excellent and seamless care to underserved minority women infected with HIV. Antepartum ART chemoprophylaxis prevents HIV-1 perinatal transimission but may result in serious maternal toxicities, despite close monitoring for adverse events.

150E. Efficacy and safety of once-daily abacavir/lamivudine fixed-dose combination (ABC/3TC) + efavirenz (EFV): ESS30009 planned 48 week analysis. Joel E. Gallant, MD, MPH[1], Allan E. Rodriguez, MD[2], Winkler G. Weinberg, MD[3], Benjamin Young, MD, PhD[4], Daniel S. Berger, MD[5], *Michael L. Lim, PharmD*[6], Qiming M. Liao, PhD[6], Lisa L. Ross, MS[6], Judy Johnson, MSN[6], Mark S. Shaefer, PharmD[6]; (1)Johns Hopkins University, Baltimore, MD; (2)University of Miami, Miami, FL; (3)Kaiser Permanente, Atlanta, GA; (4)Rose Medical Center, Denver, CO; (5)Northstar Medical Center, Chicago, IL; (6)GlaxoSmithKline, Research Triangle Park, NC.

PURPOSE: This study was designed to compare two once-daily regimens: EFV + ABC/3TC or TDF + ABC/3TC. A previously reported interim analysis demonstrated high non-response rates to TDF + ABC/3TC with high incidence of M184V ± K65R, prompting early regimen termination. The EFV + ABC/3TC arm did not raise efficacy or safety concerns and continued unchanged.
METHODS: 340 treatment-naive, HIV+ subjects randomly received open-label fixed-dose ABC/3TC + either EFV or TDF. Switching ABC to zidovudine (ZDV) was permitted for hypersensitivity (HSR). An amendment allowed TDF + ABC/3TC subjects to switch to an investigator-selected second-line regimen (SLR). A planned 48 week analysis of the EFV arm and available follow-up of TDF arm subjects following switching to SLR is reported.
RESULTS: Median baseline viral load (VL) and CD4 count was 4.7 log c/mL and 251 cells/mm3. At 48 weeks, 120/169 (71%) and 127/169 (75%) of EFV subjects achieved VL <50 and <400 c/mL, respectively [missing=failure (M=F)]. Median CD4 count at 48 weeks was 405 cells/mm3. Drug-related adverse events ≥5% in either arm included HSR (7%), rash (5%), and insomnia (4%). Following termination of the TDF + ABC/3TC regimen, 131 subjects in this arm switched to a SLR; 54/131 (41%) had VL <400 c/mL at switch. Most common SLRs included ABC/3TC + EFV, ABC/3TC/ZDV + TDF, 3TC/ZDV + EFV, and ABC/3TC/ZDV + EFV. By 24 weeks post-switch, 101/131 (77%) and 108/131 (82%) achieved VL <50 and <400 c/mL, respectively (M=F).
CONCLUSIONS: ABC/3TC + EFV is an effective and well-tolerated once-daily regimen with a very low pill-burden. TDF + ABC/3TC should not be used as a three-drug regimen in naive patients. Many subjects who initially received TDF + ABC/3TC and remained in follow-up on an SLR subsequently achieved suppression, although over one-third of this cohort had VL <400 c/mL at time of switch.
Presented at the 3rd Conference on HIV Pathogenesis and Treatment of the International AIDS Society, Rio de Janeiro, Brazil, July 24-27, 2005.

151E. Coadministration of esomeprazole (ESO) with fosamprenavir (FPV) has no impact on steady-state plasma amprenavir (APV) pharmacokinetics (APV10031). *Mark J. Shelton, PharmD*, Susan L Ford, PharmD, Mary B Wire, PharmD, Yu Lou, MS, Julie Borland, BS, Sherene S Min, MD, Zhengyu Xue, MS, Geoffrey J Yuen, PharmD; GlaxoSmithKline, RTP, NC.

BACKGROUND: Fosamprenavir (FPV, Lexiva, Telzir), the phosphate ester pro-drug of the HIV-1 protease inhibitor amprenavir (APV), is approved for the treatment of HIV infection in adults. When single doses of FPV were co-administered with antacids and administered following pre-treatment with ranitidine, plasma APV AUC(0-24) decreased by 18% and 30%, respectively. This study was conducted to evaluate the steady-state interaction between

esomeprazole (Nexium, ESO) and FPV with and without RTV.
METHODS: This was a two-arm, three-period, cross-over, study in 56 healthy adults. All subjects received esomeprazole (ESO) 20mg QD x7d in Period 1. Immediately thereafter, subjects received ESO 20mg QD with either FPV 1400mg BID or FPV 700mg/RTV 100mg BID x14d in Period 2. ESO was co-administered simultaneously with morning doses of FPV. Following a 21-28d washout, subjects received FPV 1400mg BID or FPV 700mg/RTV 100mg BID x14d in Period 3. Plasma APV and ESO concentrations were determined by LC/MS/MS. Plasma PK parameters were derived by noncompartmental methods. ANOVA was used to determine geometric least squares mean (GLSM) ratios comparing plasma APV and ESO PK parameters for the combination to each drug alone
RESULTS: Following co-administration of ESO with FPV, GLSM ratios (90% CI) for APV $AUC_{0\text{-}t}$, C_{max}, and Ctau were 0.98 (0.87-1.10), 0.97 (0.85-1.10), and 1.03 (0.90-1.19), respectively. Following co-administration of ESO with FPV/RTV, GLSM ratios (90% CI) for APV $AUC_{0\text{-}t}$, C_{max}, and C_t were 0.91 (0.84-0.98), 0.95 (0.86-1.05), and 0.93 (0.85-1.02), respectively. Following coadministration of ESO with FPV/RTV, ESO $AUC_{0\text{-}t}$ and C_{max} were unchanged. Following co-administration of ESO with FPV, ESO $AUC_{0\text{-}t}$ was increased 55% [GSLM ratio (CI) 1.55 (1.39-1.73)], but C_{max} was unchanged.
CONCLUSIONS: Co-administration of ESO 20mg QD with either FPV 1400mg BID or FPV 700mg/RTV 100mg BID had no effect on steady state plasma APV PK. Thus, FPV and FPV/RTV may be co-administered with PPIs.
Presented at the 6th International Workshop on Clinical Pharmacology of HIV Therapy, Québec City, QC, Canada, April 28-30, 2005.

152E. Safety and efficacy of antiretroviral treatment (ART) regimens containing tenofovir DF (TDF) and atazanavir/ritonavir (ATV/r) in HIV-infected adults. *Lisa A. Chamberlain, PharmD*[1], William F. Owen Jr., MD[2], David R. Warren, MD[3], Ramin Ebrahimi, MD[3], John F. Flaherty, PharmD[3], Betty J. Dong, PharmD[1]; (1)UCSF Medical Center, San Francisco, CA; (2)California Pacific Medical Center, San Francisco, CA; (3)Gilead Sciences, Foster CIty, CA.

INTRODUCTION: ART with ATV/r and TDF (plus other agents) is an option for ART-naive and experienced patients (pts) because of the convenience of QD dosing and favorable safety and resistance profiles. To assess safety and efficacy we undertook a retrospective evaluation of TDF and ATV/r use at a large urban private practice.
METHODS: Record review including demographics, prior and concurrent ART, CD4 count, plasma HIV RNA (VL), and laboratory tests (Scr, T bili, fasting lipid profile) prior to and after at least 1 month of ART with TDF and ATV/r plus other agents.
RESULTS: 82 pts were identified (81 males; mean ± SD age, 50 ± 9.6 yrs). Most were white (82%) and MSM (98%). 77 pts (94%) were experienced; 5 pts were ART-naíve. TDF and ATV/r were given for a median (range) of 10 (1–13) mos. 5 pts had treatment discontinued; 4 due to AE (1 scleral icterus, 2 dizziness/fatigue, 1 Scr elevation). 62 (81%) of the ART-experienced pts were changed to TDF and ATV/r with BL VL < 400 c/mL; all remained undetectable. 14/15 experienced pts with BL VL > 400 c/mL achieved VL < 400 c/mL on treatment. Increase from BL in CD4 count (mean ± SD) at 6 mo (n = 63) and 12 mo (n = 40) were 53 ± 194 and 36 ± 168 cells/mm^3, respectively. 5/5 naíve pts achieved VL < 400 c/mL at 12 mo. Mean ± SD change from BL in T chol and Tg were -12.8 ± 45 and -33.2 ± 118 mg/dL at 12 mo. One pt had a significant Scr elevation (grade 3); 31 (38%) and 7 (9%) pts had grade 3 and 4 hyperbilirubinemia, respectively.
CONCLUSIONS: ART with regimens including TDF and ATV/r is well tolerated and associated with favorable virologic, immunologic and lipid responses.
Presented at the 3rd Conference on HIV Pathogenesis and Treatment of the International AIDS Society, Rio de Janiero, Brazil, July 24-27, 2005.

Infectious Diseases

153E. Validation of guideline-concordant empiric antibiotic therapy for ICU patients with community-acquired pneumonia. *Christopher R. Frei, PharmD, MSc, BCPS*[1], Marcos I. Restrepo, MD, MSc[2], Eric M. Mortensen, MD, MSc[2], David S. Burgess, PharmD, FCCP[1]; (1)Univ. TX College of Pharmacy at Austin and Univ. TX Health Sci. Ctr., San Antonio, TX; (2)Univ. TX Health Sci. Ctr., Vet. Evidence-Based Res. Dissemination and Implementation Ctr., and South TX Vet. Health Care System, San Antonio, TX.

PURPOSE: Studies have demonstrated decreased mortality with guideline-concordant empiric antibiotic therapy among ward patients with community-acquired pneumonia (CAP). However, no study has yet evaluated the clinical value of guideline-concordant antibiotic therapy among ICU patients with CAP.
METHODS: Patient demographics, laboratory and physical exam findings, empiric antibiotic therapy, and hospital course were extracted from the medical records of all adult CAP patients admitted to the ICUs at five community hospitals between 1 November 1999 and 30 April 2000. Patients were stratified into guideline-concordant (GC) and discordant (GD) groups as in accordance with the 2003 IDSA and 2001 ATS guidelines. We evaluated time to clinical stability (TTCS), time to switch therapy (TTST), lengths of ICU and hospital stays (LOS), and in-hospital mortality by using regression models that included the outcome as the dependent variable, antibiotic therapy as the independent variable, and the Pneumonia Severity of Index (PSI) score as a covariate.
RESULTS: Of the 129 evaluable patients, 43 (33%) received GC antibiotic therapy. Patients in the GC group had a mean (± standard deviation) PSI score of 130 ± 40 vs. 119 ± 33 for the GD group (P=0.13). Groups were similar with respect to age, gender, comorbidities, admission from a nursing home, pre-admission antibiotics, shock, acute renal failure, and the need for mechanical ventilation. In-hospital mortality (odds ratio, 95% CI) was significantly lower among patients who received GC antibiotic therapy (12% vs. 22%; 0.34, 0.10-0.98). Other outcomes were similar between the two groups (median; risk ratio, 95% CI): TTCS (3 vs. 3 days; 0.93, 0.75-1.18), TTST (6 vs. 8 days; 1.08, 0.88-1.33), ICU LOS (2 vs. 3 days; 1.02, 0.84-1.27), and LOS (7 vs. 8 days; 1.06, 0.87-1.31).
CONCLUSION: Guideline-concordant empiric antibiotic therapy improves survival but does not impact TTCS, TTST, ICU LOS or LOS in ICU patients with community-acquired pneumonia.
Presented at the 45th Annual Interscience Conference on Antimicrobial Agents and Chemotherapy, New Orleans, LA, September 21-24, 2005.

154E. Evaluation of fluoroquinolone susceptibility breakpoints for S. pneumoniae and Enterobacteriaceae based on pharmacokinetic/pharmacodynamic principles. *Christopher R. Frei, PharmD, MSc, BCPS*, David S. Burgess, PharmD, FCCP; University of Texas College of Pharmacy, Austin, TX, University of Texas Health Science Center, San Antonio, TX.

BACKGROUND: CLSI established susceptibility breakpoints for most fluoroquinolones prior to the widespread use and acceptance of pharmacokinetic-pharmacodynamic (PK-PD) modeling. In addition, contemporary surveillance networks have detected the emergence of fluoroquinolone resistance among gram-negative pathogens. These constitute critical reasons to revisit existing CLSI breakpoints.
METHODS: Multiple 10,000-subject Monte Carlo simulations were performed using fixed MICs (0.03 to 64 µg/ml) and published pharmacokinetic parameters for standard fluoroquinolone dosing regimens. The PK-PD targets for *S. pneumoniae* and Enterobacteriaceae were a free $AUC_{0\text{-}24h}$/MIC ≥ 30 and ≥125. The PK-PD breakpoint was defined as the highest MIC at which target attainment was ≥ 90%. MIC distributions were obtained from antimicrobial surveillance networks.
RESULTS: The PK-PD breakpoints were lower than CLSI susceptibility breakpoints for both *S. pneumoniae* (1-2 fold) and Enterobacteriaceae (8 fold) (Table). Except for ciprofloxacin, the PK-PD breakpoints did not bisect the MIC distributions.

Regimen	Breakpoint (%S)			
	S. pneumoniae		*Enterobacteriaceae*	
	CLSI	PK-PD	CLSI	PK-PD
Ciprofloxacin 400mg q12h	--	--	1 (89%)	0.06 (77%)
Levofloxacin 750mg q24h	2 (99%)	1 (96%)	2 (89%)	0.25 (85%)
Gatifloxacin 400mg q24h	1 (99%)	0.5 (98%)	2 (92%)	0.12 (79%)
Moxifloxacin 400mg q24h	1 (99%)	0.25 (99%)	--	--
Gemifloxacin 320mg q24h	0.12 (100%)	0.06 (100%)	--	--

CONCLUSION: PK-PD models suggest that the CLSI fluoroquinolone susceptibility breakpoints for *S. pneumoniae* should be lowered 2-fold while breakpoints for Enterobacteriaceae should be lowered 8-fold to ensure that most patients attain PK-PD indices correlated with efficacy.
Presented at the 43rd Annual Meeting of the Infectious Diseases Society of America, San Francisco, CA, October 6-9, 2005.

155. Impact of methicillin-resistance on vancomycin MICs against staphylococci. *Roger L. White, PharmD*[1], Lawrence Friedrich, PharmD[2]; (1)Medical University of South Carolina, Charleston, SC; (2)Cubist Pharmaceuticals, Mt. Pleasant, SC.

BACKGROUND: Methicillin-resistant (MR) staphylococci are associated with increased mortality compared to susceptible (MS) strains; a contributing factor may be higher vancomycin (V) MICs with MR isolates.
METHODS: From 1984-2005, 45 studies (8,290 isolates) were evaluated to assess differences in MICs between MR and MS *S. aureus* (MRSA, MSSA), *S. epidermidis* (MRSE, MSSE), and coag-neg staphylococci (MRCNS, MSCNS). In each study, the MR/MS ratio was calculated for the MIC_{50}, MIC_{90}, Min, and Max MICs. Mean/median/range of these ratios were calculated. Differences in MIC_{50}, and MIC_{90} between MR and MS strains were assessed using the Wilcoxon test.
RESULTS: MICs (range) were: MRSA (0.12-8), MSSA (0.25-8), MRSE (0.25-4), MSSE (0.25-32), MRCNS (0.25-4), MSCNS (0.25-32). MR/MS ratios ranged from 0.25-4 for SA and SE and 0.125-2.0 for CNS.

MR/MS ratio results	*S. aureus*	S. epidermidis	Coag-neg staph
Number of ratios evaluated	45	19	15
Mean ratio (MIC_{50})	1.2	1.4	1.4
Mean ratio (MIC_{90})	1.3	1.2	1.4
% of ratios ≤ 0.5 (MIC_{50})	4	7	0
% of ratios ≤ 0.5 (MIC_{90})	2	0	0
% of ratios ≥2 (MIC_{50})	22	47	26
% of ratios ≥2 (MIC_{90})	24	20	42

Median ratios for each organism were 1; mean MR/MS ratios were all >1. MR/MS ratios ≥2 were 7-22x more likely than ratios ≤0.5, thus, ratios other than 1 were not due to random variability. MR MICs were higher ($p \leq 0.05$) for: SA MIC_{90}, SE MIC_{50} and MIC_{90}, combined (SE+CNS) MIC_{50} and MIC_{90}. Results did not appear to be influenced by MIC method, MIC value, or study year.
CONCLUSION: MR staphylococci frequently have higher V MICs than MS isolates. MIC differences were not large; however, with current V MICs, these differences have implications for pharmacodynamic profiles and efficacy. Moreover, if the prevalence of MR strains increases, the resultant higher MICs may have major implications for therapy.

156. Assessment of vancomycin MIC creep against staphylococci (1980-2005). *Roger L. White, PharmD*[1], Lawrence Friedrich, PharmD[2]; (1)Medical University of South Carolina, Charleston, SC; (2)Cubist Pharmaceuticals, Mt. Pleasant, SC.

BACKGROUND: Poor outcomes in vancomycin (V) treated patients with staphylococcal infections have been attributed to increasing V MICs, even with isolates not identified as glycopeptide-intermediate (GISA) or resistant (GRSA). A longitudinal analysis of published MICs could assess potential V "MIC creep".
METHODS: From 1980-2005, 68 studies (18,221 isolates) from US/Canada of methicillin-resistant or methicillin-susceptible *S. aureus* (MRSA, MSSA), *S. epidermidis* (MRSE, MSSE), or coagulase-negative staphylococci (MRCNS, MSCNS) were evaluated. Geometric mean (weighted on number of isolates, WGM) MIC_{50}, MIC_{90} Min, and Max were calculated. Linear regression (log WGMs vs time) and the Mann-Kendall test were used to assess trends. Since studies may have excluded GISA after 1996, the 1996-2005 subset was analyzed. Since most poor outcomes have occurred with isolates with V MICs ≥4 mg/L, the number and % of studies in which these occurred was assessed.
RESULTS: MICs (number, range) were: MRSA (6221, 0.12->32), MSSA (8142, 0.19-8), MRSE (1216,0.25-6.3), MSSE (829,0.25-16), MRCNS (1035,0.25-4), MSCNS (778,0.25-32). Most MIC_{50} and MIC_{90} values occurred over a narrow range (0.5-2.0 mg/L). The only significant ($p \leq 0.05$) slopes for WGM trends (all negative slopes) were: MRSE MIC_{90}, Max MICs for MRSE and MSSE. Mann-Kendall analysis found trends ($p \leq 0.05$) only for MRSE MIC_{90} and Max MRSE MIC. No significant trends were found from 1996-2005. Of studies with MICs ≥4 mg/L, most occurred prior to 1996 (25% of all studies, 72% of studies with MICs ≥4 mg/L) and with coagulase-negative staphylococci. These findings did not appear to be influenced by MIC test methods or range of MIC concentrations studied.
CONCLUSION: No trends detecting increasing MICs to V were found. Interestingly, higher Max MIC values (isolates currently categorized as GISA or GRSA) were noted prior to 1996, resulting in some declining MIC trends. In the last 10 years of the analysis (1996-2005), no trends in MICs were detected.

157. Potential impact of the modification of diet in renal disease (MDRD) equation on antibiotic dosing. *Winter J. Gibbs, Pharm.D.*, Richard H. Drew, Pharm.D., MS, D. Byron May, Pharm.D., Elizabeth S. Dodds Ashley, Pharm.D.; Campbell University School of Pharmacy & Duke University Medical Center, Durham, NC.

PURPOSE: Published recommendations for dosing drugs excreted renally are frequently based on creatinine clearance (ClCr) estimates using the Cockroft-Gault (CG) equation. The MDRD glomerular filtration rate (GFR) equation provides an alternate estimate of renal function. The resulting differences between estimates may result in altered dosage recommendations for many drugs, including antibiotics. The primary objective of this study was to determine the concordance rates of antibiotic dosing recommendations based on renal function estimates using the MDRD and CG equations in a cohort of hospitalized patients. The secondary objective was to determine the degree of correlation between GFR and ClCr estimates.
METHODS: This study was retrospective and observational. One hundred subjects hospitalized at Duke University Medical Center (DUMC) between 2001-2005 and receiving parenteral antibiotics were randomly selected. Dosing recommendations (according to package insert) were determined for each of the 10 most commonly prescribed antimicrobials at DUMC that require renal dosage adjustment utilizing GFR and ClCr estimates derived from the MDRD and CG equations, respectively. Descriptive statistics were used to describe the concordance rates of recommended antibiotic doses based on the two estimates. A correlation coefficient was determined to describe the correlation of GFR and ClCr values.
RESULTS: Concordance in dosing recommendations resulting from renal function estimates derived from MDRD and CG equations was observed in 781 of 1000 (78.1%) of the simulations. In 7 of the 10 antibiotics simulated, concordance rates were over 80%. Concordance was lowest for vancomycin and gentamicin (~40%), and highest for TMP/SMX and ampicillin/sulbactam (~90%). Plotting CG ClCr versus MDRD GFR reflected a correlation coefficient of 0.88.
CONCLUSIONS: While MDRD GFR and CG ClCr estimates of renal function demonstrate a high degree of correlation overall, resulting dosing recommendations vary with individual antibiotics.

158. Impact of time to antibiotic administration on hospitalization length for community-acquired pneumonia. *Christopher J. Destache, Pharm., D.*, Dawn S. Knudsen, Pharm., D.; Creighton University School of Pharmacy, Omaha, NE.

PURPOSE: A significant correlation exists in patients with CAP between TAA (if < 4 hours from time of admission) and morbidity or mortality. A retrospective medical records review was performed to ascertain TAA for CAP patients in our 332-bed university-affiliated institution.
METHODS: Adult patients admitted with CAP were identified and medical records reviewed from November 2003-October 2004. CAP patients were included if met CAP diagnostic criteria on admission (fever, productive sputum, elevated WBC, shortness of breath, + CXR). Patients were excluded for aspiration or hospital-acquired pneumonia, cancer, neutropenia (WBC < 3,000), or known HIV patient. Medical records were reviewed and data analyzed by SPSS (ver 10.0). Mean ± S.D. are reported.
RESULTS: 291 patients were identified CAP patients; 86 fulfilled inclusion criteria. There were 47 males/39 females enrolled. Mean age, weight (kgs), CAP score were 61.3 ± 16.2, 90.7 ± 36.5, and 85.6 ± 31.4, respectively. TAA was < 4 hours for 51 (59.3%) patients. If patients' TAA was < 4 hours, their length of hospitalization averaged 2 days shorter ($p > 0.05$). Forty-nine percent (17/35) of TAA > 4 hours were identified as due to either physician orders or unit clerk problems. Four patients (4.7%) expired and 9 patients (10.5%) were transferred to ICU. Four (44%) transferred patients TAA exceeded 4 hours. Transferred patients TAA > 4 hours were hospitalized 6.5 days longer ($p=0.012$). Transferred patients averaged 7 days longer hospitalization ($p<0.01$) compared to those on admitted hospital unit. Analysis by step-wise linear regression showed age and unit clerk time to take-off admission orders were significantly correlated to hospital stay ($r^2=0.88$; adj $r^2=0.874$; $p<0.001$).
CONCLUSIONS: TAA within 4 hours for CAP patients would reduce hospitalization length, significantly in critically ill patients transferred to ICU. Unit clerk time significantly affected hospitalization length.

159. Antibacterial susceptibility testing of Staphylococcus aureus **(SA) using flow cytometry**. *Qing Ma, PhD*[1], Edward Podniesinski, MEng[2], Paul Wallace, PhD[2], Patrick F. Smith, PharmD[1]; (1)University at Buffalo, Buffalo, NY; (2)Roswell Park Cancer Research Institute, Buffalo, NY.

PURPOSE: In vitro antibacterial susceptibility testing is essential in differentiating susceptible from resistant organisms. The current antibacterial testing methods depend upon growth inhibition after incubation with drugs, and include an inherent delay prior to results being available. The objective of this study was to develop a rapid and reproducible flow cytometry (FC) susceptibility test for daptomycin against SA. This assay is based on the detection of altered bacterial membrane potential (MP) following daptomycin treatment.
METHODS: MICs of 14 clinical SA isolates including 5 methicillin-resistant (MRSA) strains were determined by microbroth dilution. For FC testing, a starting inoculum (10^6 CFU/mL) was prepared and incubated with various concentrations of daptomycin at 37°C for 1 h. A mixture of permeability dye (TO-PRO-3) and MP dye ($DiOC_2(3)$) was added, incubated for 4 min, and bacterial suspension injected into the flow cytometer (FacsCalibur) for measurement of MP and cell permeability. The effective concentration (EC) was defined as the lowest daptomycin concentration that generated maximal decrease in MP as compared to growth control.
RESULTS: Daptomycin decreased MP in a concentration dependent manner. The ECs obtained by FC assay for 14 isolates were in good agreement with the results obtained by traditional MIC methods (correlation coefficient 0.93) and were without bias. Daptomycin significantly increased SA permeability at high concentrations in 10 of 14 strains. No significant correlation between permeability and MIC or MP was noted.
CONCLUSIONS: This study demonstrates that FC antibacterial susceptibility testing of SA provides rapid and reproducible results that are consistent with those obtained by conventional methods. This susceptibility testing is able to detect the varying degrees of sensitivity to daptomycin based upon membrane potential and permeability changes. Compared to permeability, MP appears to be more closely correlated with MIC.

160. PDR1-dependent and -independent gene expression programs associated with azole resistance in Candida glabrata **identified by microarray analysis**. *Kelly D. Earhart, B.S.*[1], Teresa T. Liu, B.S.[1], John-Paul Vermitsky, B.S.[2], Lijing Xu, M.S.[1], Ramin Homayouni, Ph.D.[1], Thomas D. Edlind, Ph.D.[2], P. David Rogers, Pharm.D., Ph.D.[1]; (1)University of Tennessee, Memphis, TN; (2)Drexel University, Philadelphia, PA.

PURPOSE: *Candida glabrata* has emerged as a cause of mucosal and invasive fungal infection in the U.S. Acquired azole resistance has been reported in several patient populations. In order to identify molecular mechanisms of azole resistance in *C. glabrata*, we examined changes in the gene expression profile 1) in experimentally-induced azole resistance, and 2) in response to fluconazole treatment.
METHODS: Fluconazole-resistant mutant F15 (fluconazole MIC>128 µg/mL) was derived from strain ATCC 66032 (fluconazole MIC=16 µg/mL). Isolates were grown to mid-log phase and total RNA was extracted. Isolate 200989 was exposed to fluconazole (2 X MIC) for 2.5 hours and total RNA was extracted. Gene expression profiles were compared using a custom *C. glabrata* microarray. Additional experiments were conducted with strains disrupted for *PDR1*. Differential expression was verified for selected genes by real-time RT-PCR.
RESULTS: We found 262 genes to be differentially expressed between isolates 66032 and F15. In isolate 200989 we found 631 genes to differentially expressed in response to fluconazole. Of these, 49 were common to both groups. These included *C. glabrata* homologs of *Saccharomyces cerevisiae* genes of the pleiotropic drug resistance (PDR) network such as the up-regulation of *CDR1*, *PDR1*, *YOR1*, and *RTA1*, and down-regulation of *FLR1*. Other differentially expressed genes in isolate F15 included transporter genes (*PDH1* and *QDR1*), those associated with sterol uptake (up-regulation of *SUT1* and *LAC1*), and lipid, fatty acid, and sterol biosynthesis (down-regulation of *PDR12*, *ERG20* and *ERG25*). Disruption of *PDR1* abrogated azole resistance and reduced the expression of *CDR1*, *PDH1*, *YOR1* and *RTA1* in response to azole treatment and in resistant isolates.
CONCLUSIONS: These results implicate genes involved in the azole-induced stress response and azole resistance. Some appear to be part of the *C. glabrata* PDR network, are regulated by Pdr1p, and represent novel mechanisms of azole resistance in this pathogenic fungus.

161E. Preliminary analysis of the association between fluoroquinolone (FQ) use and Clostridium difficile (C diff) **rates**. Cassandra D Salgado, MD, MS, *Patrick D. Mauldin, Ph.D.*, Lisa L Steed, Ph.D., John A Bosso, Pharm.D.; Medical University of South Carolina, Charleston, SC.

PURPOSE: *C diff* associated diarrhea can be associated with significant morbidity. Studies have suggested an association between FQ use and increased rates of *C diff* . Compared to 2000-2003, in 2004, our hospital experienced a 123% relative increase in our baseline *C diff* rate (.69 vs. 1.5 per 1000 pt days, p<0.0001). We sought to examine the relationship between FQ use and *C diff* rates.
METHODS: The quarterly *C diff* rate from 1/00 to 11/04 was calculated for the entire hospital and for each adult ward as the number of positive *C diff* toxin tests (duplicate pt isolates removed) per 1000 pt days. Similarly, FQ use was calculated as defined daily dose (DDD) per 1000 pt days. Time Series methodology and Pearson Correlation were used to examine the association between *C diff* rates and FQ use.
RESULTS: Over the study period, there was a significant positive association between hospital-wide *C diff* rates and gatifloxacin use (p=0.007). There was a significant negative association with ciprofloxacin use (p=0.028, when controlling for total FQ use). Among 9 adult wards where *C diff* occurred regularly, when an association was seen between the *C diff* rate and gatifloxacin use, it was always positive (5 were significant (p<0.05), and 2 others had strong trends (p<0.1). There was rarely any association between *C diff* rates in individual wards and total FQ use or ciprofloxacin use. Overall, the R-square values were low suggesting that additional factors may be influencing *C diff* rates in the hospital.
CONCLUSIONS: In this preliminary analysis, gatifloxacin use had a significant positive association with *C diff* rates hospital-wide and in the majority of adult units where *C diff* occurred regularly. Ciprofloxacin use appeared to have no positive association with *C diff* rates. However, other factors likely influence *C diff* rates and further study is warranted.
Presented at the 43rd Annual Meeting of the Infectious Diseases Society of America, San Francisco, CA, October 6-9, 2005.

162. Nelfinavir decreases progesterone levels and fetal weight in pregnant rats. *Trang Truong, Pharm.D., candidate*[1], Cheryl Lieb-Sargel, Pharm.D.[2], Sheila Kang, Pharm.D.[3], Clifton M. Monahan, DVM[4], Patty Fan-Havard, Pharm.D.[1]; (1)The Ohio State University, College of Pharmacy, Columbus, OH; (2)Columbus Children's Hospital, Columbus, OH; (3)Thomas Jefferson University Hospital, Philadephia, PA; (4)The Ohio State University, College of Veterinary Medicine, Columbus, OH.

PURPOSE: Hyperprogesteronegenic state is critical for pregnancy quiescense, fetal development and well-being. Premature births and low birth weight (LBW) infants have been reported with HIV-1 protease inhibitors (PIs). Nelfinavir (NFV) coadministration with oral contraceptives is known to cause reductions in the AUC of both estrogen and progestin components. The cause and effect relationship of PIs on endogenous progesterone (PG) and 17&beta-estradiol (E_2) levels during pregnancy remains unknown. We investigated the effects of NFV on PG and E_2 levels during pregnancy and fetal outcomes.
METHODS: A total of 22 female Sprague-Dawley rats were randomly assigned to control (C) (n=8), low-dose (LD) (100 mg/kg/day, n=7), or high-dose (HD) NFV-treated (400 mg/kg/day, n=7) group. Necropsy was performed on day 20 of gestation. Maternal blood samples were collected at 20 ± 1.7 hours after the last NFV dose. Serum PG and E_2 levels were quantitated using radioimmunoassay. Fetuses were isolated and weighed.
RESULTS: Necropsy was performed on 8 C (total of 100 concepti), 7 LD (118 concepti) and 7 HD NFV-treated (77 concepti) dams. A significant reduction of PG levels in LD (p<0.008) and HD NFV-treated groups (p<0.032) was observed when compared to C. The mean PG levels in C, LD, and HD NFV-treated groups were 70.7 ± 11.5 ng/ml, 55.4 ± 7.6 ng/ml, 58.2 ± 9.3 ng/ml, respectively. No significant change in E_2 levels was observed when comparing NFV-treated groups with C (p=0.185). A significantly lowered fetal weight was observed in NFV-treated groups as compared to C (p<0.001).
CONCLUSIONS: The present data suggest a significant decrease in PG levels among NFV treated dams and the perturbation in PG levels is associated with lowered fetal weight as compared to control. Clinical studies in HIV-infected pregnant women are needed to confirm the cause and effect relationship between the perturbation of PG levels and LBW infants.

163. Dangers of combining cystic fibrosis (CF) and non-cystic fibrosis (nonCF) derived Pseudomonas aeruginosa (PA) antibiotic susceptibility results in hospital antibiograms. John A Bosso, Pharm.D., *Patrick D. Mauldin, Ph.D.*, Lisa L Steed, Ph.D.; Medical University of South Carolina, Charleston, SC.

PURPOSE: Antibiograms are commonly used by hospital-based clinicians in choosing empiric antibiotic therapy. CF-derived PA are often more resistant to antibiotics than strains cultured from nonCF patients. Combining susceptibility testing results from CF and nonCF isolates to produce an average % susceptible (%S) for a hospital may therefore produce a number that is misleading to practitioners treating nonCF patients with possible PA infections.
METHODS: To test this theory, we examined susceptibility data from 3 quarters of 2004, comparing CF to nonCF susceptibility to 10 antibiotics. Further, %S for nonCF isolates were compared with the combined %S for the quarter (combined # isolates = 63, 68 and 64, respectively) as well as that reported in the annual antibiogram (n = 237). Differences were calculated as % and also assessed for statistical significance using χ^2 testing with Bonferroni correction to account for multiple testing.
RESULTS: Large % differences in %S between CF and nonCF in each quarter for aminglycosides (A) (range: 18.9-71.3) and quinolones (Q) (range: 19.1-61.5). Large differences were also observed between nonCF and combined %S in the 3 quarters (A:3.5-29.5 ; Q: 1.3-20.3) and when comparing quarterly nonCF with annual combined. Large differences were generally not seen for fl-lactams. The differences with A and Q results were frequently statistically significant.
CONCLUSIONS: Combining CF and nonCF PA susceptibility into one %S for the hospital may produce impressions that underestimate the activity of some antibiotic classes against nonCF isolates. Clinicians may make less than ideal empiric antibiotic selection choices based on such data.

164. Molecular mechanisms of acquired azole antifungal resistance in clinical isolates of Candida glabrata **identified through an integrated genetic, genomic, and proteomic approach**. *P. David Rogers, Pharm.D., Ph.D.*[1], Ziba M. Hooshdaran, Ph.D.[1], Teresa T. Liu, B.S.[1], Kelly D. Earhart, B.S.[1], John-Paul Vermitsky, B.S.[2], Yan Jiao, M.D.[1], George M. Hilliard, Ph.D.[1], Weikuan Gu, Ph.D.[1], Spencer W. Redding, D.D.S., M.Ed.[3], Thomas D. Edlind, Ph.D.[2]; (1)University of Tennessee, Memphis, TN; (2)Drexel University, Philadelphia, PA; (3)University of Texas, San Antonio, TX.

PURPOSE: Resistance of *Candida glabrata* to azole antifungals is an increasing clinical problem. The aim of this study was to identify mechanisms of azole resistance in clinical isolates of *C. glabrata*.
METHODS: Two isogenic, matched, clinical isolates were obtained from a cancer patient with oropharyngeal candidiasis during a course of fluconazole therapy (isolates 6856; MIC=8 µg/mL and 6955; MIC=64 µg/ml). Isolates were grown to early exponential phase and cell pellets and RNA were harvested. Gene expression profiles were compared using a custom *C. glabrata* microarray. The protein fraction was precipitated and subjected to 1D- or 2D-SDS-PAGE. Separated proteins were stained, imaged, and analyzed with PDQuest. Selected spots were excised and analyzed by MALDI-TOF MS. Proteins were identified by searching a custom open-reading-frame database. Differential expression was verified for selected genes by real-time RT-PCR. Genomic DNA was obtained and subjected to temperature gradient capillary

electrophoresis analysis and direct sequencing for identification of point mutations in *PDR1*.
RESULTS: In association with azole resistance we found 8% and 9% of the genome to be up- or down-regulated, respectively. Among the up-regulated genes were the putative Pdr1p targets *CDR1*, *YOR1*, *RTA1*, *RAP1*, *YMR152w*, and *YDR167w*. We identified 24 proteins as being differentially expressed in these isolates, including the up-regulated proteins Cdr1p, Erg11p, Erg1p, Erg6p, Gre2p, Sah1p, Spe3p, and Eno1p in isolate 6955. In isolate 6955 we identified a K274N mutation within a domain of *PDR1* that is conserved with *S. cerevisiae PDR1*.
CONCLUSIONS: These data suggest that acquired azole resistance likely involves increased expression of pleiotropic drug resistance genes which may be due to a gain-of-function mutation in the transcription factor Pdr1p. Transcription-independent changes in the abundance of enzymes of the ergosterol biosynthesis pathway may also contribute to the azole resistance phenotype of isolate 6955.

165. Doxycyline for treating multi-drug resistant Acinetobacter baumannii infections in a NY City hospital. *Yi Guo, Pharm.D.*, Maria Amodio-Groton, Pharm.D.; Montefiore Medical Center, Bronx, NY.

PURPOSE: According to our hospital antibiogram, approximately one-third of the Acinetobacter baumannii isolates are multi-drug resistant except to polymyxin B. A few published cases suggested doxycycline may be an effective option for treating multi-drug resistant A. baumannii. The purpose of this study was to evaluate the outcomes of our patients who received doxycycline for multi-drug resistant A. baumannii infections.
METHODS: Retrospective chart reviews were conducted for patients who received doxycycline for treating multi-drug resistant A. baumannii in 2004. Antibiotic usage was reviewed in conjunction with susceptibility data, WBC counts, vital signs, diagnoses and progress notes. Treatment outcomes were reviewed for both microbiologic and clinical outcomes. Bacteriological failure was defined as persistent positive culture of A. baumannii despite 72 hours of therapy. Clinical failure was defined as persistent fever, leukocytosis or death.
RESULTS: A total of 7 patients received doxycycline for multi-drug resistant A. baumannii infections in 2004. Five patients received monotherapy with doxycycline. Two patients received dual therapy with doxycycline and imipenem (A. baumannii isolates were intermediate to imipenem). All isolates were sensitive to doxycycline, colistin, and polymyxin B. A majority of patients (5/7, 71%) had A. baumannii bacteremia and/or pneumonia. One patient was clinically cured based on signs and symptoms; two patients had bacteriological cure but were clinical failures. The concern was raised that the patients might have colonization rather than true A. baumannii infection. Three patients (43%) died during treatment (2 patients had biological cure; 1 patient did not have any follow-up culture).
CONCLUSION: Previous case reports indicated that patients might respond to treatment with doxycycline if in vitro data shows sensitivity of A. baumannii to doxycycline. Our data was inconsistent with previous data. Larger studies are needed to confirm if doxycycline is a therapeutic option for the treatment of A. baumannii infections.

166E. Genome-wide expression profile analysis reveals genes differentially expressed in association with azole and echinocandin cross resistance in a clinical isolate of Candida glabrata. Teresa T. Liu, B.S.[1], *Kelly D. Earhart, B.S.*[1], Ramin Homayouni, Ph.D.[1], Thomas F. Patterson, M.D.[2], N. C. Villarreal, M.D.[2], Nathan P. Wiederhold, Pharm.D.[2], David S. Burgess, PharmD, FCCP[2], P. David Rogers, Pharm.D., Ph.D.[1]; (1)University of Tennessee, Memphis, TN; (2)Univ. TX College of Pharmacy at Austin and Univ. TX Health Sci. Ctr., San Antonio, TX.

PURPOSE: *Candida glabrata* has emerged as a major cause of mucosal and invasive fungal infection in the U.S. Recent reports have described the acquisition of azole and echinocandin resistance in clinical isolates. In an effort to identify genes potentially involved in azole and echinocandin resistance in *C. glabrata*, we examined changes in the gene expression profile between two isolates representing the acquisition of cross resistance to these two classes of antifungals.
METHODS: Isolates R-3562 and 03-2694 were originally isolated from a liver transplant patient with *C. glabrata* candidemia. These isolates are a matched set representing the acquisition of azole and echinocandin cross resistance during caspofungin therapy. Antifungal susceptibility testing was performed for amphotericin B (AMB), fluconazole (FLU), itraconazole (ITR), voriconazole (VOR), and caspofungin (CAS). Isolates were grown to mid-log phase and total RNA was extracted. Gene expression profiles were compared using a custom *C. glabrata* microarray. Differential expression was verified for selected genes by real-time RT-PCR.
RESULTS: MICs (µg/mL) for isolate R-3562 were: AMB 0.25, FLU 16, ITR 0.25, VOR 0.25, CAS 1.0. MICs for isolate 03-2694 were: AMB 0.125, FLU >64, ITR >16, VOR 8, CAS 64. We found 263 genes to be up-regulated and 191 genes to be down-regulated in isolate 03-2694. These included homologs of yeast genes of the pleiotropic drug resistance (PDR) network such as the up-regulation of *CDR1*, *PDH1*, *PDR1*, *YOR1*, *RSB1*, *RPN4*, *HSP12*, *RTA1*, *QDR2*, and *YPL088w*. Other up-regulated genes included those associated with lipid, fatty acid, and sterol metabolism (*SUT1*, *LAC1*, *LCB5*, *ARE1*, *CSR1*), cell structure (*SAC7*, *RHO5*) and cell wall maintenance (*DAN4*, *TIR1*, *DDR48*, *ECM38*, *FLO1*, *FLO5*, *FLO10*, *POG1*, *SKN1*).
CONCLUSIONS: These results implicate genes potentially involved in azole resistance through the *C. glabrata* PDR network, and suggest potential novel mechanisms of azole and echinocandin resistance in this pathogenic fungus.
Presented at the 45th Interscience Conference on Antimicrobial Agents and Chemotherapy, New Orleans, LA, September 21-24, 2005.

167. Evaluation of a febrile neutropenia algorithm with respect to empiric antifungal therapy in adult hematology/oncology patients. *Nadine Shehab, Pharm.D.*[1], Daryl D. DePestel, Pharm.D.[1], Bradley J. McCloskey, Pharm.D., candidate[2], Emily R. Stuntebeck, Pharm.D.[1], Curtis D. Collins, Pharm.D., M.S.[1], James G. Stevenson, Pharm.D.[1]; (1)The University of Michigan Health System and College of Pharmacy, Ann Arbor, MI; (2)The University of Michigan College of Pharmacy, Ann Arbor, MI.

BACKGROUND: An algorithm for the management of febrile neutropenia (FN) was implemented at the University of Michigan Health System recommending voriconazole as an alternative to liposomal amphotericin B (LAMB) for the empiric treatment of invasive fungal infections (IFIs) in persistently febrile adult hematology/oncology patients. Objectives: (1) To assess utilization of the new algorithm; and (2) to compare the safety and effectiveness of voriconazole to LAMB for management of FN in clinical practice.
METHODS: This was a single center, retrospective chart review. Patients who were initiated on LAMB (Group 1) or on voriconazole (Group 2) over a two-year period for FN were identified. Patients with a suspected or documented IFI at antifungal initiation were excluded.
RESULTS: Sixty-six patients were identified; 29 patients in each group were evaluable. Baseline variables (age, diagnosis, duration of ANC < 500, fever duration, use of antifungal prophylaxis, and duration of therapy) were similar. Three patients in each group experienced a breakthrough IFI. Resolution of fever was observed in 62% of patients in Group 1 versus 59% of patients in Group 2. Mean duration of therapy with intravenous voriconazole was 5.7 days, compared to 11.1 days with LAMB. More patients in Group 2 were alive at 7 days after end of therapy. In Group 1, infusion-related reactions and serum creatinine elevations were observed in 14% and 24% of patients, respectively. In Group 2, 7% and 10% of patients experienced visual disturbances and elevation in liver enzymes, respectively. Overall, results are comparable to outcomes previously reported in clinical trials.
CONCLUSIONS: An algorithm incorporating voriconazole for the management of FN was associated with comparable outcomes to LAMB and a lower incidence of adverse effects. Voriconazole may be considered as a viable and potentially safer alternative to LAMB for the empiric treatment of FN in this patient population.

168E. Antibacterial activity of colistin (C) and polymyxin B (PB) against multidrug-resistant (MDR) Pseudomonas aeruginosa **(PSA),** Alcaligenes xylosoxidans **(AX), and** Stenotrophomonas maltophilia **at a cancer center**. Kimberly A. Nguyen, Pharm., D.[1], *Elizabeth A. Coyle, Pharm., D.*[2], Vincent H. Tam, Pharm., D.[2], Kenneth V. I. Rolston, M. D.[1], Randall A. Prince, Pharm., D.[2]; (1)University of Texas M D Anderson Cancer Center, Houston, TX; (2)University of Houston College of Pharmacy, Houston, TX.

BACKGROUND: Increasing resistance of gram-negative bacteria in the immunocompromised host has renewed interest on the utilization of previously employed antimicrobial agents, such as C and PB. Despite the lack of reliable breakpoint data, the seriousness of the MDR issue warrants further research. The purpose of this study was to evaluate the activity of C and PB against MDR PSA, SM, and AX at a major Cancer Center.
METHODS: Clinical isolates of MDR PSA, SM, and AX from MD Anderson Cancer Center from September 2002 to July 2004 were retrieved. Isolate source and susceptibility profile were collected to determine MDR. MICs for C and PB were determined via E test. Quality controls were performed with PSA ATCC strain 27853. C and PB MIC 50s and MIC 90s against PSA, SM and AX were determined from susceptibility results.
RESULTS: Susceptibility testing was performed on 97 MDR isolates (63 PSA, 27 SM, 7 AX). Isolates were obtained from lung, blood, and urine specimens with PSA and SM primarily from the lung and AX the blood. The C MIC ranges were 0.5–32 µg/mL for PSA, 0.25->1024 µg/mL for SM, and 12-64 for AX. For PB, MIC ranges were 1-16 µg/mL for PSA, 0.125-24 µg/mL for SM and 8-24 µg/mL for AX. The C MIC 50s/90s against PSA, SM and AX were 8/24, 1.5/12, and 16/32 µg/mL, respectively. For PB, MIC 50s/90s against PSA, SM, and AX were 6/12, 1/4, and 8/12 µg/mL, respectively.
CONCLUSIONS: This study documents the in vitro activity of C and PB against clinical isolates at a Cancer Center. The data suggests good activity of C and PB against SM with more varied activity against PSA and AX. With limited options for the treatment of MDR gram-negative infections, more research is needed to determine the role of C and PB these infections,

particularly in the immunocompromised host.
Presented at the 44th Interscience Conference on Antimicrobial Agents and Chemotherapy, Washington, D.C., October 30–November 2, 2004.

169E. The efficacy and safety of tigecycline in the treatment of complicated intra-abdominal infections: results of pooled clinical trial data. *Evelyn J. Ellis-Grosse, PhD*[1], Timothy Babinchak, MD[1], Nathalie Dartois, MD[2], Gilbert M. Rose, MD[1], Evan Loh on behalf of the 301 and 306 Study Groups, MD[1]; (1)Wyeth Research, Collegeville, PA; (2)Wyeth Research Paris, Paris, France.

PURPOSE: To evaluate the pooled results of 2 phase 3, multicenter, double-blind, randomized trials that compared the clinical efficacy and safety of tigecycline monotherapy with imipenem/cilastatin (IMI/CIL) in 1,642 adults with complicated intra-abdominal infections (cIAI).
METHODS: One study was conducted in 96 centers in 17 countries (North America, Europe, Latin America, India, and Asia), and other study was conducted in 94 centers (27 countries in Europe, South Africa, and Asia). Patients were randomly assigned to receive either tigecycline (100 mg initial dose then 50 mg intravenously every 12 hours) or IMI/CIL (500/500 mg intravenously every 6 hours) for 5 to 14 days. The population was hospitalized adult patients who were candidates for or had undergone a laparotomy, laparoscopy, or percutaneous drainage of an intra-abdominal abscess and had a known or suspected diagnosis of cIAI. The primary endpoint was the clinical response at the test-of-cure visit (12 to 42 days after therapy) in the co-primary endpoint microbiologically evaluable (ME) and microbiologically modified intent-to-treat (m-mITT) populations. The noninferiority efficacy of tigecycline compared with IMI/CIL was evaluated for clinical and microbiologic responses by using a two-sided 95% confidence interval (CI) for the true difference in efficacy (tigecycline minus IMI/CIL).
RESULTS: For the ME group, clinical cure rates were 86.1% (441/512) for tigecycline versus 86.2% (442/513) for IMI/CIL (95% CI –4.5, 4.4; p<0.0001 for noninferiority). Clinical cure rates in the m-mITT population were 80.2% (506/631) for tigecycline versus 81.5% (514/631) for IMI/CIL (95% CI –5.8, 3.2; p<0.0001 for noninferiority). Nausea (24.4% tigecycline, 19.0% IMI/CIS [p=0.01]), vomiting (19.2% tigecycline, 14.3% IMI/CIS [p=0.008]), and diarrhea (13.8% tigecycline, 13.2% IMI/CIS [p=0.719]) were the most frequently reported adverse events.
CONCLUSION: This pooled analysis of 2 phase 3 clinical trials demonstrates that tigecycline was efficacious and well-tolerated in treatment of patients with cIAIs and statistically noninferior to IMI/CIL.
Presented at the Biennial Congress of the International Society of Chemotherapy, Manila, Philippines, June 4-6, 2005.

170E. Tigecycline is safe and effective in the treatment of skin and skin structure infections: results of two double-blind phase 3 comparison studies with vancomycin/aztreonam. *Evelyn J. Ellis-Grosse, PhD*[1], Timothy Babinchak, MD[1], Nathalie Dartois, MD[2], Gilbert M. Rose, MD[1], Evan Loh on behalf of the 300 and 305 cSSSI Study Groups, MD[1]; (1)Wyeth Research, Collegeville, PA; (2)Wyeth Research Paris, Paris, France.

PURPOSE: Two phase 3, randomized, double-blind studies were conducted in hospitalized patients with complicated skin and skin structure infections (cSSSI) to determine tigecycline safety and efficacy compared with vancomycin/aztreonam (V/A).
METHODS: North American/South American study (NA) was conducted in 53 centers in 8 countries. Worldwide (EU) study was conducted in 65 centers in 21 countries. Patients received either tigecycline or V/A for up to 14 days. Primary objective was to evaluate clinical efficacy of tigecycline versus V/A. Secondary objectives were microbiological efficacy and in vitro susceptibility to tigecycline of a range of bacteria that cause cSSSI. Physical examination, laboratory results, and adverse events (AE) were recorded.
RESULTS: Patient numbers were similar: 537 and 520 patients in NA and EU studies (clinical modified intent-to-treat, c-mITT), 397 and 436 were clinically evaluable (CE) and 228 and 312 were microbiologically evaluable, respectively. In NA study, cure rates in the c-mITT and CE at test-of-cure (TOC) were similar in tigecycline (76% [95%CI 69.9, 80.4] and 83% [77.0, 87.9]) and V/A (77% [71.3, 81.9] and 82% [76.3, 87.4]) groups. Cure rates in the EU c-mITT and CE at TOC were 84% [79.3, 88.5] and 90% [84.9, 93.3] for tigecycline and 87% [82.1, 90.7] and 94% [90.4, 97.1] for V/A. Percentages of patients with microbiological eradication at subject level at end of therapy were similar in NA (75% [67.9, 80.8] for tigecycline and 72% [64.6, 78.5] for V/A) as in EU (73% [95% CI 65.1, 79.2] and 81% [73.8, 87.0], respectively). In both studies, overall frequency of AEs and treatment-emergent AEs were similar in the 2 groups. Patients treated with tigecycline had more nausea and vomiting events; however, rash and increased ALT and AST levels were more frequent in V/A.
CONCLUSION: Tigecycline monotherapy is as safe and efficacious as V/A combination in the treatment of cSSSI.
Presented at the Western Pacific Congress on Chemotherapy and Infectious Diseases, Bangkok, Thailand, December 1-5, 2004.

171E. Pharmacokinetic/pharmacodynamic profile of amphotericin B deoxycholate and the relationship between interferon-gamma and interleukin-10 and mycological efficacy in invasive pulmonary aspergillosis. *Nathan P. Wiederhold, Pharm.D.*[1], Vincent H. Tam, Pharm.D.[2], Jingduan Chi, Ph.D.[2], Randall A. Prince, Pharm.D.[2], Dimitrios P. Kontoyiannis, M.D., Sc.D.[3], Russell E. Lewis, Pharm.D.[2]; (1)University of Texas at Austin & University of Texas Health Science Center at San Antonio, San Antonio, TX; (2)University of Houston College of Pharmacy, Houston, TX; (3)University of Texas M.D. Anderson Cancer Center, Houston, TX.

PURPOSE: We conducted an in vivo dosage-fractionation study to characterize the pharmacodynamic/pharmacokinetic (PK/PD) parameter most closely associated with amphotericin B deoxycholate (AMBd) efficacy in invasive pulmonary aspergillosis (IPA). Interferon-gamma (IFNg) and interleukin-10 (IL-10) concentrations in bronchial alveolar lavage (BAL) fluid were also determined to assess their relationship to mycological response.
METHODS: Immunosuppressed mice were inoculated intranasally with *Aspergillus fumigatus* conidia. AMBd plasma concentrations measured by HPLC following single intraperitoneal doses (0.25, 1.0, and 3.0 mg/kg) were analyzed by nonparametric population pharmacokinetic analysis. Three dosage groups (0.5, 0.75, and 1.0 mg/kg) fractionated into 3 dosing intervals (q8, q24, or q72 hr) were used to evaluate the PK/PD effects (C_{max}/MIC, AUC/MIC, Time>MIC) at clinically achievable exposures. Lungs were harvested and pulmonary fungal burden was measured by quantitative real-time polymerase chain reaction. IFNg and IL-10 concentrations from BAL fluid were measured by enzyme-linked immunosorbent assay. Differences in fungal burden and survival were assessed for significance by analysis of variance and Kaplan-Meier analysis, respectively. Linear regression analysis was used to assess relationships between fungal burden, survival, and IFNg/IL-10 ratios.
RESULTS: Concentration-dependent reductions in pulmonary fungal burden compared to controls were observed in each dosage-fractionation group with the dose resulting in the highest C_{max} concentration ($p<0.05$) and were maximized at a C_{max}/MIC ratio of 2.4. Survival was also improved in a concentration-dependent fashion. Linear regression analysis demonstrated that reductions in pulmonary fungal burden and improvements in survival were associated with higher IFNg/IL-10 ratios ($r^2 = 0.85$ & 0.78, respectively).
CONCLUSIONS: AMBd demonstrated concentration-dependent pharmacodynamics in the treatment of IPA, with C_{max}/MIC the parameter most closely associated with efficacy. Increasing IFNg/IL-10 ratios were also associated with mycological efficacy.
Presented at the 44th Interscience Conference on Antimicrobial Agents and Chemotherapy, Washington, D.C., October 30–November 2, 2004.

172. Utility of antibiotic synergy studies in patients with cystic fibrosis. *William L. Musick, PharmD*[1], Jennifer L. Barrow, PharmD[1], Dennis M. Williams, PharmD[2], Ralph H. Raasch, PharmD[2]; (1)University of North Carolina Hospitals, Chapel Hill, NC; (2)UNC-Chapel Hill, School of Pharmacy, Chapel Hill, NC.

PURPOSE: While there exists no published literature linking the use of antibiotic synergy testing (AST) to improve clinical outcome in cystic fibrosis (CF) exacerbations, these *in vitro* assays are becoming more commonplace. Although prospective outcome studies are underway, central to the use of these assays are their interpretation and application. This retrospective cohort study seeks to evaluate the clinical utilization of AST at a single CF center.
METHODS: Subjects were identified by ICD-9 code from hospital admission data. Subsequently, microbiology data (culture dates, isolate, and two-drug AST results) and demographic information were gathered from the electronic medical record. All patients were >16 years old, admitted to a medicine service and had a history of known colonization with either multi-drug resistant (MDR) *Pseudomonas* or *Burkholderia*. Subjects were excluded if respiratory cultures were not obtained upon admission, admission was for other than a CF exacerbation, or records were incomplete. The empiric antibiotic regimen was judged either appropriate or inappropriate based on historical AST results relevant to the date of admission.
RESULTS: Two hundred twenty-nine admissions were evaluated between 1/1/2003 and 12/31/2004, with 48 of these meeting inclusion criteria (19 *Burkholderia* and 29 *Pseudomonas*). AST yielded synergistic combinations in 18% (4 of 22) and 44% (14 or 32) of *Burkholderia* and *Pseudomonas* isolates, respectively. Chloramphenicol was a synergistic agent in 50% of *Burkholderia* AST. Empiric regimens were appropriate in 32% of *Burkholderia* admissions and 66% of *Pseudomonas* admissions. Antibiotic allergies influenced the regimen in only 2 (10%) and 1 (3%) admissions in the *Burkholderia* and *Pseudomonas* cohorts, respectively.
CONCLUSION: Two-drug AST are unlikely to yield true synergistic combinations of antibiotics in MDR isolates from CF patients, especially among *Burkholderia spp*. Further, results from AST in *Burkholderia* isolates are often not utilized appropriately when constructing empiric antibiotic regimens.

173. Methicillin-resistant Staphylococcus aureus **(MRSA) in Riyadh, Saudi Arabia: where do we stand?** Manal M. Baddour, MD, PhD.[1], *Amal J. Fatani, PhD*[1], Manal M AbuElKhair, B.pharm[1], Marie F. Bohol, B.Sc[2], Mohammad A. AlAhdal, PhD[2]; (1)King Saud University, Riyadh, Saudi Arabia, Riyadh 11459, Saudi Arabia; (2)King Faisal Specialist Hospital & Research Centre, Riyadh 11459, Saudi Arabia.

Methicillin-resistant Staphylococcus aureus (MRSA), is a major pathogen. Few studies have been done to report the prevalence of MRSA in Saudi Arabia.
PURPOSE:(1) To track and clarify the prevalence of MRSA and to identify major lineages of MRSA present among major hospitals in Riyadh, Saudi Arabia. (2) To initiate a national database of MRSA Pulsed Field Gel Electrophoresis (PFGE) profiles that would help identify major lineages of MRSA present in Riyadh, Saudi Arabia, to be used as a clinical tool to investigate suspected outbreaks and to evaluate nosocomial transmission. (3) To compare between PFGE outcomes using two different techniques and choose the most appropriate.
METHODS: (1) Isolates were identified as MRSA strains according to The National Committee for Clinical Laboratory Standards (NCCLS) guidelines. (2) Molecular typing of MRSA in major hospitals in Riyadh, Saudi Arabia by Pulsed Field Gel Electrophoresis (PFGE) using SmaI enzyme which is the "gold standard" for typing MRSA. (3) A comparative study has been carried out between PFGE according to the Matushek technique and the standardized European technique. (4) Surveillance of MRSA with decreased susceptibility to vancomycin according to National Committee for Clinical Laboratory Standards (NCCLS) guidelines
RESULTS: (1) 300 isolates have been identified as MRSA from 7 major hospitals. (2) PFGE was carried out for the secured isolates and correlation between patterns is being studied. (3) The Matushek PFGE has been found to be superior to the standardized European PFGE technique and hence was adopted as the standard technique throughout the study. (4)To date, none of the studied isolates has been found to have decreased sensitivity to vancomycin.
CONCLUSIONS: pending. Acknowledgements: The authors wish to acknowledge KFSHRC for providing the means for carrying out this study. We also acknowledge KACST for the grant approval for funding this project.

174. Single-dose comparative bioavailability study of film-coated and sugar-coated ethionamide tablets in healthy volunteers. *Joan Korth-Bradley, PharmD, PhD*, Philip Mayer, PhD, Debra Mansfield, MT(ASCP), Hal Tucker, DO, David Wu, MD; Wyeth Research, Collegeville, PA.

PURPOSE: Trecator-SC (ethionamide sugar-coated) tablets have been reformulated to film-coated tablets (Trecator). A randomized, single-dose, two-way crossover study was conducted to compare the relative bioavailability of the reformulated and reference formulations.
METHODS: After providing consent, and screening procedures, 40 healthy fasting subjects randomly received a single 250-mg dose of either the reformulated or reference formulation. Serial blood samples were collected before and 0.5, 1, 1.5, 1.75, 2, 2.25, 2.5, 3, 4, 5, 6, 8, 10, 12, 16, and 24 hours post dose. Seven days later, subjects fasted, received the other formulation, and serial blood samples were collected as before. The blood samples were processed to provide plasma samples, which were frozen until assay. Ethionamide concentrations were measured using a validated LC/MS/MS method with the lower limit of quantitation of 50 ng/mL. Pharmacokinetic parameters were determined using noncompartmental methods with subsequent evaluation for bioequivalence using SAS.
RESULTS: A total of 40 subjects (37 males, 3 females; mean age 28 years; mean weight 74 kg) completed the study. Seven subjects reported 10 adverse events (5 with each dosage form) that were all of mild severity and possibly related to drug treatment. None resulted in discontinuation from the study. The pharmacokinetic parameters (mean ± sd) observed were: Reformulated: C_{max} 2160 ± 614 ng/mL; t_{max} 1.0 ± 0.5 hr; ke 0.369 ± 0.053 h^{-1}; $t_{1/2}$ 1.92 ± 0.272 h; AUC 7668 ± 1688 ng•h/mL Reference: C_{max} 1484 ± 636 ng/mL; t_{max} 1.5 ± 0.9 hr; ke 0.232 ± 0.114 h^{-1}; $t_{1/2}$ 4.06 ± 2.52 h; AUC 6594 ± 1764 ng•h/mL
CONCLUSION: Comparing AUC values, the reformulated product and the reference product were bioequivalent. The maximum concentrations observed for the reformulated product were higher, but more consistent (CV 28%) compared with the reference formulation (CV 43%).

175E. Impact of NCCLS M39-A guideline recommendations for duplicate isolate removal on Pseudomonas aeruginosa **antibiogram data: a four-year analysis**. *Samaneh T. Wilkinson, PharmD*, Melinda K. Lacy, PharmD, Rebecca T. Horvat, PhD, Dennis W. Grauer, PhD, Brian J. Barnes, PharmD, Rick Couldry, MS; University of Kansas Medical Center, Kansas City, KS.

PURPOSE: Recent guidelines (NCCLS M39-A) have directed that antibiogram data be tabulated using only the first isolate of a given species per patient per year or analysis period while omitting all duplicates. Pseudomonas aeruginosa (PSA) is frequently identified in successive cultures from the same patient. Inclusion of all isolates may lead to biased reporting of lower susceptibility rates on hospital antibiograms since results would be skewed to those most heavily cultured. This study analyzed the number of inpatient PSA duplicate isolates and determined the impact of repeat isolates on reported susceptibility rates for imipenem (IMI), ceftazidime (TAZ), ciprofloxacin (CIP), and gentamicin (GENT) over a recent 4-year period at our institution.
METHODS: Data for PSA was transferred from the laboratory computer (MISYS) into Microsoft Access to detect duplicate patient isolates. Susceptibility rates were calculated for each year and collectively by using all inpatient isolates and then by eliminating all duplicates. Rates of IMI, TAZ, CIP, and GENT PSA susceptibility (all isolates vs. elimination of duplicates) were statistically compared by the χ^2 test with Yates Correction.
RESULTS: Cumulative results for the 4-year period analyzed indicate that % susceptible PSA rates were as follows for all isolates vs. duplicates excluded: IMI 70% (880/1259) vs. 80% (580/727), p<0.0001; TAZ 69% (814/1180) vs. 76% (546/715), p=0.0007; CIP 67% (804/1200) vs.74% (493/670), p=0.0036; and GENT 72% (857/1191) vs. 84% (558/668), p<0.0001.
CONCLUSIONS: These data show that susceptibility of common antipseudomonal antibiotics is significantly higher when duplicate PSA strains are eliminated as recommended in the NCCLS M39-A guidelines. Elimination of duplicate PSA strains results in a more accurate reflection of IMI, TAZ, CIP, and GENT-susceptibility for PSA and may ultimately impact appropriate empiric antibiotic selection.
Presented at the 45th Interscience Conference on Antimicrobial Agents and Chemotherapy, New Orleans, LA, September 21-24, 2005.

176. Mupirocin resistance in clinical methicillin-resistant Staphylococcus aureus. *Kerry L. LaPlante, Pharm, D.*, Kia Lor, B.S.; University of Rhode Island and Veterans Affairs Medical Center, Providence, RI.

PURPOSE: Nasal decolonization of methicillin-resistant Staphylococcus aureus (MRSA) is recommended in surgical and dialysis patients. Mupirocin, a topical antibiotic is the compound of choice in decolonizing these patients. Mupirocin resistance in MRSA is currently unknown because mupirocin resistance testing is not routinely conducted in clinical laboratories. This emphasizes the need to evaluate mupirocin resistance in clinical Staphylococcus aureus isolates. We examined the inhibitory activity of mupirocin against several clinical strains of MRSA.
METHODS: One hundred randomly collected, clinical strains of MRSA were obtained from patients at the VAMC in Providence, RI. These strains were collected and provided by the clinical microbiologist at the VAMC, Providence, RI. All bacteria were previously isolated and stored in 20% glycerol, and frozen at -80 ∫C prior to use. MIC's were performed using methodologies described by CSLI (formally NCCLS) guidelines.
RESULTS: Of the 100 clinical MRSA isolates, 10.1% were from blood, 20.2% from nares, 24.2% from tissue, 27.3% from sputum, 12.1% from urine and 6.1% were from other sites (i.e., ear swab, catheter site, ect.). Two isolates, both from nares demonstrated high-level mupirocin resistance with a minimum inhibitory concentration (MIC) of >1024mg/L and one isolate from a urine specimen demonstrated low-level resistance with a MIC of 12mg/L. The rest of the isolates were susceptible with MIC's ranging between 0.094 to 2mg/L. The MIC90 of all isolates tested was 1.5mg/L.
CONCLUSIONS: Mupirocin resistance is present in clinical Staphylococcus aureus isolates. If this topical antibiotic is recommended for MRSA decolonization in patients, it is important that clinical laboratories conduct resistance testing.

177E. Successful treatment of catheter-related bacteremia with daptomycin: report from a registry. Yoav Golan, MD[1], Rene Russo, PharmD[2], *Kenneth C. Lamp, PharmD*[2], Lawrence Friedrich, PharmD[2]; (1)Tufts-New England Medical Center, Boston, MA; (2)Cubist Pharmaceuticals, Mt. Pleasant, SC.

PURPOSE: Catheter-related bacteremia (CRB) is the most common form of healthcare-associated bacteremia and is frequently caused by antibiotic-resistant Gram positive bacteria for which treatment options are limited. We describe the effectiveness of daptomycin (DAP), a novel lipopeptide antibiotic with rapid bactericidal activity including against stationary phase bacteria, in the therapy of CRB.
METHODS: Using a standard data-collection form, clinicians in the Cubicin® Outcomes Registry and Experience (CORE) at 45 institutions collected data on patients with CRB treated with DAP. Data included demographics, comorbidities, disease severity, pathogens and clinical and outcomes.
RESULTS: Of 92 treated patients, response to therapy was determined in 71 patients who were included in the analysis. A high number of patients were in the ICU (35%); 51% were female; 63% were >50 years. Comorbidities included cardiovascular disease (42%), malignancy (35%), chronic renal failure requiring dialysis (31%), diabetes mellitus (20%), immuno-suppression (13%). Infecting pathogens included MRSA (31%), coagulase-negative staphylococci (31%), and VRE (25%). 67% received concomitant antibiotics, most frequently aminoglycosides (24%) and cephalosporins

(23%). Clinical success (defined as cure or improved) was achieved in 89% of patients (63), of which 71% (45) were cured. The likelihood of a favorable response was not associated with type of comorbidities, pathogens, or ICU stay. The median time to response to therapy was 2 days and the average length of therapy was 14 days.
CONCLUSIONS: In this cohort of critically ill patients with severe underlying comorbidities, treatment of CRB with daptomycin was successful in 89%. Of particular interest is the high success rate in treating VRE-related CRB, which was not reported previously.
Presented at the 43rd Annual Meeting of the Infectious Diseases Society of America, San Francisco, CA, October 6-9, 2005.

178. Characterization of community-acquired methicillin resistant Staphylococcus aureus **(CA-MRSA) infections and outcomes**. *Kari A. McCracken, Pharm.D.*, Krystal K. Haase, Pharm.D., Ronda L. Akins, Pharm.D.; Texas Tech University Health Sciences Center School of Pharmacy, Amarillo, TX.

PURPOSE: To compare patients with CAMRSA to those with community acquired methicillin sensitive *S. aureus* (MSSA) infections; and to identify factors that affect presentation and outcome.
METHODS: Patients were identified from laboratory records. All patients with *S. aureus* cultures taken ≤48 hours from admission and no risk factors for hospital-acquired MRSA were included in this population-based analysis. Demographic data, potential risk factors, type and severity of infection, culture, susceptibility, and antibiotic selection were documented. Treatment outcomes (length of hospitalization, surgical intervention) were recorded. Patients were screened for readmission at 30 days. Data were analyzed to determine predictors of CAMRSA. Treatment selection was correlated to patient outcomes.
RESULTS: 900 medical records were screened. CAMRSA was more common than MSSA (8.1% vs. 5.8%). Of the 52 MSSA and 73 suspected CAMRSA infections included in this analysis, most occurred in males (62% vs. 58%) with wound being the most common infection site (69%). Patients with CAMRSA were older (median 47 vs. 38 years), although children constituted 18% of both groups. Documented necrosis (38% vs. 34%) was slightly more common in CAMRSA patients. Length of stay was similar (9 vs. 8 days), but more CAMRSA patients required surgical intervention (74 vs. 52%). The percent susceptibilities for CAMRSA isolates were: clindamycin 86%, erythromycin 5%, levofloxacin 48%, trimethoprim/sulfamethoxizole 100%, and tetracycline 97%. Two documented treatment failures occurred due to non-compliance with outpatient IV antibiotics. Treatment success occurred in 98% of patients despite 33% of patients treated with "inactive" antibiotics.
CONCLUSIONS: CA-MRSA infections are an emerging problem that may more frequently affect males and older patient than traditionally are seen with MSSA. Differentiating MSSA and CAMRSA is difficult. CAMRSA should be suspected in cases of necrosis requiring surgical debridement. Treatment failures were infrequent in this study population, limiting the ability to correlate treatment selection and outcomes.

179E. Daptomycin in the treatment of non-catheter related bacteremia. George Sakoulas, MD[1], Rene Russo, PharmD[2], Kenneth C. Lamp, PharmD[2], *Lawrence Friedrich, PharmD*[2]; (1)New York Med. Coll., Valhalla, NY; (2)Cubist Pharmaceuticals, Mt. Pleasant, SC.

PURPOSE: The emergence of multi-drug resistance has limited clinicians' therapeutic options against Gram positive bacteremia. Daptomycin (DAP) is a novel lipopeptide antibiotic with potent in vitro Gram-positive activity, yet data describing the clinical effectiveness of DAP for the treatment of non-catheter related bacteremia (nCRB) are limited.
METHODS: The Cubicin Outcomes Registry and Experience is a Phase IV retrospective analysis of patient clinical outcomes treated with DAP (45 institutions). Only those patients with nCRB were evaluated.
RESULTS: Seventy-six patients were identified with the following demographics: (male 54%, female 46%; age >50 yrs 79%; infection developed in a nosocomial setting 74%). Comorbidities included diabetes (17%) and renal failure (29%). DAP doses ranged from 2.5 to 10 mg/kg QD. The most frequent dosing regimens were 4mg/kg QD (51%), and 6mg/kg QD (26%). The median duration of DAP therapy was 8.5 days. The most common organisms cultured prior to DAP were Enterococcus spp. (36%, of which 70% were VRE), S. aureus (36%, of which 85% were MRSA), and coagulase-negative staphylococci (22%). 78% of patients received concomitant antibiotic therapy, most commonly with aminoglycosides (22%), cephalosporins (25%) or quinolones (20%). In those patients in whom clinical outcome could be determined (n=55), cure, improvement, and failure were reported in 56%, 33%, and 11%, respectively. Time to clinical response occurred in a mean of 4.6 days (n=29). The presence of low creatinine clearance (<30ml/min) was associated with a higher rate of treatment failure (20% vs. 3%, p=0.06).
CONCLUSIONS: DAP provided effective therapy for the treatment of Gram positive nCRB in a sample of patients that included a sizeable subset of infections with multi-drug resistant pathogens. While direct head-to-head comparison studies of DAP versus current standard therapies for nCRB are in progress, these data suggest that DAP shows promise in the treatment of Gram positive nCRB.
Presented at the 43rd Annual Meeting of the Infectious Diseases Society of America, San Francisco, CA, October 6-9, 2005.

180. Daptomycin for the treatment of enterococcal bacteremia: post marketing experience in a registry. Joseph C. Chan, MD[1], Kenneth C Lamp, PharmD[2], *Lawrence Friedrich, PharmD*[2], Rene Russo, PharmD[2]; (1)Mount Sinai Med. Ctr., Miami, FL; (2)Cubist Pharmaceuticals, Mt. Pleasant, SC.

PURPOSE: Daptomycin (DAP) is approved for complicated skin and skin structure infections. Despite potent in vitro activity for Enterococcus sp., there is limited data in enterococcal infections.
METHODS: Cubicin® Outcomes Registry and Experience (CORE) is a retrospective observational chart review (45 institutions) to quantitate characteristics and clinical outcome of patients (pts) receiving DAP. Of the 1160 pts in CORE, 114 had Enterococcus sp. pathogens with infections other than lone skin involvement and received > 3 days of DAP. Nonevaluable pts were excluded (N=23, 20%) and 91 pts with an outcome assigned were further divided into a group (BAC) with definite bacteremia and all others (NBAC).
RESULTS: There were 51 pts in BAC and 40 in NBAC. The two groups were similar in demographics except BAC were older with more sepsis, cardiac arrhythmias, valvular heart disease (dz), anemia/hem dz, and cancer. NBAC had more diabetes and fractures/ orthopedic procedures. The most common infections were (BAC: catheter-related, 45%, and noncatheter-related, 31%, bacteremia and endocarditis, 24%) and (NBAC: osteomyelitis, 25%; UTI, 18%; necrotizing infection, 18%). Vancomycin-resistant Enterococcus sp. were high in both groups; BAC 65%, NBAC 60%. 26% BAC and 33% NBAC reported polymicrobial infections. A high percentage received antibiotics (abx) prior to DAP in both groups; BAC 98%, NBAC 75%. The initial DAP dose was ≥6mg/kg in BAC 35% and NBAC 30%. 75% of BAC and 70% of NBAC received concomitant abx with DAP. The mean duration of DAP was 19 days and similar for both groups. The reported success (cure and improved) and failure rates were; BAC: 94%, 6%; NBAC: 90%, 10%. There were 7 BAC and 4 NBAC pts switched to alternative abx at the end of DAP.
CONCLUSIONS: DAP appears to have clinical utility treating enterococcal infections. Additional studies of DAP for this difficult pathogen are warranted.

181E. Endocarditis treated with daptomycin: experience from a registry. Donald P. Levine, MD[1], *Kenneth C. Lamp, PharmD*[2]; (1)Wayne State Univ., Detroit, MI; (2)Cubist Pharmaceuticals, Halstead, KS.

PURPOSE: Daptomycin (DAP) is approved for treatment of skin and skin structure infections due to Gram-positive pathogens. There is limited data available for DAP in infections such as endocarditis.
METHODS: Cubicin® Outcomes Registry and Experience (CORE) is a retrospective observational chart review (45 institutions) to quantitate characteristics and clinical outcome of patients (pts) receiving at least one dose of DAP. Investigators completed case report forms which collected demographic, disease state, clinical and microbiologic data. Outcomes were defined using standard definitions; there was no follow up beyond the initial treatment period. Nonevaluable pts had insufficient information available to the investigator. This analysis describes the pts with endocarditis.
RESULTS: Of 1160 pts in CORE, 49 were diagnosed with endocarditis, 26 left-sided (LE), 11 right-sided (RE) and 12 with right and left-sided disease (combined with LE for analysis). Many had co-morbid conditions. Renal failure was most common (55% had a CrCl < 30 ml/min; 29% on hemodialysis). Staphylococcus aureus (59%; MRSA 83%) and Enterococcus sp. (29%; VRE 43%) were the commonest pathogens. Most pts (88%) received other antibiotic therapy before beginning DAP. The initial DAP dose was ≥6 mg/kg in 63% LE and 27% RE. For those reported as cured or improved, the mean duration of DAP was 29 and 26 days for LE and RE, respectively. 11 pts, including 4 who were reported cured, were switched to other antibiotics to conclude treatment (vancomycin 6, cephalosporin 2, 1 each of linezolid, penicillinase-resistant penicillin and unknown). The combined cure and improved rates were 66% LE and 55% RE. The failure rate was 8% LE and 9% RE. A high percentage (29%) were nonevaluable.
CONCLUSIONS: In this non-randomized sample of IE pts, including many with renal failure and other co-morbid conditions, the outcomes justify further clinical trials.
Presented at the 43rd Annual Meeting of the Infectious Diseases Society of America, San Francisco, CA, October 6-9, 2005.

182. Population susceptibility profiles (PSPs) for P. aeruginosa **strains with overproduction of different Mex-Opr multidrug efflux pumps**. *Sarah M. McCabe, B.Sc.*, Kara L. Smith, B.Sc., Jeffrey R. Aeschlimann, Pharm.D.; University of Connecticut School of Pharmacy, Farmington, CT.

PURPOSE: *P. aeruginosa* causes a variety of human infections. Strains that

overproduce 3-protein Mex-Opr efflux pumps expel all fluoroquinolone antibiotics and have been isolated from patients. Whether efflux pump overproduction (EPO) is consistent amongst all cells is unknown. Heterogeneous EPO may not be detected using standard clinical laboratory methods. Accordingly, we performed population susceptibility profiles (PSPs) on strain pairs of *P. aeruginosa* with EPO to determine resistance heterogeneity.
METHODS: PAO1 (*P. aeruginosa* genome project strain, no EPO) and four mutants overproducing MexAB-OprM (PAO1-ABM), MexCD-OprJ (PAO1-CDJ), MexEF-OprN (PAO1-EFN), or MexXY-OprM (PAO1-XYM) were evaluated. Baseline minimum inhibitory concentrations (MICs) were determined via E-tests®. PSPs were determined in duplicate by plating an inoculum of 10^8 cells/ml of test strains on agar containing $^1/_4$ to 2xMIC of ciprofloxacin (CIP) or levofloxacin (LEV). Viable colony counts were compared to the total plated inoculum.
RESULTS: Baseline CIP/LEV MICs for PAO1, PAO1-ABM, PAO1-CDJ, PAO1-EFN, and PAO1-XYM were 0.125/0.25, 0.19/1.0, 0.25/0.75, 0.25/1.0, and 0.25/0.75 mg/L. CIP PSPs were homogeneous up to $^3/_4$ x MIC for all strains. At 1xMIC there was ≥3 $\log_{10}$ reduction in viable inoculum for PAO1, PAO1-CDJ, and PAO1-XYM. At 2xMIC, CIP inhibited detectable growth of only the PAO1-CDJ strain; there was a ≥5 $\log_{10}$ growth reduction in all strains except for PAO1-EFN(1.3 $\log_{10}$ reduction). LEV PSPs were heterogeneous at $^1/_2$ x MIC for PAO1-CDJ and PAO1-EFN and at $^3/_4$ x MIC for PAO1-ABM and PAO1-XYM. At 1xMIC there was ≥3 $\log_{10}$ reduction in viable inoculum only for the PAO1-CDJ strain. LEV inhibited detectable growth at 2xMIC for all strains excluding PAO1. Overall, EPO affected CIP PSPs more than LEV PSPs.
CONCLUSION: EPO resistance was not consistently homogeneous and varied by pump type and antibiotic. Confirmation of these results in additional strains would support development of additional methods to detect EPO in clinical isolates of *P. aeruginosa*.

183. Impact of linezolid compared with vancomycin on the length of stay of elderly patients with complicated skin and soft-tissue infections due to suspected or proven MRSA. *Marianne McCollum, R.Ph., Ph.D., BCPS*[1], Larry Z. Liu, MD, PhD[2]; (1)University of Colorado School of Pharmacy, Denver, CO; (2)Pfizer Inc., New York, NY.

PURPOSE: To compare length of stay (LOS) between linezolid and vancomycin for the treatment of complicated skin and soft-tissue infection (cSSTI) due to suspected or proven methicillin-resistant Staphylococcus aureus (MRSA) in elderly U.S. patients.
METHODS: Data were obtained for 163 subjects 65 years of age and older from 717 subjects treated in the United States as part of a multinational, open-label, comparator-controlled study enrolling 1200 hospitalized subjects with cSSTIs due to suspected or proven MRSA. Subjects were randomized 1:1 to receive either linezolid 600 mg q12h intravenous (IV) or oral (PO), or vancomycin 1 g q12h IV for 7-21 days. LOS was compared for the intent-to-treat (ITT) group and patients with confirmed MRSA.
RESULTS: Linezolid significantly reduced LOS compared with vancomycin in the ITT group (n=163; mean 3.5 days shorter, P=0.0004) and LOS trended lower in the MRSA patients (n=65; mean 3.9 days shorter, P=0.1988). Clinical cure rates were comparable in the linezolid and the vancomycin groups in both the ITT (88.7% vs 81.3%, P = 0.2392) and MRSA (80.0% vs 71.4%, P = 0.5124) populations. IV duration was significantly shorter for linezolid compared with the vancomycin in both the ITT (1.4 days vs 10.9 days) and MRSA populations (1.3 days vs 13.9 days, both P < 0.0001). After adjusting for other factors, patients in the ITT population who received linezolid were 57% less likely to have a LOS > 7 days (OR=0.43, 95% CI 0.21-0.87) than were patients who received vancomycin. Factors associated with LOS > 7 days included history of chronic renal failure, malnutrition, and a clinical diagnosis of infected ulcer.
CONCLUSION: Linezolid has the potential to reduce patient LOS and IV duration without affecting clinical outcomes among elderly patients with cSSTI due to suspected or proven MRSA.

184. Increased prevalence of multi-drug resistant E. coli **in clinical urinary isolates.** *Donna R. Burgess, RPh*[1], Christopher R. Frei, PharmD, MSc, BCPS[2], Debra A. Garza, RPh, MBA[1], David S. Burgess, PharmD, FCCP[2]; (1)Univ. TX College of Pharmacy at Austin and Methodist Hospital Dept. of Pharmacy, San Antonio, TX; (2)Univ. TX College of Pharmacy at Austin and Univ. TX Health Sci. Ctr. Dept. of Medicine and Pharmacology, San Antonio, TX.

PURPOSE: The therapeutic management of urinary tract infections (UTIs) has become increasingly complex due to the rapid emergence of antibiotic resistance among gram-negative bacteria. This study evaluated the susceptibility profile of several antibiotics against the most common cause of UTIs.
METHODS: We evaluated all hospitalized adult patients discharged from a private health-system between Jan-Dec 2002 and July 2003-June 2004 with a primary diagnosis of UTI (DRG 320 and 321). Only patients with a positive urine culture for *E. coli* were included in this analysis. When a single patient had multiple cultures within a year, only the first *E. coli* isolate was evaluated. The susceptibility profiles for ampicillin (AMP), ceftriaxone (CRO), gentamicin (GEN), levofloxacin (LEV), and trimethoprim/sulfa-methoxazole (SXT) were recorded. Multi-drug resistance was defined as non-susceptible to ≥3 antibiotics. All isolates were tested for production of ESBL according to CLSI (formerly NCCLS) guidelines.
RESULTS: Overall, 158 (64 in 2002, 94 in 2003-04) patients with a non-duplicate *E. coli* isolate were identified. The age (mean ± SD) was 64.5 ± ;20.5 yrs with the majority (79%) being female. None of these isolates produced ESBLs. During this study, susceptibility declined for AMP (52% vs. 45%), SXT (68% vs. 59%), LEV (86% vs. 76%), and GEN (97% vs. 83%, p=0.0038). Additionally, multi-drug resistance was significantly higher in 2003-04 vs. 2002 (23 % vs. 11%, p=0.0445). In contrast, all isolates except for 1 were susceptible to CRO for the entire study period.
CONCLUSIONS: Multi-drug resistant *E. coli* has increased among hospitalized patients with UTIs at our institution. CRO maintained the most favorable susceptibility profile against multi-resistant *E. coli*.

185E. Evaluation of bacterial kill when modeling the bronchopulmonary pharmacokinetic profile of moxifloxacin (MOX) and levofloxacin (LVX) against parC containing isolates of S. pneumoniae (SPN). *C. Andrew DeRyke, Pharm.D.*, Xiaoli Du, Ph.D., David P. Nicolau, Pharm.D.; Center for Anti-Infective Research & Development, Hartford Hospital, Hartford, CT.

BACKGROUND: The increasingly recognized prevalence of first step *parC* mutants in SPN and the development of de novo resistance while on fluoroquinolone therapy is of concern. Previous work by our group demonstrated the ability of MOX, but not LVX, to eradicate *parC* mutants. The objective of this experiment is to determine if either AUC/MIC ratios or inherent differences in target site binding explain the difference in efficacy between these agents.
METHODS: An *in vitro* pharmacodynamic model was used to simulate the epithelial lining fluid (ELF) concentrations of LVX 500mg q24h and MOX 400mg q24h in older adults. Additionally, a range of AUC/MIC ratios were also modeled. Five different SPN containing first step *parC* mutations were tested for 48 hours and time-kill curves were constructed. Samples at 0, 24, and 48 hours were collected for phenotypic and genotypic profiling. HPLC was used to ensure the correct exposure.
RESULTS:

Drug	Isolate#	AUC/MIC MIC (µg/ml)	³16-fold increase in MIC*	No change in MIC
LVX	1610	1.5	126; 233	529
	3104	1.5	43; 112	232; 497
	18705	2	75; 190	410
	759	1	193	406
	403	1	173	
MOX	1610	0.25	188	380; 756
	3104	0.19	256	555; 1040

*acquisition of gyrA mutation (except exposure 233) bold = simulated human ELF exposures

CONCLUSIONS: Similar efficacy exists between the two antimicrobial agents when comparable AUC/MIC ratios are evaluated. LVX at standard doses does not maintain bactericidal activity, leads to >16-fold increase in MIC and the common acquisition of a *gyrA* mutation. Due to the much higher exposures obtained with standard MOX dosing, bactericidal efficacy is maintained with no development of resistance at 48 hours.
Presented at the 45th Interscience Conference on Antimicrobial Agents and Chemotherapy, New Orleans, LA, September 21-24, 2005.

186E. Increasing incidence of sterile-site infections due to community-associated methicillin-resistant Staphylococcus aureus **among hospitalized patients.** *Garrett E. Schramm, Pharm.D.*[1], Jennifer Johnson, MD[2], Scott T. Micek, Pharm.D.[1], Josh A. Doherty, BS[3], Marin H. Kollef, MD[2]; (1)Barnes-Jewish Hospital, Saint Louis, MO; (2)Washington University School of Medicine, Saint Louis, MO; (3)BJC Healthcare, Saint Louis, MO.

PURPOSE: Community-associated methicillin-resistant *Staphylococcus aureus* (CAMRSA) has emerged as an important pathogen in sterile-site infections in hospitalized patients. The objective of the study was to characterize the susceptibility pattern of sterile-site MRSA infections over a 3-year period.
METHODS: Retrospective study of patients hospitalized at Barnes-Jewish Hospital (St. Louis, MO) with sterile-site infections (blood, BAL, peritoneal and pleural fluid, and CSF) caused by MRSA from January 1, 2002-December 31, 2004, evaluating in vitro susceptibility results for the following antimicrobial agents: trimethoprim-sulfamethoxazole, gentamicin, clindamycin, ciprofloxacin, and erythromycin.
RESULTS: 574 cases of MRSA were identified. 322 (56.1%) cases were from cultures obtained within the first 48 hours of hospital admission. A significant increase in in vitro susceptibility was observed for erythromycin (3.4% to 9.2%; p=0.022), ciprofloxacin (3.4% to 10.0%; p=0.028), and clindamycin (16.3% to 39.3%; p<0.001) from 2002 to 2004. No change in

susceptibility was observed for all other antimicrobials tested. 39 (6.8%) isolates demonstrated susceptibility to at least 4 of the antimicrobials tested.
CONCLUSIONS: The change in susceptibility patterns for erythromycin, ciprofloxacin, and clindamycin could indicate an increasing incidence of sterile-site CAMRSA infections in hospitalized patients.
Presented at the 45th Interscience Conference on Antimicrobial Agents and Chemotherapy of the American Society for Microbiology, New Orleans, LA, September 21-24, 2005.

187E. Safety of isoniazid or rifampin prophylaxis for the prevention of latent tuberculosis in liver cirrhotic patients during transplant candidacy. *Thao Tran, Pharm.D.*, Lanchi Bui, Pharm.D., James Joyner, M.D.; University of California, Irvine Medical Center, Orange, CA.

PURPOSE: This study evaluated the safety and tolerability of either INH or rifampin prophylaxis in liver transplant candidates during the pre-transplant period at our institution.
METHODS: We reviewed the medical records of liver transplant candidates with a positive PPD who were receiving INH or rifampin prophylaxis in the pretransplant period between January 2000 to February 2005. Data collected included patient demographics, undelying liver diseases, liver functionl tests (LFTs), adverse events and tolerability.
RESULTS: One hundred and sixty five (165) charts were reviewed. Twenty two patients met the inclusion criteria. Eight patients received INH and 7 patients received rifampin. Most INH patients have had no hepatotoxicity while on treatment. One out of 8 INH patients had increased LFTs more than 2 times from their baseline. Rifampin prophylaxis did not adversely effect hepatic function. All patients receiving INH or rifampin prophylaxis during pre-transplant tolerated treatment well.
CONCLUSION: INH and rifampin prophylaxis in pre-transplant patients during transplant candidacy appears to be safe and well tolerated.
Presented at the Western States Conference, Asilomar, CA, May 15-18, 2005.

188E. Prevalence of enterococcal virulence genes in E. faecium **and** E. faecalis **isolated among human, retail food, and farm animals in the United States.** *Vanthida Huang, Pharm.D.*[1], Susan M. Donabedian, M.Ph.[2], Mary B. Perri, M.Ph[2], Dora Vager, B.S.[2], Marcus J. Zervos, M.D.[2], Shabbir Simjee, M.D.[3]; (1)Mercer University Southern School of Pharmacy, Department of Clinical and Administrative Sciences, Atlanta, GA; (2)William Beaumont Hospital, Royal Oak, MI; (3)U.S. Food and Drug Administration, Centers for Veterinary Medicine, Laurel, MD.

PURPOSE: Enterococci are commensal organisms of both the human and animal gut. These species have emerged as a leading cause of nosocomial infections. Enterococcus ability to rapidly acquire & disseminate antimicrobial resistance genes will lead to treatment challenge. Furthermore, there is concern that the use of antibiotics in animal environment may select for antibiotic-resistant enterococci. Alternatively, animal enterococci may pass through the human gut, and in transit pass resistance genes to the resident human gut enterococci.
METHODS: Evaluate 5 enterococcal virulence genes (*gelE, cylB, cpd, cob, esp*) in *E. faecium* strains isolated from human (n=29: 21 clinical & 6 stool), retail food (n=17), & farm animals (n=36) and *E. faecalis* strains isolated from human (n=14) & retail food (n=13). Isolates included streptogramin-, vancomycin-, & gentamicin-resistant *E. faecium & faecalis*. Streptogramin resistance determinants, *vatD & vatE*, were determined.
RESULTS: One human & 16 farm animal *E. faecium* isolates tested positive for *vatE* and no *vatD* detected. Only *esp* was detected in resistant *E. faecium* in human. Virulence genes were widely dispersed in resistant *E. faecium* in farm animals: *gelE* (n=14) & *cpd* (n=10) but not retail food isolated. Among resistant *E. faecalis*, we detected all 5 virulence genes in both human [*gelE* (n = 13), *cylB* (n=6), *cpd* (n=14), *cob* (n=7), *esp* (n=5)] and retail food [*gelE* (n=12), *cylB* (n=5), *cpd* (n=13), *cob* (n=13), *esp* (n=6)]. Three resistant *E. faecalis* isolated from human & 4 isolated from retail food contained all 5 virulence genes tested.
CONCLUSION: Theses findings suggest that among resistant *E. faecium*, virulence determinants are more widespread in isolates recovered from farm animals than human. Among resistant *E. faecalis*, virulence genes evaluated were recovered equally from both human and retail food. This data supports the premise that enterococci of animal origin are not adapted to colonize the human gut.
Presented at the 2nd International Conference on Enterococci of the American Society Microbiology and the Federation of European Microbiological Societies, Helsingoer, Denmark, August 28-31, 2005.

189E. Monte Carlo simulation versus S. pheumoniae **of levofloxacin 500 mg, 750 mg, and 1000 mg once daily compaired to gatifloxacin 200 mg and 400 mg once daily administered to hospitalized patients with community-acquired pneumonia (CAP).** *Ayman M. Noreddin, MSc., Ph.D.*[1], Daryl Hoban, PhD[2], George G. Zhanel, Pharm.D., Ph.D.[3], N. Ajide, B. Anderson, T. Marras, C. Chan; (1)College of Pharmacy, Univeristy of Minnesota, Duluth, MN; (2)International Health Management Associates, Inc., Schaumburg, IL; (3)Univeristy of Manitoba, Winnipeg, MB, Canada.

PURPOSE: This study aimed to assess the probability of levofloxacin (Levo) compared to gatifloxacin (Gati) achieving favorable pharmacodynamic (PD) targets for bacterial eradication and prevention of resistance development in *P. aeruginosa*. Various doses of Levo as well as Gati 400 mg OD dosing were simulated and target attainment potential was estimated in critically ill patients.
METHODS: Previously described and validated population pharmacokinetic (PK) models of Levo and Gati in critically ill hospitalized patients were utilized to simulate Levo as well as Gati PKs. Free-drug $AUC_{0\text{-}24}$ were simulated in plasma (P) using Levo dosing at 500 mg, 750 mg and 1000 mg OD as well as Gati 400 mg OD. Use of Monte Carlo simulation allowed for the full variability of encountered drug clearance to be accounted. *P. aeruginosa* susceptibility data were obtained from the North American Urinary Tract Infection Surveillance Study (NAUTICA). The NAUTICA study collected 2000 outpatient and 2000 inpatient urinary isolates from all geographic regions in Canada and the US (ICAAC 2003).
RESULTS: Probability of target attainment (free $AUC_{0\text{-}24}$/MIC of 125 and 250) of Levo and Gati is shown in the following table.

Levo	125	250
500 mg	28.5%	15.4%
750 mg	39.7%	22.7%
1000 mg	45.4%	25%
Gati400 mg	19.3%	14.9%

CONCLUSIONS: For critically ill patients, Levo 500 mg, 750 mg and 1000 mg as well as Gati 400 mg OD showed low probability for target attainment of free $AUC_{0\text{-}24}$/MIC of 125 or 250 against *P. aeruginosa*. For treatment of *P. aeruginosa* infections using the highest dose possible of fluoroquinolone in combination with another antibiotic is imperative.
Published in Pharmacotherapy 2005;25(3):464.

190. Clinical evaluation of continuous infusion amphotericin B deoxycholate. *Sarah X. Gao, Pharm.D.*, Gonzalo Ballon-Landa, M.D., Harminder Sikand, Pharm.D.; Cardinal Health and Scripps Mercy Hospital, San Diego, CA.

PURPOSE: Standard infusion of amphotericin B deoxycholate (AmBD) is associated with high incidence of nephrotoxicity (34%) and infusion-related side effects (54%). Studies show up to 40% reduction in AmBD toxicity when given over a 24-hour period. This study evaluates the tolerability and effectiveness of continuous infusion AmBD (CI-AmBD).
METHODS: Data was collected prospectively and retrospectively in patients treated with CI-AmBD for diagnosed or suspected fungal infections, excluding patients with fungal urinary tract infection or on hemodialysis. The primary endpoints were the incidence of nephrotoxicity, infusion-related side effects and electrolyte abnormalities. The secondary endpoints included infection reoccurrence and mortality.
RESULTS: A total of 56 patients were evaluated. The mean duration of therapy was 9 days with mean daily dose of 0.56 mg/kg. The average change in creatinine clearance was 21.8 ml/min. The incidence of nephrotoxicity was 14.3% with no correlation to age, dose or duration of therapy. The incidence of fever and chills was 10.7% and 1.8%, respectively. While 55.4% of the patients developed hypokalemia, 35.7% developed hypomagnesemia. The mortality rate was 8.9% and 12.5% of the patients experienced breakthrough infections.
CONCLUSION: In comparison to published literature with CI-AmBD, our study showed similar incidence of nephrotoxicity, infusion-related side effects and mortality. As a cost-effective option, CI-AmBD is as well tolerated as liposomal amphotericin B and is at least as effective as both standard infusion AmBD and liposomal amphotericin B.

Managed Care

191. Prescribers respond favorably to drug safety alert mailings from Blues plans. *Patrick P. Gleason, PharmD, BCPS*[1], Steven C. Hartwig, RPh, MS[1], David Lassen, PharmD[1], Alan H. Heaton, PharmD[2], Bob Schultz, RPh[3]; (1)Prime Therapeutics LLC, Eagan, MN; (2)Blue Cross Blue Shield of Minnesota, Eagan, MN; (3)Blue Cross Blue Shield of Wyoming, Cheyenne, WY.

PURPOSE: To assess the utility and results of the one-page anonymous prescriber fax-back evaluations from two different retrospective drug utilization review (RetroDUR) safety alert letters sent in 2005.
METHODS: On January 7, 2005, BCBS Minnesota (BCBSM) mailed the "Safety Alert: Bextra 20mg Daily Dose" letter to 2385 provider caring for 3250 members who had recent chronic Bextra 20mg daily dose claims. On February 15, 2005 BCBS Wyoming (BCBSWY), mailed the "Controlled Substances Use Pattern Requiring Further Evaluation" letter to 516 providers

caring for 288 members with claims indicating multiple controlled substance prescriptions and/or multiple prescribers and/or filled at multiple pharmacies.
RESULTS: Of the 2139 delivered Bextra Safety Alert letters, 220 (10.3%) prescribers faxed back an evaluation. 86% rated the letter as "useful" or "very useful." 89% responded "Yes, information provided was accurate." 42% responded they would "discontinue or modify the drug regimen" and 60% responded they would "discuss the information with my patient(s)." 17% of written comments were "Thank you" or "Excellent" and 13% were critical of the letter. Of the 499 delivered Controlled Substance Alert letters, 83 (17%) prescribers faxed back an evaluation. 90% rated the letter as "useful" or "very useful." 90% responded "Yes, information provided was accurate." 21% responded they would "discontinue or modify the drug regimen" and 54% responded they would "discuss the information with my patient(s)." 19% of written comments were "Thank you" or "Appreciate Info" and 4% were critical of the letter.
CONCLUSIONS: Evaluation of two different RetroDUR safety alert letters in two different Blues plans resulted in each having greater than 1 of 10 prescribers responding with very similar positive feedback. Prescribers overwhelming found the information useful and accurate. The Blues plans found the one-page prescriber fax back responses helping in assessing prescriber value of RetroDUR safety alerts.

192. Effectiveness of a valdecoxib safety alert letter. *Patrick P. Gleason, PharmD, BCPS*[1], Carol Walters, MBA[1], Steven C. Hartwig, RPh, MS[1], David Lassen, PharmD[1], Alan H. Heaton, PharmD[2]; (1)Prime Therapeutics LLC, Eagan, MN; (2)Blue Cross Blue Shield of Minnesota, Eagan, MN.

PURPOSE: In December 2004, new valdecoxib (Bextra) cardiovascular safety concerns were identified. BlueCross BlueShield Minnesota (BCBSM) sent letters to prescribers describing this new safety concern with a list of their patient(s) and valdecoxib claim information. The letter asked prescribers to re-evaluate therapy. The primary objective was to assess if there was an association between letter and valdecoxib discontinuation.
METHODS: January 7, 2005, BCBSM mailed a "Safety Alert: Bextra 20mg Daily Dose" letter to 2385 providers caring for 3511 members who had recent claims indicative of chronic valdecoxib 20mg daily use. The reference group was a BCBS plan that did NOT mail the letter. Criteria for evaluation included: valdecoxib 20mg daily dose with a supply on January 10, 2005, continuous enrollment, and letter deliverable. Using pharmacy claims, the primary endpoint was a change: to valdecoxib 10mg a day, to another NSAID, or discontinuation. Statistical comparison was done using the Kaplan-Meier proportional hazard analysis method adjusting for age and gender. Costs were defined as development, printing, materials, and postage.
RESULTS: Of the 3,511 BCBSM members intervention group, 1,240 (35.3%) met criteria for evaluation. The comparison BCBS plan had 455 letter eligible members. At the end of the 60-day evaluation, change in therapy occurred for 612 (49.4%) of BCBSM members and 173 (38.0%) of comparison BCBS members, p<0.001. BCBSM rate of discontinuation was 18% higher over the follow-up period, proportional hazard ratio 1.18 (95% confidence interval 1.06–1.32). Using the comparison BCBS plan's valdecoxib 20mg persistence, an additional 141 BCBSM members had a change in their therapy. Program cost was $2,790.45.
CONCLUSIONS: A safety alert prescriber letter was associated with a significant absolute 11.4% decrease in valdecoxib 20mg utilization. Safety alert letters may be an effective means to notify prescribers of new medication safety information and change prescribing behavior.

193. Serotonin norepinephrine reuptake inhibitors (SNRIs) trends and utilization management opportunity in a Midwest Blues plan. *Patrick P. Gleason, PharmD, BCPS*, Carol Walters, MBA, Kirsten Tiberg, RPh, David Lassen, PharmD, M Jeanie Brown, RPh, MBA; Prime Therapeutics LLC, Eagan, MN.

PURPOSE: Serotonin selective reuptake inhibitors (SSRIs) and SNRIs (venlafaxine, duloxetine) are equally efficacious with similar tolerance. Three generic SSRIs are available while SNRIs are only available as brand, resulting in average claim cost differences. During May 2005, the average SSRI and SNRI paid per claim were $62.88 ($40.18 plan and $22.70 member) and $118.76 ($83.29 plan and $35.47 member), respectively. We sought to investigate SSRI and SNRI utilization trends and assess utilization management opportunities.
METHODS: All SSRI and SNRI pharmacy claims during 2002 through 2004 (3-years) were identified for a current 210,000 member midwest BlueCross BlueShield plan. Utilization and cost trends are presented using the compounded annual growth rate (CAGR). The first SNRI claim for each member was identified from 01JAN2004 to 31MAR2005. A "new SNRI start" member had no claims with an SNRI day supply in the previous 120 days. Identical logic was used for previous SSRI use.
RESULTS: From 2002 through 2004, annual SSRI utilization per 1000 members remained at 84 and plan paid per utilizing member decreased from $276 to $247 (-3.6% CAGR) while SNRI utilization increased from 13 to 19 (13.5% CAGR) and $383 to $510 (9.9% CAGR). During the 15-month SNRI new start evaluation, of all 4616 SNRI utilizers, 2894 (62.7%) were new starts. Of new SNRI starters, 763 (26.4%) had previously tried an SSRI. SNRI utilizers had an average of 5 claims per year. Using recent utilization patterns, a step-therapy program requiring prior SSRI use could avoid SNRI use in up to 2131 members x 5 claims = 10,655 SNRI claims. If an SSRI could instead be used, there is a potential $136,064 member and $459,444 plan savings.
CONCLUSION: Due to large differences in costs and similar efficacy/safety, step-therapy requiring SSRI use prior to SNRI use may result in considerable plan and member savings.

Medication Safety

194E. Comparative safety of atorvastatin 80 mg versus 10 mg derived from analysis of 49 completed trials. *Connie Newman, MD*, Margaret Essex, PharmD, John Tsai, MD, Michael Szarek, MS, Don Luo, PhD, Eric Gibson, PhD, Donald Pittman, PharmD; Pfizer Human Health, New York.

PURPOSE: Clinicians continue to associate high-dose statin use with increased adverse events (AEs). We thus compared the safety of atorvastatin (Atv) 80 mg, Atv 10 mg, and placebo (Pbo) in 14,236 patients with varying CV risk in 49 trials completed by September 15, 2004.
RESULTS: The most frequent treatment-associated AEs were related to the digestive system (≤6.2% in all groups). No cases of rhabdomyolysis were reported. Incidence of myalgia was low and similar for both Atv groups. Incidence of CPK elevations >10xULN was 0%, 0.2%, and 0.5% in the Pbo, Atv 10 mg, and Atv 80 mg groups, respectively.* One patient with a stress fracture in the 80 mg group and 2 in the 10 mg group also had muscle symptoms. Incidence of LFT (ALT/AST) elevations >3xULN was 0.6%, 0.6%, and 3.3% for Pbo, Atv 10 mg, and Atv 80 mg, respectively.* There were no cases of treatment-related albuminuria and treatment-related hematuria was rare (≤0.05% in all groups).
CONCLUSIONS: Across 49 trials, Atv 80 mg had an AE profile similar to Atv 10 mg, although incidence of LFT elevations >3xULN was higher in the 80 mg group. Contrary to the perception that the incidence of muscle-related AEs increases with statin dose, no such relationship was evident.

Population	Pbo, n (%)	Atv 10 mg, n (%)	Atv 80 mg, n (%)
Pt # (pt-yrs exposure)	2180 (907)	7258 (4925)	4798 (4681)
Pt experiencing ≥1 AE[a]	270 (12.4)	983 (13.5)	699 (14.6)
Serious AEs[a]	92 (4.2)	12 (0.2)	25 (0.5)
Myalgia[a]	15 (0.7)	99 (1.4)	72 (1.5)[b]
Persistent CPK >10xULN*	0	0	2 (0.06)[c]
Persistent LFTs >3xULN*	3 (0.2)	8 (0.1)	26 (0.6)

[a]Treatment-associated events; [b]One case of reported myopathy with CPK 1.4xULN; [c]Both cases were without muscle symptoms; *Denominators for incidences are the # of pts with lab values during treatment
Presented at the 75th European Atherosclerosis Congress, Prague, Czech Republic, April 23-26 2005.

195E. Absence of electrocardiographic findings with daily tiotropium in patients with chronic obstructive pulmonary disease. *Craig S. Conoscenti, MD*, Cara Cassino, MD, Steven Kesten, MD; Boehringer Ingelheim, Ridgefield, CT.

PURPOSE: Although uncommon, increases in heart rate may be associated with inhaled anticholinergics. Tiotropium, an inhaled anticholinergic, provides 24-hour efficacy with once-daily dosing. While peak plasma levels occur within 5 minutes, steady state occurs following several weeks of treatment. We sought to examine electrocardiographic findings of tiotropium in COPD patients following acute and chronic dosing.
METHODS: 12-week, randomized, double-blind, placebo-controlled study in COPD patients included ECGs (pre-dose and 5 minutes post-dose) and 24-hour Holter monitoring at baseline and following 8 and 12 weeks of tiotropium 18mcg daily or placebo. Efficacy measures were included to confirm improvements observed in previous tiotropium studies.
RESULTS: 196 patients were randomized: mean age=65 years; %males=58%; mean FEV_1=1.022L. Mean change from baseline in heart rate was similar between groups:

DHeart Rate (beats/min)	Tiotropium		Placebo	
	8 wks	12 wks	8 wks	12 wks
ECG pre-dose	0.87	-0.35	1.06	1.55
ECG post-dose	-1.73	-2.09	-0.11	0.65
24-hour Holter	0.26	0.2	0.73	0.55

There were no differences in %patients developing abnormalities in rhythms or conduction. Frequency of premature beats, and mean and maximal changes in PR, QRS, QT, QTcB and QTcF were similar between groups. No patients developed new onset QT or QTc >500 msec; no differences in %patients developing new QT prolongation <30 msec, 30-60 msec or >60

msec. Cardiac adverse events were observed in 1 tiotropium and 4 placebo patients. At 12 weeks, improvements with tiotropium over placebo in morning pre and post-dose FEV_1 were 184 and 265 mL ($p<0.001$); prn use of albuterol was reduced by 25% ($p<0.05$). COPD Global ratings by physicians and patients, and EQ5D visual analogue scale were improved with tiotropium ($p<0.05$).
CONCLUSIONS: Tiotropium was not associated with electrocardiographic evidence of changes in heart rate, rhythm, QT intervals and conduction. Tiotropium provided spirometric and symptomatic benefits to COPD patients.
Funding: Boehringer Ingelheim
Published in Chest 2004;126(4):837S.

196. Implementation and a randomized controlled evaluation of pharmacist medication assessments in a surgical pre-admission clinic. *Yvonne Kwan, BScPhm*[1], Olavo Fernandes, PharmD[1], Jeff Nagge, PharmD[1], Gary Wong, BScPhm[1], Jin Huh, BScPhm[1], Deborah Hurn, RN, MA[1], Jana Bajcar, MScPhm, EdD, FCSHP[2]; (1)University Health Network, Toronto, ON, Canada; (2)Leslie Dan Faculty of Pharmacy, University of Toronto, Toronto, ON, Canada.

PURPOSE: Post-operative hospital admission is a key vulnerable moment where patients are at increased risk of medication discrepancies. This study measures the impact of a combined intervention of structured pharmacist medication assessments in a surgical pre-admission clinic (PAC) and a post-operative order form on reducing medication discrepancies.
METHODS: In this randomized, prospective, parallel study, patients who had a PAC appointment prior to undergoing surgical procedures (ENT, Urology, Gynecology Oncology, Plastics, General Surgery, and Thoracics) were eligible for inclusion. Patients were excluded if they were scheduled for discharge the same day as their surgery. Eligible patients were randomly assigned to the intervention arm (structured pharmacist medication assessment and generation of a post-operative medication order form) or standard care (nurse-conducted medication histories and surgeon-generated orders). Primary endpoint was the incidence of patients with at least one post-operative medication discrepancy related to home medications. Discrepancies were systematically characterized and their clinical impact was independently assessed.
RESULTS: From April 19, 2005 to June 3, 2005, 310 patients completed the study after exclusions due to pending and cancelled surgeries and admissions to in-patient units not participating in the study. Of the 310 patients, 154 were randomized to the intervention arm and 156 to the standard care arm. In the intervention arm, 30 (19.5%) patients had at least one post-operative medication discrepancy related to home medications, compared to 68 (43.6%) in the standard care arm ($p<0.001$). Eight (17.0%) of these discrepancies in the intervention arm were classified with the potential to result in "probable" patient discomfort and/or clinical deterioration versus 46 (36.8%) in the standard care arm.
CONCLUSIONS: A combined intervention of pharmacist medication assessments and a post-operative order form can reduce post-operative medication discrepancies related to home medications. Pharmacist involvement in the PAC may be beneficial at improving patient safety during post-operative hospital admission.

197. Lack of hypersensitivity reactions to hyaluronidase ovine (Vitrase®). *Karl Buetner, M.D., Ph.D*[1], Tim Mcnamara, Pharm.D.[2], Lisa Grillone, Ph.D.[2]; (1)Solano Clinical Research, Davis, CA; (2)ISTA Pharmaceuticals, Inc., Irvine, CA.

PURPOSE: To investigate the potential for developing hypersensitivity reactions to Vitrase®, ovine hyaluronidase, an FDA approved pharmaceutical product containing animal derived proteins.
METHODS: Two, identical, single center, clinical trials were conducted, each in 65 normal healthy volunteers, to determine the incidence of hypersensitivity reactions to highly purified hyaluronidase ovine (Vitrase®). Both open label, clinical trials evaluated the response to a 30µl intradermal injection of hyaluronidase ovine versus an equal volume of saline control. Normal healthy volunteers, who had previously not been exposed to hyaluronidase, received a single intradermal injection each of hyaluronidase ovine and saline given 10 cm apart ventral surface of the left forearm. One study used vials of Vitrase® 6200 USP Lyophilized Ovine for injection, which was reconstituted to deliver 3 USP units in a single injection. The other study utilized Vitrase® 200 USP units/ml injection, to deliver approximately 4 USP units in a single injection. Both hyaluronidase ovine and control injection sites were examined 5 minutes after injection and observation continued for 30 minutes. Evidence of hypersensitivity was a positive reaction that consisted of wheal formation with pseudopods appearing within 5 minutes of injection, persisting for 20 to 30 minutes and accompanied by local itching. Transient vasodilatation (e.g. erythema) at the site of the test was not a positive reaction.
RESULTS: No hypersensitivity reactions to hyaluronidase ovine alone, were observed in either trial. No adverse reactions were observed during the study.
CONCLUSIONS: Highly purified hyaluronidase ovine is not associated with hypersensitivity reactions in subjects who have not previously received the drug.

Nephrology

198E. The hemoglobin response to rapid, high-dose intravenous iron sucrose therapy in anemic chronic kidney disease patients not receiving hematopoietic hormone therapy. *Michael H. Schwenk, Pharm, D*[1], Daniel A. Blaustein, MD[2], Jyoti Chattopadhyay, PhD[2], Harinder Singh, MD[2], Radha Venkatramanan, M.D.[2], Morrell Avram, MD[2]; (1)The New York Hospital Medical Center of Queens, Flushing, NY; (2)The Long Island College Hospital, Brookyln, NY.

PURPOSE: The widespread use of epoetin in anemic end stage renal disease patients has resulted in correction of the anemia, but the response may be blunted by the presence or development of iron deficiency. The hemoglobin response to iron therapy (without concomitant epoetin therapy) in anemic CKD patients is an area which has received relatively little attention. The purpose of this study was to gauge the hemoglobin (Hgb) response in anemic patients with chronic kidney disease (APCKD) after a rapid, high-dose IV iron sucrose dosing regimen.
METHODS: APCKD were included for study if they had Hgb ≤ 12.5 g/dL, ferritin < 500 ng/ml, and TSA < 40%. Epoetin, darbepoetin, androgens, intravenous iron therapy and transfusions were not administered for 6 months prior to, or up to 6 months after iron sucrose dosing. Iron sucrose 500 mg IV over 3h on 2 consecutive days was given. At baseline and 1 and 6 months after iron dosing, Hgb, ferritin, TSAT and GFR (MDRD) were obtained.
RESULTS: There were 29 APCKD enrolled in the study, age 63.6 ± 10.3 years, 22F/7M. Intravenous iron sucrose in this prescribed regimen was well tolerated in this cohort.

	Hgb (g/dL)	Ferritin (ng/ml)	TSAT (%)	GFR mL/min
Baseline	11.0 ± 1	150 ± 145	19.8 ± 8	32.4 ± 13.1
1 month	11.7 ± 1*	430 ± 219*	26.2 ± 7.2*	36.4 ± 16.6
6 months	12.1 ± 1.4*	332 ± 225	24.9 ± 9.6	34.1 ± 17.4

*$p<0.05$, compared with baseline

CONCLUSIONS: We conclude that a rapid, high-dose intravenous iron sucrose dosing regimen is safe and effective in repleting/maintaining body iron stores during the ensuing, clinically significant hemoglobin response. These results were obtained without the concomitant use of hematopoietic hormone therapy, confirming previous small studies, and may simplify treatment of anemia in APCKD.
Published in J Am Soc Nephrol 2004;15:549A.

199. The pharmacokinetics and pharmacodynamics of enoxaparin in end-stage renal disease. *Donald F. Brophy, Pharm.D., M.Sc.*[1], Erika J. Martin, MT, (ASCP)[2], Jurgen Venitz, MD, PhD[1], Todd W.B. Gehr, MD[1], Marcus E. Carr, Jr., MD, PhD[1]; (1)VCU Medical College of Virginia, Richmond, VA; (2)Hemodyne, Inc., Richmond, VA.

PURPOSE: The pharmacodynamic parameters Thrombin Generation Time (TGT), Platelet Contractile Force (PCF) and Clot Elastic Modulus (CEM), have been identified as novel monitors for the effects of low molecular weight heparin drugs in high-risk populations, such as those with end-stage renal disease (ESRD). A pharmacokinetic-pharmacodynamic study determined the relationships between antifactor Xa activity (the pharmacokinetic marker) and TGT, PCF and CEM (the pharmacodynamic markers) in ESRD patients following enoxaparin administration.
METHODS: Eight controls and eight ESRD subjects received single-dose enoxaparin 1 mg/kg subcutaneously. Blood sampling for antifactor Xa activity, TGT, PCF and CEM was performed at baseline, 4, 8 and 12 hours post-dose. Antifactor Xa concentrations were determined using a validated amidolytic method. TGT, PCF and CEM were determined using the Hemodyne™ hemostasis analyzer. The pharmacokinetics of enoxaparin's antifactor Xa activity were determined by noncompartmental analysis. Area under the effect curves (AEUC) were constructed for the pharmacodynamic variables PCF, CEM and TGT. Inter-group comparisons of the PK and PD parameters were performed using the student's *t*-test. The significance level was set at $p \leq 0.05$.
Results:

Group	A_{max} (IU/mL)	T_{max} (h)	AUC (U/mL*min)	$T_{1/2}$ (h)	Vd/F (L)
Control	0.6 ± 0.1	4	279 ± 76	4.7 ± 3.5	8.5 ± 2.8
ESRD	0.5 ± 0.1	4	249 ± 71	5.1 ± 1.6	9.6 ± 2.8

(table continued)

Group	Cl/F (ml/min)	AEUC PCF (kdynes/h)	AEUC CEM (kdynes/cm²/h)	AUEC TGT (mins/h)
Control	30.8 ± 9	79.4 ± 18.9	188.5 ± 27.2	91.3 ± 14.3
ESRD	33.0 ± 10	64.1 ± 21.7	172.9 ± 54.2	115.8 ± 34.6[a]

Mean ± S.D., [a]significant difference vs. control ($p<0.05$)

CONCLUSIONS: These findings suggest similar antifactor Xa disposition between groups, however, the TGT AUEC is more prolonged in the ESRD

subjects compared to controls. This suggests that the ESRD group is more anticoagulated compared to controls, despite a seemingly similar antifactor Xa pharmacokinetic profile. Antifactor Xa activity may not adequately explain the degree of anticoagulation in ESRD patients who receive enoxaparin. Further large-scale trials are needed to confirm these results.

200. Stability of vancomycin in icodextrin peritoneal dialysis solution. *Rowland J. Elwell, Pharm.D.*, Adwoa O. Nornoo, Ph.D., David Goodman, Pharm.D. Candidate; Albany College of Pharmacy, Albany, NY.

PURPOSE: There are limited data describing the compatibility of vancomycin and icodextrin peritoneal dialysis (PD) solution. The objective of this study was to assess the chemical stability of vancomycin in icodextrin PD solution in polyvinyl chloride containers over a seven-day period.
METHODS: Study samples were prepared by adding 2000 mg vancomycin HCl to commercially available 2.0 liter bags of icodextrin 7.5% PD solution. Nine bags were prepared and stored in the following conditions: 3 under refrigeration (5°C), 3 at room temperature (24°C), and 3 at body temperature (37°C). Samples were withdrawn from each bag immediately after preparation and at predetermined intervals over the subsequent 7 days. Solutions were visually inspected for precipitation, cloudiness or discoloration at each sampling interval. All samples were immediately frozen (-80°C) after collection and stored prior to assay. Total concentration of vancomycin in dialysate fluid was determined by high performance liquid chromatography.
RESULTS: The solutions were clear in appearance and no color change or precipitation was observed during the study. Under refrigeration, a mean of 99.7 ± 0.5 % of the initial vancomycin concentration remained at 168 hours (7 days). At room temperature, 97.5 ± 3.4 % remained at 168 hours. At body temperature, 94.3 ± 3.9 % remained at 24 hours. Stability was not assessed beyond these respective time points.
CONCLUSION: Pre-mixed vancomycin-icodextrin PD solutions whether stored refrigerated or at room temperature were found to be stable for up to 7 days. However, it is recommended that these be kept refrigerated whenever possible. Solutions stored at body temperature were stable up to 24 hours permitting the practice of pre-warming solutions prior to administration.

201. The effects of oxandrolone on nutritional parameters in hemodialysis patients: a pilot study. *Jason J. Kotsko, Pharm.D.*[1], Edward F. Foote, Pharm.D.[1], Jonathan L. Ritter, B.S.[1], Bradley Kulp, B.S.[1], Marie Roke-Thomas, Ph.D.[1], Steven Young, D.O.[2], John A. Rothschild, M.D.[2]; (1)Wilkes University, Wilkes Barre, PA; (2)Renal Consultants of Wyoming Valley, Wilkes Barre, PA.

PURPOSE: Malnutrition Inflammation Complex Syndrome (MICS) is characterized by protein energy malnutrition and inflammation. MICS is common in HD patients and is associated with excess morbidity and mortality. MICS has also been observed in AIDS, cancer and COPD. Oxandrolone, an anabolic steroid, has been shown to improve MICS in other disease states. No studies have been done in HD patients. The purpose of this pilot study is to evaluate its potential benefit in this population.
METHODS: This was an open label, prospective, pilot study in which patients were given oxandrolone, 5 mg twice daily for 8 weeks. Assessments of inflammation [C-reactive protein (CRP) and ferritin levels] and nutrition (weight, albumin, prealbumin) was performed at baseline (week 0) and every 4 weeks while on the drug (weeks 4,8), and 4 weeks after drug discontinuation (week 12). A paired *t*-test was used to determine statistical significance.
RESULTS: Seven patients were enrolled in the study; only 5 patients were available for analysis. One patient died and another withdrew consent, both shortly after starting oxandrolone. Mean Prealbumin levels increased from baseline and throughout the study but only reached statistical significance by week 12 (18.8 to 26.3 mg/dL, p=0.047). Albumin also increased from baseline but again, did not reach statistical significance until week 12 (3.28 to 3.54 g/dL (p=0.049). Inflammatory markers were high at baseline but were not affected during study. Total body weight (post dialysis) did not change during the study but this may have been confounded by fluid balance.
CONCLUSIONS: This is the first published data on the use of oxandrolone in HD patients. The data presented suggest that oxandrolone may have nutritional benefits; however, the mechanism does not appear related to an anti-inflammatory effect. Further large-scale, prospective trials are warranted before the drug can be recommended in this patient population.

202E. Intravenous iron requirement in adult hemodialysis patients. *Timothy V. Nguyen, PharmD*; Holy Name Hospital, Teaneck, NJ.

PURPOSE: Chronic hemodialysis patients often require maintenance intravenous iron, as iron is an essential component for effective erythropoiesis. The Anemia Work Group (NKF/KDOQI) anemia guidelines suggests a maintenance IV iron dose of 25 mg to 125 mg, but optimal maintenance dose regimen remains to be difficult to determine. K/DOQI recommended optimal iron parameters: TSAT ∞›20% to <50%, ferritin ∞›100 to <800 ng/mL. We present the assessment of our maintenance dose regimen.
METHODS: A total of 40 adult chronic hemodialysis patients received regular maintenance IV iron sucrose 100 mg either every other week or every month based on their ferritin and transferrin saturation (TSAT) levels. Every other week if ferritin levels 100 to less than 500 ng/mL and TSAT levels 20% to less than 30%. Every month if ferritin levels 500 to 700 ng/mL or TSAT 30% to 45%. Ferritin and TSAT levels were monitored quarterly.
RESULTS: After the first quarter, 38% of patients maintained the same regimen; 53% of patients required regimen adjustment either discontinued or at a decreased interval, 45% and 8% respectively; 10% of patients required additional IV iron supplementation.
CONCLUSIONS: Iron sucrose 100 mg administered on maintenance regimen of every other week or every month exceeded most patients' requirement. Maximum IV iron maintenance doses for adult chronic hemodialysis patient are difficult to determine and maintenance iron requirement varies from patient to patient.
Presented at the Annual Meeting of the New Jersey Society of Health-System Pharmacists, New Brunswick, NJ, April 21, 2005.

203. Effects of angiotensin converting enzyme inhibitors and angiotensin II receptor blockers on protection of cardiovascular disease in peritoneal dialysis patients. Wei-Hsuan Lo, B.S.Pharm.[1], Ming-Cheng Wang, M.D.[2], Shu-Min Kao, M.S.C.P.[1], *Yea-Huei Kao Yang, B.S.Pharm.*[1]; (1)Institute of Clinical Pharmacy, College of Medicine, National Cheng Kung University, Tainan, Taiwan; (2)Department of Internal Medicine, National Cheng Kung University Hospital, Tainan, Taiwan.

PURPOSE: Angiotensin-converting enzyme inhibitors (ACEI) and angiotensin II receptor blockers (ARB), an effective treatment for hypertension and cardiovascular disease, are known to improve prognosis in chronic renal failure and hemodialysis patients. The CV protection effects of ACEI and ARB in peritoneal dialysis (PD) patients remain unclear. We investigated whether ACEI or ARB reduces CV morbidity and mortality in chronic PD patients.
METHODS: Clinical data and medical treatment were extracted from 245 PD patients therapy between 1990 and 2005. We excluded patients who were receiving PD therapy less than 6 months, with underlying malignancy, younger than 18 years, or incomplete information. CV events and mortality were compared between patients treated with or without ACEI and/or ARB.
RESULTS: Forty-two patients had been treated with ACEI and/or ARB at for least 6 months (treated group) and 107 patients (untreated group) had never been treated by either drugs. Blood pressure was higher in the treated group during the entire follow-up period. Compared with the untreated group, CV events were decreased significantly in the treated group, with a risk reduction of 70% (RR, 0.30, 95% CI 0.10, 0.96). All-cause mortality (RR, 0.98, 95% CI 0.94, 1.01) and CV-related mortality (RR, 0.98, 95% CI 0.93, 1.03) did not differ between 2 groups.
CONCLUSIONS: These preliminary findings suggest that ACEI or ARB may dramatically reduce CV events in PD patients. However, there is no evidence to show beneficial effects from ACEI or ARB in terms of all-cause mortality and CV-related mortality.

204. Comparison of sevelamer hydrochloride and aluminum hydroxide in treatment of hyperphosphatemia. Hye Won Kim, M.S.[1], Wan Gyoon Shin, Pharm.D, Ph.D[2], Miae Kim, M.S.candidate[3], *Jee Hyun Suh, M.S. candidate*[1]; (1)Graduate school of pharmacy, Seoul National University, Seoul; (2)Graduate School of Pharmacy, Seoul National University, Seoul, South Korea; (3)Graduate school of pharmacy, Seoul National University, seoul, South Korea.

PURPOSE : The study prospectively compares the effect and the safety of sevelamer hydrochloride, calcium and aluminum free phosphate binder, with aluminum hydroxide for the treatment of hyperphosphatemia in Continous Ambulatory Peritoneal Dialysis(CAPD) patients.
METHODS : 11 CAPD patients who had a concentration of serum phosphate higher than 6.0 mg/dL or a calcium phosphate product (Ca x P) higher than $60mg^2/dL^2$ were prospectively analyzed. They received 1~3 Tablets of (400~1200 mg) sevelamer three times a day in proportion to their serum phosphate for 8 weeks. After they had had a 2 week "washout period", they were treated with 1~3 Tab. (300~900 mg) of aluminum hydroxide three times a day. A paired *t* test was done and a P value of ∞‹ 0.05 was considered significant.
RESULTS: In the sevelamer group, serum phosphate concentration was 7.96 ± 1.62 mg/dL during the washout period, and dropped to 7.76 ± 1.63 mg/dL after 2 weeks of treatment, 7.27 ± 1.44 mg/dL after 4 weeks of treatment and insignificantly rose to 8.09 ± 1.35. In the aluminum group, serum phosphate dropped insignificantly from 9.07 ± 2.41 mg/dL during the washout period to 5.83 ± 0.50 mg/dL after 2 weeks of treatment 6.90 ± 1.08 mg/dL after 4 weeks of treatment) 6.40 ± 1.01 mg/dL after 8 weeks of treatment. The changes in serum calcium levels were consistent. Ionized calcium dropped significantly from 1.27 ± 0.12 to 1.12 ± 0.11 mmol/L in the sevelamer group but not in the aluminum group.
CONCLUSION: Sevelamer hydrochloride and aluminum hydroxide

insignificantly decrease serum phosphate. Sevelamer is recommended in combination with therapy in the treatment of hyperphosphatemia in peritoneal dialysis patients, especially those who cannot use calcium-based phosphate binders due to hypercalcemia. Study evaluating the efficacy of sevelamer in dialysis patients who have hypercholesterolemia is needed.

205. An evaluation of ACE-Inhibitors in contrast nephropathy. Craig D. Cox, PharmD, BCPS[1], James P. Tsikouris, PharmD[2], Miranda C. Peek, BS[1], *Charles F. Seifert, PharmD, FCCP, BCPS*[1]; (1)Texas Tech University Health Sciences Center School of Pharmacy, Lubbock, TX; (2)University of Pittsburgh School of Pharmacy, Pittsburgh, PA.

PURPOSE: One significant complication of coronary interventions is contrast-induced nephropathy (CN), occurring in approximately 15% of patients. Many patients undergoing cardiac procedures receive ACE-Inhibitors, yet their relationship to CN is unknown. Herein, we describe a retrospective review investigating ACE-Inhibitors and the development of CN.
METHODS: A retrospective review of patients undergoing cardiac catheterization at University Medical Center from 1999 to 2005 was conducted. CN was defined by a rise of 0.5 mg/dL in serum creatinine (SCr) from baseline occurring within three days of contrast. Of the patients identified, only those at high risk for CN (baseline SCr ≥1.3) were considered. Patients receiving ACE-Inhibitors within 24 hours of contrast were compared to a control group of patients not receiving an ACE-Inhibitor. Following cardiac procedures, SCr concentrations up to 72 hours from baseline were recorded to identify patients who developed CN.
RESULTS: The analysis included 79 patients. CN developed in 17.9% (7/39) of patients not receiving an ACE-Inhibitor and 35% (14/40) of patients receiving an ACE-Inhibitor (p=0.144). In addition, patients with diabetes or CHF reported a significant increase in CN, regardless of ACE-Inhibitor use (p <0.0011; p <0.008, respectively). Among those receiving ACE-Inhibitors, non-CHF patients (n=60) showed a trend toward greater risk of CN (29.6% vs. 9.1%, p=0.0872), while non-diabetic patients (n=48) did not (p=0.7118). No significant differences in preventative strategies, contrast volume, baseline SCr, or age were found.
CONCLUSIONS: Confirming prior studies, CHF and diabetes were major risk factors for development of CN in this analysis. When looking at patients who received ACE-Inhibitors, they had a two-fold greater risk of developing CN compared to those not receiving ACE-Inhibitors; however, these findings were not statistically significant. Diabetes and CHF may have contributed to this observation, but this cannot be clearly determined. Continued investigation is warranted and ongoing.

206E. An optimized formulation of lanthanum carbonate is effective and well tolerated. *Jaime Weres, Pharm.D.*[1], Jeremy W. Sharp, Pharm.D.[1], Stephen Haworth, M.D.[1], Rajnish Mehrotra, M.D.[2], Katie Blanck, MSHS[1]; (1)Shire Pharmaceuticals, Wayne, PA; (2)Harbor UCLA Medical Center, Los Angeles, CA.

Clinical research has demonstrated that lanthanum carbonate (LC), a non-aluminum, non-calcium phosphate binder, is safe and effective at doses up to 3,000 mg/day in end-stage renal disease patients. We assessed the efficacy and safety of a new optimized formulation of LC in the control of serum phosphate at doses up to 4500 mg/day. In Part 1 of the study, patients underwent a 4-week open-label titration to LC doses ranging between 1500-3000 mg/d. At the end of Part 1, patients were classified as either responders or non-responders (serum phosphate level >5.5 mg/dL). Depending on response, patients either continued open-label treatment (responder = LC doses of 1500-3000 mg/day) or were randomized in a double-blind fashion to higher doses of LC (non-responder = LC doses of either 3000, 3750 or 4,500mg/day) for an additional 4 weeks. To date, 88 of the 199 subjects that have entered part I have completed the open label dose-titration phase. After 4 weeks of LC therapy (1500-3000 mg/d), 59% of patients achieved K/DOQI recommendations for P control (3.5-5.5 mg/dL); the remainder entered the double-blind randomized cohort. Mean baseline values (preliminary data from Part I; n=23, 13 men, 12 white, mean age of 62 yrs) for P, calcium-phosphorus product (Ca x P), calcium (Ca), and parathyroid hormone (PTH) were: 7.1 mg/dL, 64.1 mg2/dL2, 9.4 mg/dL, and 263 pg/mL, respectively. Following 4 weeks of LC treatment, mean values for P, Ca x P, Ca, and PTH decreased to: 5.3 mg/dL, 50.5 mg2/dL2, 9.4 mg/dL, and 241 pg/mL, respectively. Preliminary adverse events are consistent with prescribing information with no serious adverse events related to LC. The optimized formulation of LC appears to be well tolerated and effective in the management of hyperphosphatemia at doses up to 3 g/day and leads to an improvement in phosphate control in the majority of patients.
Presented at the Spring Clinical Meeting of the National Kidney Foundation, Washington, D.C., May 4-8, 2005.

207E. Lanthanum carbonate: preference and satisfaction. *Jaime Weres, Pharm.D.*[1], Jeremy W. Sharp, Pharm.D.[1], Stephen Haworth, M.D.[1], Rajnish Mehrotra, M.D.[2], Katie Blanck, MSHS[1]; (1)Shire Pharmaceuticals, Wayne, PA; (2)Harbor UCLA Medical Center, Los Angeles, CA.

Dosing frequency, pill burden, and side effects are just some of the obstacles to phosphate-binder compliance in the dialysis patient. Here, we assess physician and patient preference and satisfaction with a new optimized formulation of lanthanum carbonate (LC) and evaluate these parameters relative to prior treatment. This formulation of LC has a reduced tablet size, compared with the original formulation, and is available in additional strengths (750 mg and 1 g) which permits 1 tablet/meal dosing that physicians and subjects may find more appealing, thus facilitating compliance. Patients included in this analysis took part in a phase IIIb, multi-center, parallel group, randomized trial with 2 cohorts (LC 1500-3000 mg/day and LC 3000-4500 mg/day). Patient and physician satisfaction and preference of LC vs. previous phosphate binders were evaluated using questionnaires; Preliminary data (LC doses of 1500-3000 mg/day; n=24) are presented in this abstract with additional data to be incorporated and presented at the time of the meeting. Following 4 weeks of LC treatment, most patients "strongly agreed" or "agreed" they were satisfied with: pill burden (82%), ease of administration (86%), duration of effect (70%) and compliance (71%) and "strongly disagreed" or "disagreed" they experienced bothersome side effects (85%). The majority of physicians (>76%) "strongly agreed" or "agreed" LC was easy to take, effective for hyperphosphatemia and related symptoms, and subjects were compliant; Most physicians were satisfied with the effectiveness of LC (80%). Additionally, the majority of patients preferred LC over previous phosphate therapy (sevelamer, n=14; calcium acetate/carbonate, n= 10) when questioned on pill burden (62%) and compliance (59%). In conclusion, the majority of patients and physicians reported overall satisfaction with the optimized formulation of LC and patients appear to prefer this treatment over previous therapies.Presented at the Spring Clinical Meeting of the National Kidney Foundation, Washington, D.C., May 4-8, 2005.

208E. Lack of adverse effects on hematological parameters during lanthanum carbonate treatment. *Jeremy W. Sharp, Pharm.D.*, Stephen Haworth, M.D., Scharmen Confer, Shire Pharmaceuticals, Wayne, PA.

The efficacy and tolerability of the new phosphate binder lanthanum carbonate (LC) have been demonstrated in an extensive clinical trial program. Here, we review data relating to effects on mean levels of hematological parameters (iron, transferrin, ferritin, hemoglobin, folate, vitamin B12, or mean cell volume (MCV) from four Phase III trials and open-label extensions. No significant changes were seen during a randomized, double-blind study with LC (n=50) vs. placebo (n=44) in any of the parameters assessed (p > 0.5). After 6 months of treatment with LC (n = 455) or calcium carbonate (CC; n = 92), no siginificant difference between treatment groups was seen with any parameter (p > 0.1) except MCV, which showed a significantly greater increase in the CC group (p<0.0001). After 6 months, mean (± SD) MCV was 97.6 ± 6.9 fL in the LC group compared with 101.5 ± 7.1 fL in the CC group. No significant difference in MCV, or any other hematologic parameter assessed, was seen after 1 year of treatment in a randomized study of LC (n = 49) vs. CC (n = 49; p > 0.2). In a randomized study comparing LC (n = 680) with standard therapy (calcium or aluminum salts, or sevelamer; n = 674), no significant between-group differences were seen in any of the parameters assessed after 2 years of treatment (p > 0.1). Treatment with LC for up to 3 years has been assessed in open-label trials. Changes in hematological parameters throughout treatment were slight and not considered to be clinically significant. In conclusion, lanthanum carbonate did not appear to adversely affect hematological parameters when compared with currently available phosphate binders.
Presented at the Spring Clinical Meeting of the National Kidney Foundation, Washington, D.C., May 4-8, 2005.

209E. Further evidence for the long-term safety and tolerability of lanthanum carbonate. *Steve Woods, Pharm.D.*[1], Jeremy W. Sharp, Pharm.D.[1], G. Siami, M.D.[2], W. Backs, M.D.[3]; (1)Shire Pharmaceuticals, Wayne, PA; (2)VA Medical Center, Vanderbilt University, South Nashville, TN; (3)Dialysepraxis Barmbek, Hamburg, Germany.

The efficacy and tolerability of the new phosphate binder, lanthanum carbonate, have been demonstrated in randomized, controlled trials and open-label extensions for periods of up to 3 years continuous treatment. Patients from four such studies were enrolled into an additional open-label trial to further assess long-term safety and maintenance of phosphorus control during continued lanathanum carbonate treatment. Patients who participated in any of four previous studies of lanthanum carbonate and continued to require phosphate binder therapy were eligible to enter this 2-year, open-label extension. Patients who were withdrawn from a previous study before randomization, or were withdrawn as a result of adverse events classed as 'related' or 'possibly' related to study medication, were not eligible for this open-label study. Safety of lanthanum carbonate was assessed by adverse event recording and by monitoring of laboratory values and vital signs. Adverse events were also categorized according to length of exposure to

lanthanum carbonate. Efficacy was assessed as control of pre-dialysis serum phosphorus levels. Control of serum phosphorus was defined as <=.9 mg/dL (1.9 mmol/L) for patients previously enrolled in US studies, and <=.6 mg/dL (1.8 mmol/L) for those previously enrolled in European studies. Data will be presented demonstrating the long-term safety, tolerability and efficacy of lanthanum carbonate in patients who have received up to 5 years of treatment.
Presented at the Spring Clinical Meeting of the National Kidney Foundation, Washington, D.C., May 4-8, 2005.

210E. Relative pharmacological potency of the phosphate binders, lanthanum carbonate and sevelamer hydrochloride. *Steve Woods, Pharm.D.*[1], Jeremy W. Sharp, Pharm.D.[1], Valerie Autissier[2], Stephen Damment, Ph.D.[3]; (1)Shire Pharmaceuticals, Wayne, PA; (2)Chemistry, School of Natural Sciences, University of Newcastle, UK, United Kingdom; (3)Shire Pharmaceuticals Development Ltd., Basingstoke, United Kingdom.

Control of serum phosphate to the K/DOQI target, high pill burden, and poor patient compliance remain significant problems in the management of ESRD. We reported previously, that the new phosphate binding drug, lanthanum carbonate, has a potency advantage over existing products, exhibiting similar efficacy compared to aluminum, and greater efficacy compared to sevelamer and calcium carbonate in animal models of chronic renal failure (Damment & Webster (2003), JASN, 14, 204A). To further investigate relative potency, we have measured the equilibrium binding affinities of phosphate to lanthanum carbonate and sevelamer hydrochloride under identical conditions, over a range of phosphate concentrations (5-100 mM), binder concentrations (134-670 mg/50mL) and pH (3-7). Phosphate concentration in the solution was determined by ICP-AES. Lanmuir plots were generated, from which K1 (affinity constant for phosphate binding) and K2 (Langmuir capacity constant; maximum amount of phosphate that binds per unit weight of binder) were determined. In all cases, the Langmuir plots were straight lines. At all pH levels, lanthanum carbonate had a higher affinity for phosphate compared to sevelamer. Thus, for lanthanum carbonate, K1 = 6.1 was independent of pH, whilst for sevelamer hcl, K1 was pH-dependent, increasing from 0.025 at pH 3 to 1.45 at pH 5-7. The values obtained for sevelamer hcl were in agreement with those reported earlier (Swearingen et al. (2002), J Pharm Biomed Anal, 29, 195-201), where phosphate concentrations were determined by GLC. These results indicate that the binding affinity of lanthanum carbonate for phosphate is > 200-fold higher at gastric pH (3) and 4-fold higher at intestinal pH (5-7) compared to sevelamer. They provide an explanation for the greater potency observed with lanthanum carbonate in vivo, and indicate the importance of trapping dietary phosphate in the acidic milieu of the stomach and duodenum before phosphate can be absorbed in the small intestine.
Presented at the Spring Clinical Meeting of the National Kidney Foundation, Washington, D.C., May 4-8, 2005.

211. Vasoactive medication use and vascular access patency: a U.S. renal data system study. *Robert Sanchez, RPh, MS*, Alexander S Yevzlin, MD, Emily L Ebenhoe, MD, Henry N Young, PhD, Bryan Becker, MD; University of Wisconsin, madison, WI.

PURPOSE: Several medications have been proposed to improve hemodialysis vascular access outcomes based on potentially favorable anticoagulant, antiplatelet, or pleiotrophic properties. A recent international observational study suggested that treatment with calcium channel blockers, angiotensin-converting enzyme inhibitors, and aspirin was associated with improved vascular access patency. The purpose of this study is to further evaluate the relationship between medication use and vascular access patency.
METHODS: We conducted a historical cohort study of the U.S. Renal Data System Dialysis Mortality and Morbidity Wave-2 study to identify patients with an AV fistula, PTFE graft, or a permanent catheter. Cox Regression analysis adjusted for age, gender, race, history of coronary artery disease, peripheral vascular disease, or bypass graft was used to model the relative risk of permanent vascular access failure.
RESULTS: Of the 4029 patients in the Wave 2 study a total of 946 (23%) met the criteria for the AV fistula, PTFE graft, or a permanent catheter placement analysis. PTFE graft patency was better for males (relative risk [RR], 0.73; p=0.02) and for those younger in age (RR, 0.99; p=0.04). Treatment with antiplatelet medications, ticlopidine and persantine, was associated with significantly better AV fistula access patency (RR, 2.92; p=0.048). Treatment with HMG-CoA reductase inhibitors, angiotensin converting enzyme inhibitors, anti-anginal agent, calcium channel blockers, aspirin, and anticoagulants was not associated with improved patency.
CONCLUSION: These findings may help guide a prospective, interventional trial of antiplatelet therapy for vascular access preservation.

212. Paricalcitol versus calcitriol in the treatment of secondary hyperparathyroidism in hemodialysis patients. *Marina B. Rabinovich, PharmD*, Ted Walton, PharmD; Grady Health System, Atlanta, GA.

PURPOSE: Treatment of secondary hyperparathyroidism involves administration of calcium supplements or vitamin D (calcitriol). Limitations of treatment are development of hypercalcemia, hyperphosphatemia, and increased calcium and phosphorus product (Ca x P). Paricalcitol is a synthetic vitamin D analogue shown to reduce parathyroid hormone (PTH) levels with minimal effects on calcium (Ca) and phosphorus (P) levels. Limited data is available comparing efficacy of intravenous paricalcitol to intravenous calcitriol. The primary objective was to compare efficacy of paricalcitol to calcitriol in outpatient hemodialysis patients. Secondary objectives included safety of paricalcitol and calcitriol and direct costs associated with these agents.
METHODS: This was a retrospective, cross-over study of hemodialysis patients who received at least 8 weeks of both therapies from March 2002 to March 2004. Primary outcomes included percentage of patients achieving > 50 % reduction in baseline PTH levels; change in PTH levels from baseline to end of therapy; time to achieve > 50 % reduction in baseline PTH concentrations. Secondary outcomes included percentage of patients experiencing hypercalcemia, hyperphosphatemia, and/or elevated Ca x P; percentage of patients hospitalized secondary to side effects of these agents.
RESULTS: Serum PTH levels were similar between two agents at baseline; however, there was statistically non-significant median percent decrease in PTH concentrations from baseline to the end of treatment phase (paricalcitol–1.5 %, calcitriol–8.3 %, p=0.8). A similar number of patients in both treatment groups were able to achieve > 50 % reduction in baseline PTH concentration. This endpoint was achieved faster in paricalcitol-treated patients but was non-significant (p > 0.05). The incidence of side effects between the two agents was similar.
CONCLUSION: Due to unclear beneficial effects of paricalcitol and limited data comparing this agent to calcitriol, additional research is required before paricalcitol becomes the standard of care in patients with secondary hyperparathyroidism.

213. Effect of nesiritide on renal function in acute decompensated heart failure or open-heart surgery. *Haley Papps, Student*[1], Judith L. Kristeller, PharmD, BCPS[1], Russell Stahl, MD[2]; (1)Wilkes University, Wilkes-Barre, PA; (2)Community Medical Center, Scranton, PA.

PURPOSE: Nesiritide improves hemodynamics and symptoms in patients with acute decompensated heart failure (ADHF). Patients undergoing open-heart surgery (OHS) have physiologic characteristics similar to ADHF, thus providing a theoretical rationale for the benefit of nesiritide in OHS patients. Nesiritide was used in both patient populations at our institution. For OHS, nesiritide was used primarily for renal protection in patients at risk for renal insufficiency. A recent publication however raised concern about worsening renal function in ADHF patients receiving nesiritide. This study evaluated the effect on renal function of nesiritide in OHS and ADHF patients.
METHODS: We retrospectively assessed renal function in 84 ADHF and 29 OHS patients from 9/2004 to 3/2005. Within each group, renal function was compared between patients receiving nesiritide and those who did not. For OHS patients, only those with a CrCl <60ml/min were included in the study. Worsening renal function was defined as an increase in peak serum creatinine by > 0.5mg/dl. We used the χ^2 test to determine statistical significance.
RESULTS: Forty patients with a primary diagnosis of ADHF received nesiritide. This group was compared to 44 similar ADHF patients not receiving nesiritide. The mean baseline creatinine in both groups was 1.5mg/dl. Worsening renal function occurred in 14/40 (35%) nesiritide and 7/44 (16%) non-nesiritide patients (p<0.05). Nesiritide was administered to 12 OHS patients with an initial CrCl <60ml/min. This group was compared to 17 similar OHS patients not receiving nesiritide. Worsening renal function occurred in 7/12 (58%) nesiritide and 4/17 (23%) non-nesiritide patients (p<0.1).
CONCLUSION: The incidence of worsening renal function is significantly higher in ADHF patients who receive nesiritide. OHS patients who received nesiritide demonstrated a trend of worsening renal function.

214. Renal reserve is maintained in patients with hepatitis C. *Gary R. Matzke, Pharm.D*[1], Thomas C. Dowling, Pharm.D., Ph.D.[2], Kristine Schonder, Pharm.D[1], Ghazal Vessal, Pharm.D.[2], Raman Venkataramanan, PhD[1], Paul Palevsky, M.D.[1]; (1)University of Pittsburgh, Pittsburgh, PA; (2)University of Maryland, Baltimore, MD.

PURPOSE: Liver disease is known to alter some aspects of renal function. Many patients with pre-ascitic hepatic insufficiency do not have overt abnormalities of renal function, but may be unable to excrete a sodium load or to escape from the sodium retaining effect of mineralocorticoids. This may be a reflection of reduced glomerular and/or tubular renal function reserve. We assessed the degree of glomerular reserve in patients with hepatitis C to test the hypothesis that glomerular reserve will be significantly reduced in this patient population.
METHODS: Seven patients with hepatitis C [HC] and Child-Pugh scores of 6 to 8 [age 49.6 (2.3) years] and 6 healthy volunteers[NH][age 47.6 (5) years]

had glomerular filtration rate [GFR] and effective renal plasma flow [ERPF] measured via a continuous infusion of iothalamate and p-aminohippurate prior to, during and post an intravenous protein challenge with an amino acid (AA) solution. The changes in GFR and ERPF were considered indices of glomerular reserve.
RESULTS: Baseline renal function was similar between groups, and slight increases in renal reserve were observed in both groups following AA infusion.

		Before AA inf.	During AA inf.	P value
NH (n=6)	GFR	118.8	122.4	0.66
	ERPF	494.7	510.2	0.67
	Filtration fraction	0.244	0.248	0.76
HC	GFR	127.8	132.6	0.64
	ERPF	549.7	574	0.66
	Filtration fraction	0.240	0.232	0.67

These data refute the recent findings of Woitas and colleagues in patients with mild liver disease (child-pugh scores < 6) which indicated dissociation between changes in GFR and ERPF after an IV AA challenge. Thus the decrease in renal sodium, water, calcium, phosphorous and magnesium excretion in patients with liver disease may be due to alterations in tubular function and reserve rather than glomerular reserve. Further studies are in progress to confirm these observations and ascertain the mechanisms responsible.

215. Assessment of quality of life in hemodialysis patients receiving pharmaceutical care. *Amy B. Pai, Pharm.D.*[1], Alex Boyd, BS[1], Alicia Chavez, BS[1], Harold J. Manley, Pharm.D.[2]; (1)University of New Mexico, Albuquerque, NM; (2)Albany College of Pharmacy, Albany, NY.

PURPOSE: End-stage renal disease(ESRD) and the initiation of hemodialysis(HD) affects quality of life(QoL). There are no data evaluating the effect of continued pharmacist intervention on QoL in HD patients. This study's purpose is to determine the impact of provision of pharmaceutical care on QoL using a disease-specific QoL survey.
METHODS: Patients at the largest dialysis unit in New Mexico were randomized to receive Pharmaceutical Care(Pharm); in-depth monthly medication reviews conducted by a nephrology-trained clinical pharmacist or Standard Care(Std); medication reviews conducted by nursing staff. The Renal Quality of Life Profile(RQLP) was administered by the same interviewers to both groups at baseline and at medication reviews 6 and 12. The RQLP is a 43-item questionnaire with a 5-point Likert response scale providing scores in 5 dimensions; eating/drinking(A), physical activities(B), leisure time(C), psychosocial activities(D) and impact of treatment(E). An increase in overall score reflects a decrease in QoL.
RESULTS: A total of 115 patients were enrolled in the study (Pharm: n=63, Std: n=52). Baseline demographic data were not significantly different between the groups. There was no difference in baseline total RQLP scores. Mean ± SD total RQLP scores at the 6th medication review were significantly higher in Std compared to Pharm (88 ± 30 vs 71 ± 34, p=0.03). Significant increases in dimensions A(5.9 ± 3.3 vs 4.4 ± 3.1, p=0.04), B(37 ± 13.6 vs 30 ± 16.3, p=0.04) and C(8.3 ± 3.4 vs 5.9 ± 3.6, p=0.03) were also observed in Std compared to Pharm. At the 12th medication review there was only a significant increase in dimension C(7.5 ± 3.1 vs 5.2 ± 3.9, p=0.04) in STD, attributable to a significant number of drop-outs, death and loss to follow-up.
CONCLUSION: These data indicate that patients who have clinical care provided by pharmacists maintain QoL compared to patients not receiving pharmacists' interventions.

Neurology

216. A randomized, double-blind, placebo controlled trial of melatonin add-on therapy in epileptic children on valproate monotherapy: effect on glutathione peroxidase and glutathione reductase enzymes. *Madhur Gupta, MD*[1], Y.K. Gupta, MD[2], S Aneja, MD[1], K Kohli, MD[1]; (1)Lady Hardinge Medical College, New Delhi, India; (2)All India Institute of Medical Sciences, New Delhi, India.

PURPOSE: To compare the effect of add-on melatonin with placebo on the antioxidant enzymes (glutathione peroxidase and glutathione reductase) in epileptic children on valproate monotherapy.
METHODS: In a double-blind, randomized, placebo controlled trial, the effect of add-on melatonin administration on the antioxidant enzymes in epileptic children on valproate monotherapy was assessed. Out of 31 patients, 16 patients were randomly allocated to receive add-on melatonin, and 15 to receive add-on placebo. Blood samples were collected for baseline values of glutathione peroxidase and glutathione reductase enzymes, and then after 14 days of add-on melatonin/placebo. Blood was then centrifuged, sera separated, and stored in deep freezer until assay of glutathione reductase. Heparinized blood was collected and stored at -20 degrees C in the deep freezer for assay of glutathione peroxidase. All activity assays were performed on the Ames (Technicon) RA 50 chemistry analyser.
RESULTS: Fifteen patients in the add-on melatonin group and 14 patients in the add-on placebo group were finally assessed. There was an increase in the activity of antioxidant enzymes, glutathione peroxidase (GSH-Px) and glutathione reductase (GSSG-Rd), in the add-on melatonin group as compared with a reduction in the same in the add-on placebo group. On administration of melatonin/placebo, the post-treatment concentrations of GSSG-Rd in the valproate + placebo group decreased from 92.0 U l(-1) to 67.0 U l(-1) and increased from 82.0 U l(-1) to 113.0 U l(-1), in the valproate + melatonin group, respectively, the difference between them being statistically significant (P = 0.05). The percentage change in the values of GSSG-Rd in the two groups was statistically significant (P = 0.005).
CONCLUSIONS: Melatonin exerts neuroprotection due to its antioxidant, antiexcitotoxic and free radical scavenging properties within the central nervous system. Melatonin, thus, as an adjunct, can be a putative neuroprotector in conditions involving oxidative stress like epilepsies.

217. Botulinum toxin for cervical dystonia in myasthenia gravis: a case study. *Jack J. Chen, PharmD*[1], David M. Swope, MD[2], Laura Nist, MD[2]; (1)Western University of Health Sciences and Movement Disorders Clinic, Loma Linda University, Pomona, CA; (2)Loma Linda University, Loma Linda, CA.

PURPOSE: To discuss the safety and effectiveness long-term botulinum toxin type-A (BTX-A) treatment for cervical dystonia in a 73-year-old woman with pre-existing myasthenia gravis (diagnosed by positive AChR antibodies).
METHODS: At the age of 63 years, the patient was initiated on BTX-A treatment for management of focal dystonia. Her myasthenia gravis was in remission and managed with azathioprine, pyridostigmine, and prednisone. Muscles that were consistently injected over a 10-year period were the left and right splenius capitus, left and right masseters, and left and right temporalis. Occasionally, injections were also administered in the muscles of the upper and lower face and thyroarytenoid (vocalis). BTX-A treatment continued for 10 years at which time the patient moved and was lost to follow-up.
RESULTS: The patient was successfully treated with BTX-A on 24 occasions over 10 years with a cumulative BTX-A (Botox®, Allergan, Irvine, CA) dose of 5380 units (approximate mean total dose of 225 units per treatment). Her average duration of clinical improvement associated with BTX-A injections was approximately 8 weeks. Over the 10 year course of BTX-A treatment, the patient experienced excessive neck weakness on two occasions that were correlated with injections to the splenius capitus. These episodes of neck weakness lasted 2 and 6 weeks, respectively. She did not develop dysphagia. The patient was able to live alone independently and did not experience any exacerbation of myasthenic weakness attributable to BTX-A treatment. She did not experience any episodes of myasthenic crisis.
CONCLUSIONS: To the best of our knowledge, this case represents the longest duration of safe and effective BTX-A therapy in a patient with established myasthenia gravis. BTX-A can be used safely and effectively in patients with myasthenia gravis in remission.

218. Zonisamide for the treatment of essential tremor: a case study. *Jack J. Chen, PharmD*[1], David M. Swope, MD[2], Rowena S. Gascon, PharmD[1]; (1)Western University of Health Sciences and Movement Disorders Clinic, Loma Linda University, Pomona, CA; (2)Loma Linda University, Loma Linda, CA.

PURPOSE: To discuss the effectiveness of zonisamide in the treatment of essential tremor in an 83-year-old, right-handed man. Symptoms included bilateral postural and action tremor of the distal upper extremities and a horizontal head tremor. Voice tremor was absent. The tremor resulted in limitations in physical and social functioning. Functional disability included difficulty with holding and drinking from a cup, handwriting, and with utilizing eating utensils without spilling food. In the past, monotherapy with beta-blockers, gabapentin, and primidone provided partial symptomatic benefit but was discontinued due to side effects.
METHODS: Zonisamide 100 mg at bedtime was initiated and, given the absence of side effects, increased to 200mg after two weeks. Objective assessments included baseline and on-treatment videotaped neurologic examinations, freehand cursive writing samples, and spiral hand drawings. Subjective assessment was also documented. A dosage increase beyond 200mg was not attempted due to side effect concerns.
RESULTS: Treatment with zonisamide resulted in objective and subjective improvements of action and postural tremors and ability to perform cup-to-cup water transfer, handwriting, and spiral drawing. Head tremor remained unchanged. Zonisamide was well tolerated with the exception of drowsiness, at the 200mg dose, which improved over time.
CONCLUSION: Zonisamide may be effective and well tolerated as monotherapy for treating essential tremor. Additional investigations are warranted.

219. Low incidence of cognitive and behavioral adverse events in rasagiline-treated patients with early to advanced Parkinson's disease (PD). *Jack J. Chen, PharmD*[1], Richard C. Berchou, PharmD[2]; (1)Western University of Health Sciences and Movement Disorders Clinic, Loma Linda University, Pomona, CA; (2)Wayne State University, Detroit, MI.

PURPOSE: Effective management of PD motor symptoms with current treatments is often complicated by treatment emergent cognitive and behavioral adverse events (CBAEs), such as confusion, depression, hallucinations, somnolence, and other sleep disorders. Rasagiline [N-propargyl-1(R)-aminoindan] mesylate is a novel, potent, second-generation, selective, irreversible monoamine oxidase type-B inhibitor that has demonstrated symptomatic efficacy in multicenter, randomized, placebo-controlled, 26-week trials in patients with early PD (TEMPO, n=404) and moderate-to-advanced PD (PRESTO, n=472). This analysis was performed to determine the incidence of CBAEs and effects on mental function in patients treated with rasagiline 1 mg once daily as compared to placebo.
METHODS: In both TEMPO and PRESTO, the incidence of CBAEs and the change from baseline in the Unified Parkinson's Disease Rating Scale (UPDRS) Part I mental subscores were analyzed. The UPDRS is a validated multi-item rating scale commonly utilized in PD clinical research. The UPDRS Part I subscale evaluates cognitive impairment, thought disorder, depression, and motivation/initiative.
RESULTS: No CBAEs in either the rasagiline or placebo groups exceeded 10% of the patients in that treatment group. In either study, the difference between rasagiline 1mg and placebo in CBAEs did not exceed 3% and there was no adverse change compared to placebo on the UPDRS mental subscore after 26 weeks of treatment. Frequency of CBAEs resulting in early withdrawal did not notably differ between rasagiline 1mg and placebo groups.
CONCLUSIONS: In addition to improving symptoms in early and moderate-to-advanced PD patients, once daily rasagiline was well tolerated and was not associated with a significant incidence of CBAEs or adverse effects on mentation, behavior and mood. This study was supported by Teva Pharmaceutical Industries, LTD, HLundbeck A/S, and Teva Neuroscience Inc., now in partnership with Eisai Inc.

220. Rasagiline is effective as monotherapy in patients with early Parkinson's disease (PD) and as adjunctive therapy in moderate to advanced PD. *Jack J. Chen, PharmD*[1], Richard C. Berchou, PharmD[2]; (1)Western University of Health Sciences and Movement Disorders Clinic, Loma Linda University, Pomona, CA; (2)Wayne State University, Detroit, MI.

OBJECTIVE: To evaluate the efficacy of rasagiline (N-propargyl-1[R]-aminoindan) mesylate, a potent, selective, second-generation, irreversible MAO-B inhibitor as monotherapy and as adjunctive therapy for the treatment of symptoms in idiopathic PD.
METHODS: Two multicenter, randomized, double-blind, placebo-controlled, 6-month trials investigated the effects of once-daily rasagiline 1 mg on PD symptoms. The TEMPO study (n=404) evaluated rasagiline monotherapy in early PD. The PRESTO study (n=472) evaluated rasagiline vs placebo in patients with moderate to advanced PD experiencing motor fluctuations despite optimized levodopa/carbidopa (LD/CD) treatment. Endpoints included change in total Unified Parkinson's Disease Rating Scale (UPDRS) from baseline as the primary measure of efficacy of TEMPO and change in total daily "off" time measured by patient daily diaries for PRESTO.
RESULTS: For the rasagiline 1mg treatment groups, disease duration was 0.92 ± 1.24 years (n=134) in TEMPO and 8.8 ± 5.4 years (n=149) in PRESTO. In both trials, rasagiline was superior to placebo for change in total UPDRS ($p<0.0001$ and $p=0.0084$, TEMPO and PRESTO, respectively). As adjunct therapy, rasagiline provided an incremental significant reduction in total daily "off" time compared to LD/CD alone (-0.94 hours, $p<0.0001$). This significant effect included those patients (70%) also taking other dopaminergic therapy in addition to LD/CD. No effect on postural instability/gait disorder was observed in either study. Rasagiline was well tolerated in both trials with a low incidence of dopaminergic adverse events.
CONCLUSION: These findings suggest that once daily rasagiline provides significant symptom benefit as initial monotherapy in early PD and as adjunct therapy to LD/CD in moderate to advanced PD. Disclosures: This study was supported by Teva Pharmaceutical Industries, LTD, HLundbeck A/S, and Teva Neuroscience Inc., now in partnership with Eisai Inc.

221. Rasagiline provides significant management of motor symptoms in early and moderate-to-advanced Parkinson's disease (PD). *Richard C. Berchou, PharmD*[1], Jack J. Chen, PharmD[2]; (1)Wayne State University, Bingham Farms, MI; (2)Western University of Health Sciences and Movement Disorders Clinic, Loma Linda University, Pomona, CA.

INTRODUCTION: Rasagiline (N-propargyl-1[R]-aminoindan) mesylate is a potent, selective, second-generation, irreversible MAO-B inhibitor.
METHODS: Two multicenter, randomized, double-blind, placebo-controlled, 6 month trials investigated the effects of once-daily rasagiline 1 mg on PD symptoms. The Unified Parkinson's Disease Rating Scale (UPDRS) was the primary efficacy measure in the TEMPO study (N=404), which evaluated rasagiline monotherapy in early PD patients (mean age 60.8 ± 10.8 years, disease duration 1.0 ± 1.24 years). UPDRS was a secondary efficacy measure in PRESTO (N=472), which evaluated rasagiline + optimized levodopa/carbidopa (LD/CD) vs placebo + LD/CD in moderate-to-advanced patients (mean age 63.3 ± 9.5 years, PD duration 9.3 ± 5.3 years).
RESULTS: In TEMPO and PRESTO, rasagiline was superior to placebo for total UPDRS ($p<0.0001$; $p=0.0084$, respectively) and motor subscale ($p<0.0001$; $p=0.0011$). Motor score analyses were conducted post-hoc, without correcting for multiple comparisons. In TEMPO and PRESTO, rasagiline reduced tremor ($p=0.002$; $p=0.0021$, respectively) and bradykinesia ($p<0.0001$; $p=0.0493$), vs placebo. Rasagiline patients also experienced less rigidity in PRESTO ($p=0.0239$) vs placebo + LD/CD.
Conclusion: These findings demonstrate that rasagiline has significant motor symptom effects as initial monotherapy in early PD and as adjunct therapy in advanced PD.
This study was supported by Teva Neuroscience Inc., in partnership with Eisai Inc., and H. Lundbeck A/S.

222. Clinical and economic outcomes of pharmacist-managed epileptic drug therapy in hospitalized Medicare patients. *C. A. (CAB) Bond, Pharm.D., FASHP, FCCP*, Cynthia L. Raehl, PHarm.D., FASHP, FCCP; Texas Tech University-HSC-School of Pharmacy, Amarillo, TX.

PURPOSE: This study explores the associations between pharmacist provided epileptic drug management in hospitalized Medicare patients who had diagnoses indicating the need for these drugs and major heath care outcomes: death rate, length of stay, Medicare charges, drug charges, laboratory charges, complications, and adverse drug reactions.
METHODS: Data was drawn from the 1998 MedPAR and 1998 National Clinical Pharmacy databases. Pharmacists management of drug therapy was evaluated in a study population composed of 9380 Medicare patients treated in 794 hospitals. This study population was derived from the 38,311 hospitalized Medicare patients who had epilepsy or seizure disorders (MedPAR).
RESULTS: In hospitals that did not have pharmacist provided epileptic drug management, death rates were 121% higher-304 excess deaths (X^2 (1) = 5.983, p =0.014, odds ratio = 1.553, 95%CI (1.102, 2.189), length of stay was 14.68% higher- 8069 patient days (U = 3833132, p=0.0009), total Medicare charges were 11.19% higher $14,372,550 in excess total Medicare charges (U = 3644199, p=0.0003), drug charges were $115/patients lower, however, these differences were not statistically significant, laboratory charges were 32.24% higher-$5,664,970 in excess laboratory charges, aspiration pneumonia was 54.61% higher (U = 3411054, $p<0.0001$), $X^2 = 5.848$, df = 1. p=0.015, odds ratio = 1.233, 95%CI (1.081,1.901), and while the incidence of other complications and side effects were higher, these differences were not statistically significant when compared to hospitals that had pharmacists managing epileptic drugs.
CONCLUSION: Clinical and economic outcomes were mostly improved among Medicare patients who did receive epileptic drugs management by pharmacists.

223E. Duration of human mu-opiate receptor blockade following naltrexone: measurement by 11C-carfentanil PET. *Edward M. Bednarczyk, PharmD*, David Wack, MA, Michael S Haka, PhD, Elizabeth Shang, PhD, Linda Hershey, MD, PhD, Richard L O'Sullivan, MD, Terence Fullerton, PharmD; University at Buffalo, Buffalo, NY.

BACKGROUND: Naltrexone is a mu opiate receptor antagonist approved for the treatment of alcohol dependency. Previous reports have suggested a duration of receptor occupancy of naltrexone that greatly exceeds that predicted by it's 4 hour $T^1/_2$, or the 13 hour $T^1/_2$ of beta-naltrexol, the predominant metabolite. We undertook a double blind, placebo controlled, randomized study of receptor occupancy using the highly selective mu opiate receptor ligand 11C-carfentanil.
METHODS: Healthy volunteers underwent PET imaging with 11C-carfentanil at baseline, 3 24, 72 and 144 hours following a single oral dose of placebo, 12.5, 50 or 100mg of naltrexone. Regional analysis was undertaken using a statistical parametric mapping approach (SPM2).
RESULTS: 22 subjects have completed all phases of the study. Regions of significantly ($p<0.001$) lower activity were mapped in all known regions of brain mu receptors 3 and 24 hours following all doses of naltrexone. This effect was measurable at 72 hours for 50 and 100mg dose. At 144 hours, significant blockade remained in the left temporal lobe for 100 mg dose.

Baseline vs	Placebo N=6	12.5mg N=6	50 mg N=5	100 mg N=5
3H	NS	P<0.001	P<0.001	P<0.001
24H	NS	P<0.001	P<0.001	P<0.001
72H	NS	NS	P<0.001	P<0.001
144H	NS	NS	NS	P<0.001

CONCLUSIONS: Our findings provide tomographic evidence of a persistence

of blockade of the mu opiate receptor for up to 144 hours following naltrexone, with no evidence of a receptor level placebo effect. Correlation with plasma naltrexone and beta naltrexol is planned.
Published in J Nucl Med 2005;46(5):288P.

Nutrition

224. Does medication use change during a weight loss program? *Margaret Malone, PhD, FCCP*[1], Sharon Alger-Mayer, MD[2], Drew Anderson, PhD[3]; (1)Albany College of Pharmacy, Albany, NY; (2)Albany Medical College, Albany, NY; (3)Dept of Psychology-SUNY, Albany, NY.

PURPOSE:To determine the change in medication use by participants in a weight loss program.
METHODS: Adult patients were recruited from an outpatient University teaching hospital to participate in a 20 week structured weight loss program. Demographic data including medication use were recorded at the start, 6, 12 and 20 week time points. The charge for the program was $200/person which was self paid. All data are reported as mean ± SD.
RESULTS: Ninety patients (74 female) age 48 ± 10 years were recruited. At the start of the program weight was 228 ±46 lbs (BMI 37 ± 6 kg/m^2). At 10 weeks 83/90 (92%) remained in the program, % wt loss was 3 (3). At 20 weeks the % wt loss of completers (n=59) was 4.8 (5.0). Patients had multiple diseases including: type 2 diabetes mellitus [DM] (n=23); hypertension [HT] (n=48); depression [D](n=18) and dyslipidemia [L] (n=9). At baseline, the # of medications per patient used to treat obesity related comorbid (ORM) disease was 2.7 ± 2.6 [median=2.0], # of non ORM medications was 1.3 ±1.5 [median=1.0], # of nutritional supplements was 1.0 ±1.2 [median=1.0]. The number of types of ORM by therapeutic category at baseline was 47 DM, 118 HT, 48 D and 21 L. Nine participants were not taking any medication or supplements at baseline. Fifteen participants had medication discontinued during the program. The cost savings per patient per 30 days of therapy (using AWP 2004) ranged from $6-$523 (Mean $155 ± 153). Diabetic patients who lost weight had improved blood glucose control; 13 medications for diabetes were discontinued in nine patients.
CONCLUSION: Patients taking medication for DM who experienced weight loss, had cost savings per month which were equal to or greater than the total cost of the program. Antidepressants, lipid lowering agents and antihypertensives were rarely discontinued.

225E. Treatment of diminished bone mineral density with intravenous pamidronate in patients receiving chronic home parenteral nutrition. *John K. Siepler, Pharm.D.*, Reid A Nishikawa, Pharm.D., Tom Diamantidis, Pharm.D., Rod Okamoto, RpH; Nutrishare, Inc, Elk Grove, CA.

RATIONALE: Patients receiving home TPN (HPN) may develop osteoporosis requiring treatment. In patients with short bowel (SBS), IV pamidronate (IVP) has been used. We evaluated serial bone densitometry studies (DEXA) in HPN patients with SBS to determine if therapeutic response can be correlated with any specific patient parameter.
METHODS: Patients requiring HPN for SBS on IVP were included. An initial DEXA (T score: spine (S) and left femoral neck (FN)) was performed. DEXA was repeated yearly while on IVP. Clinical data recorded was age, gender, and underlying disease. Statistical analysis included logistic regression and student's T test.
RESULTS: Results were available for 23 patients. Duration of IVP use was 4.8 ± 1.8 years. Improvement in DEXA was seen in 87% S and 78% FN. Age, gender, IVP dose, days/week of HPN, underlying disease, corticosteroid use, and Calcium dose was not associated with improvement in DEXA. Duration of IVP use (years) correlated with % improvement in S DEXA (OR 3.6; 95%CI:1.5-8.3, p=0.03) and FN DEXA (OR 2.9;95%CI:1.2-2.9, p=0.02). Patients on IVP greater than 3 years had a greater probability of DEXA improvement of FN DEXA (OR 6.6;95%CI:1.3-33,p=0.024). No patient developed a long bone fracture during IVP treatment. Discussion: HPN patients may develop osteoporosis and require treatment with IVP. Data documenting effectiveness of IVP in these patients are limited. We demonstrate an improvement in DEXA in HPN patients on IVP. Longer duration of IVP use correlate with improved DEXA. Improvement in DEXA while on IVP is not associated with age, gender, underlying disease, IVP dose, Calcium dose, corticosteroid use, or frequency of HPN use. Further investigation is required in this area to establish a role of bisphosphonate therapy in patients on HPN.
Published in the 27th Congress of the European Society of Clinical Nutrition and Metabolism, Brussels, Belgium, August 27-30, 2005.

226E. Weaning from chronic home parenteral nutrition in patients with short bowel syndrome: identification of clinical parameters associated with success. *John K. Siepler, Pharm.D.*, Vanessa Kumpf, Pharm.D., Tom Diamantidis, Pharm.D., Rod Okamoto, RpH, Reid Nishikawa, Pharm.D.; Nutrishare, Inc, Elk Grove, CA.

BACKGROUND: Patients with short bowel(SBS) may require home TPN(HPN). We evaluated HPN patients from 1 home-care provider to determine if there were clinical parameters which were associated with ability to wean off HPN(wean).
METHODS: The records of every HPN patient with SBS from one provider were examined. HPN was any patient requiring HPN for >1 year and not expected to WHPN in the future. Inclusion criteria consisted of bowel anatomy after resection (length of small bowel, presence of ileocecal valve, and/or colon). Data included demographics, anthropomorphics, underlying disease, bowel anatomy, bowel length, and attendance at a bowel rehabilitation program. Data was analyzed using logistic regression to determine if clinical parameters were associated with the ability to Wean.
RESULTS: 94 patients met inclusion criteria. The mean age and weight were 38.4 ± 19 years and 55.9 ± 18.5 kg. There were 56(59.6%) females. The patients had been on HPN for 14.9 ± 7 years. There were 13(13.8%) patients able to wean. Small bowel length >1cm/kg was associated with a greater chance of weaning (See table). Underlying disease, age, gender and attendance at bowel rehab program was not associated with being able to wean.
CONCLUSIONS: In HPN population, mall bowel length >1cm/kg is associated with a greater chance of being able to wean. Underlying disease, age, and gender were not predictors for being able to wean. These results are limited to patients who are on chronic HPN.

Table 1 Probability to Wean and SB length
Sb length total weaned

Cm/kg	n	n (%)	p	OR	95% C.I.
> 0.5	81	13 (16)	0.072	6.7	0.84–53
> 1.0	62	12 (19)	0.019	6.4	1.36–29
> 1.5	53	11 (21)	0.014	5.3	1.4–20
> 2.0	40	10 (25)	0.004	6.1	1.8–21
> 2.5	35	10 (29)	0.001	7.8	2.3–27

weaned = cumulative number of patients

Presented at the Digestive Disease Week of the American Gastroenterological Association, Chicago, IL, May 14-19, 2005.

227. Utilization of parenteral nutrition in patients receiving isolated kidney or simultaneous pancreas/kidney transplantation. *Gordon S. Sacks, Pharm.D., B.S.*, Kenneth A. Kudsk, MD; The University of Wisconsin–Madison, Madison, WI.

PURPOSE: To characterize the utilization of parenteral nutrition (PN) in patients with a history of an isolated kidney (KID) or simultaneous pancreas/kidney (SPK) transplantation.
METHODS: Medical records of consecutive adult patients receiving transplantations or admitted to the hospital with complications related to a previous transplantation between April 2004 and May 2005 were retrospectively reviewed. Data collected and analyzed included: demographic data, indications for PN, days of PN, preoperative albumin concentrations, and postoperative prealbumin and CRP concentrations. Patient outcome parameters including length of hospitalization, transition to oral diet, and mortality for were also recorded.
RESULTS: Medical records of 25 patients were identified for being hospitalized during the review period. A total of 7 patients were admitted for their initial SPK with the remaining patients requiring admission for complications related to SPK (n=10) or KID (n=8)transplantations from previous hospitalizations. Ileus, persistent nausea/vomiting, and gastroparesis were the most common indications for initiation of PN. Approximately 25% (6/25) of patients required significantly fewer days of PN before tolerating enteral nutrition/oral diet compared to the remaining patients (4.7 ± 0.8 vs. 11.3 ± 6.4 days, $p < 0.001$, *t*-test). Factors differentiating this subgroup from the rest of the patients included a significantly higher preoperative serum albumin (4.13 ± 0.5 vs. 3.49 ± 0.7 mg/dL, $p < 0.03$, *t*-test), undergoing an initial SPK transplantation (57% vs. 17%, $p < 0.05$, χ^2 test), and having a diagnosis of ileus as the indication for PN initiation (57% vs. 11%, p<0.05, chi square test).
CONCLUSIONS: Our data suggest that ileus and persistent nausea/vomiting are two primary reasons for institution of PN in isolated KID and SPK transplantation patients. Well-nourished patients undergoing their first SPK transplantation who develop a postoperative ileus receive PN < 7 days and,thus, may not need nutritional intervention.

Oncology

228. Patient motivations surrounding participation in phase I and phase II clinical trials of cancer chemotherapy. *Zubeir Nurgat, M.Sc.*; Aberdeen Royal Infirmary, Aberdeen, United Kingdom.

Successful advances in the treatment of advanced malignant diseases rely on recruitment of patients into clinical trials of novel agents. However, there is a genuine concern for the welfare of individual patients. The aim of this study

was to examine motives of patients entering early clinical trials of novel cancer therapies using a questionnaire survey with both open- and close-ended questions. The patients were surveyed after they had given informed consent and before or during the first cycle of treatment. In all, 38 phase I/II trial patients participated and completed the survey. Obtaining possible health benefit was listed by 89% as being a 'very important' factor in their decision to participate, with only 17% giving reasons of helping future cancer patients and treatment. Other items cited as a 'very important' motivating factor were 'trust in the doctor' (66%), 'being treated by the latest treatment available' (66%), 'better standard of care and closer follow-up' (61%), and 'closer monitoring of patients in trials' (58%). Only 47% patients indicated that someone had explained to them about any 'reasonable' alternatives to the trial. In total, 71% strongly agreed that 'surviving for as long time as possible was the most important thing (for them)'. Nearly all (97%) indicated that they knew the purpose of the trial and had enough time to consider participation in the trial (100%). In this survey, most patients entering phase I and II clinical trials felt they understood the purpose of the research and had given truly informed consent. Despite this, most patients participated in the hope of therapeutic benefit, although this is known to be a rare outcome in this patient subset. Trialists should be aware, and take account of the expectations that participants place in trial drugs.

229. Transport of vincristine by xenobiotic efflux transporters. *Rong (Steph) Huang, M.S.*[1], Daryl J. Murry, Pharm.D.[2], Stephen D. Hall, Ph.D.[3], David R. Foster, Pharm.D.[1]; (1)Purdue University, Department of Pharmacy Practice, Indianapolis, IN; (2)The University of Iowa, College of Pharmacy, Clinical and Administrative Pharmacy Division, Iowa City, IA; (3)Indiana University, Division of Clinical Pharmacology, Indianapolis, IN.

PURPOSE: Membrane transporters including p-glycoprotein (MDR1), and membrane resistance proteins 1-3 (MRP's1-3) actively efflux many drugs across cell membranes, and can cause resistance to cancer chemotherapy. This study characterized interactions between efflux transporters and vincristine (VCR), using immortalized cell lines with differential transporter expression.
METHODS: Caco-2 (expresses MDR1, MRP's1-3), LS174T (expresses MDR1, MRP1), and A549 (expresses MRP's1-3) cells were used. To study VCR transport (effective permeability, P_{eff}), [^{3}H]VCR (1-500nM) was added to donor chambers of permeable supports containing Caco-2 monolayers, and receiving chamber concentrations were measured. Cytotoxicity experiments were conducted with all cell lines. To determine the contribution of MDR1 to VCR transport/cytotoxicity, experiments were also conducted with LY335979 (LY), a specific MDR1 inhibitor.
RESULTS: VCR P_{eff} was 2 x 10^{-6}cm/s; LY increased P_{eff} in a dose dependent manner (up to 7-fold with 1mM LY). Cytotoxicity results are shown in table.Table: Cell viability (%, mean ± s.d.) following 72 hour treatment with VCR and VCR+LY 1uM (*adjusted for multiple comparisons; NS, not significant)

VCR conc. (nM)	Caco-2			LS174T		
	VCR	VCR+LY	p*	VCR	VCR+LY	p*
5	60.9 ± 7.7	9.4 ± 4.3	0.004	80.8 ± 6.7	69.2 ± 11.9	NS
10	66.8 ± 4.0	8.8 ± 7.4	0.002	101.7 ± 8.8	40.3 ± 5.6	0.004
50	49.7 ± 3.1	30.5 ± 5.0	0.034	78.3 ± 16.2	30.3 ± 4.7	0.055
100	47.0 ± 4.4	15.4 ± 4.8	0.008	78.1 ± 12.8	25.6 ± 12.5	0.049
200	41.3 ± 5.6	8.9 ± 1.3	0.004	66.1 ± 7.9	11.5 ± 1.7	0.002
500	49.3 ± 1.1	11.4 ± 2.3	<0.001	63.0 ± 3.0	30.0 ± 2.2	0.001
1000	50.1 ± 3.9	19.9 ± 11.7	NS	63.9 ± 4.7	15.1 ± 2.7	0.001

(table continued)

	A549		
	VCR	VCR+LY	p*
5	81.8 ± 7.3	87.9 ± 13.7	NS
10	78.7 ± 9.6	75.3 ± 6.5	NS
50	75.6 ± 6.9	75.2 ± 11.2	NS
100	78.4 ± 8.0	68.7 ± 11.9	NS
200	66.4 ± 4.2	75.1 ± 6.4	NS
500	60.2 ± 9.4	88.6 ± 11.6	NS
1000	51.8 ± 8.1	61.9 ± 17.1	NS

CONCLUSIONS: MDR1 may play an important role in VCR efflux; MDR1 inhibition increased VCR P_{eff} in Caco-2 cells, and increased VCR cytotoxicity in Caco-2 and LS174T cells (both express MDR1), but not A549 cells (minimal MDR1 expression). Inhibition of MDR1 may be a viable strategy to overcome VCR resistance in tumors expressing MDR1.

230E. Final hematologic results: epoetin alfa (EPO) 40,000 U QW vs darbepoetin alfa (DARB) 200 µg Q2W in anemic cancer patients (pts) receiving chemotherapy (CT). Roger Waltzman, MD[1], Christopher Croot, MD[2], Denise Williams, MD[3], *Samir Mody, PharmD, MBA*[4]; (1)Saint Vincent's Comprehensive Cancer Center, New York, NY; (2)North Mississippi Hematology & Oncology, Ltd, Tupelo, MS; (3)Johnson and Johnson Pharmaceutical Research and Development, Raritan, NJ; (4)Ortho Biotech Clinical Affairs, LLC, Chapel Hill, NC.

PURPOSE: To compare hematologic outcomes, QOL, and safety for EPO and DARB using dosing regimens commonly prescribed in anemic cancer pts receiving CT.
METHODS: Randomized, open-label trial enrolled pts ≥18y with solid tumors, baseline (BL) Hb ≤11g/dL, scheduled for ≥12 weeks of CT. Pts stratified by ±platinum CT then randomized to EPO 40,000U SC QW or DARB 200mcg SC Q2W for 12-16 weeks; dose adjustments per NCCN guidelines. 150 pts per arm ensured 90% power to detect ≥20% difference in primary endpoint, Hb response rate (HRR; proportion of pts with Hb increase ≥1g/dL within first 4 weeks). Interim analysis of primary endpoint was planned after the first 300 pts completed 4 weeks.
RESULTS: 358 pts were randomized to EPO (178) or DARB (180). Primary endpoint achieved based on interim analysis of first 305 pts (EPO 151, DARB 154) demonstrating HRR was significantly higher for EPO (47%) vs DARB (33%) (p=0.0078). Mean BL Hb was 10.2g/dL (EPO) and 10.1g/dL (DARB). Mean Hb change and median time to 1g/dL rise are reported below. Incidence of RBC transfusion (week 5 to end of study) was 11% (EPO) and 16% (DARB) (p=0.2078). QOL change scores were similar between groups. Clinically relevant thrombovascular events occurred in 11% of EPO and 9% of DARB pts. 13% of EPO and 16% of DARB pts died on study.
CONCLUSIONS: Hb response rates were higher and time to 1g/dL Hb rise was shorter in pts with CT-induced anemia treated with EPO 40,000U QW compared with DARB 200 µg Q2W.

Table:

	EPO (n=175)	DARB (n=177)
Mean Hb change (g/dL)*		
4 weeks	0.7†	0.3
8	1.0†	0.5
12	1.3†	0.7
16 (final)	1.2†	0.8
Median time to 1g/dL Hb increase (days)	35†	48

*4 EPO and 5 DARB pts excluded due to missing BL or post-BL Hb. †P ≤.007 vs DARB

Published in Proc Am Soc Clin Oncol 2005;23(16S Part I of II):736s.

231. Empiric therapy for neutropenic fever: piperacillin/tazobactam in combination with tobramycin or levofloxacin. *Jill R. Blancett, Pharm.D.*, Susanne E. Liewer, Pharm.D., BCOP, Kelly M. Smith, Pharm.D., Jeremy D. Flynn, Pharm.D., Robert P. Rapp, Pharm.D., FCCP, Val R. Adams, Pharm.D., BCOP, FCCP; University of Kentucky Chandler Medical Center, Lexington, KY.

PURPOSE: The use of levofloxacin in combination with piperacillin/tazobactam in neutropenic fever (NF) treatment is an emerging practice, although the efficacy of this regimen has not been fully demonstrated. The objective of this study is to determine if piperacillin/tazobactam plus levofloxacin is equivalent to piperacillin/tazobactam plus tobramycin for empiric NF therapy.
METHODS: Retrospective pilot study of all patients hospitalized with NF between June 2001 and December 2004 treated with piperacillin/tazobactam and levofloxacin (Group A) or piperacillin/tazobactam and tobramycin (Group B). Primary endpoint was success rates between groups, defined as resolution of NF without altering antibiotic regimen. Appropriate addition of vancomycin was not considered a failure of therapy. Secondary endpoints included duration of therapy, length of stay, time to neutrophil recovery, colony stimulating factor use, time to defervesence, superinfection and subsequent infection rates. Statistical analysis was performed using the Mann-Whitney *t*-test and Fisher's exact test.
RESULTS: Two-hundred and ninety-one events were identified and 36 patient admissions met the inclusion/exclusion criteria. Thirteen patients in Group A were compared with 23 patients in Group B. No difference in success rate between Group A and B (76.9% vs. 78.3%, respectively) (P = 1.0) was found. Secondary endpoints of length of stay (mean, 6.5 vs. 8.9 days) (P = 0.59), time to defervesence (mean, 3.9 vs. 2.9 days) (P = 0.29) and duration of neutropenia (mean, 4 vs. 3.4 days) (P = 0.48) were similar between groups A and B, respectively.
CONCLUSION: These findings suggest levofloxacin in combination with piperacillin/tazobactam may be as effective as tobramycin plus piperacillin/tazobactam for empiric NF therapy and therefore warrants additional study.

232. First and subsequent cycle pegfilgrastim significantly reduces the incidence of febrile neutropenia, hospitalizations, and IV anti-infective use in patients with breast cancer receiving docetaxel: a phase 3, randomized, double-blind study. *Charles Vogel, MD*[1], Roger Dansey, MD[2]; (1)Cancer Research Network, Inc., Plantation, FL; (2)Amgen Inc., Thousand Oaks, CA.

PURPOSE: The pivotal pegfilgrastim studies demonstrated substantial clinical benefit in a chemotherapy regimen with an expected 40% risk of febrile neutropenia (FN). Patients at lower risk of FN may also benefit from first-

cycle use of growth factors. A study of patients with breast cancer receiving docetaxel 100 mg/m^2 Q3W (expected FN incidence of 20% without growth factor support) demonstrated that patients receiving pegfilgrastim experienced a significant reduction in FN compared with placebo (1% versus 17%; p<0.0001). Additionally, pegfilgrastim significantly reduced the incidence of FN-associated hospitalizations and IV anti-infective use. Lyman has shown ~50% of initial neutropenic events occur in cycle 1 for non-Hodgkin's lymphoma patients. We analyzed our study to determine if breast cancer patients also experience neutropenic events early in therapy.
METHODS: Breast cancer patients (ECOG 0 to 2) received either pegfilgrastim 6mg (n=463) or placebo (n=465) on the day after docetaxel for up to 4 cycles. FN was defined as temperature ≥38.2°C and absolute neutrophil count <0.5x10^9/L (within 1 day after temperature ≥38.2°C).
RESULTS: For patients receiving placebo, most neutropenic events occurred in cycle 1. For patients receiving pegfilgrastim, few FN events occurred and a pattern could not be discerned.

		Placebo (n=465)	Pegfilgrastim (n=463)
Febrile Neutropenia, % (95% CL)	Cycle 1	11 (8.5, 14.4)	<1 (<0.1, 1.6)
	Cycles 2 to 4	6 (3.7, 8.1)	<1 (0.2, 2.2)
FN-associated hospitalizations, % (95% CL)	Cycle 1	9 (6.8, 12.3)	1 (0.4, 2.5)
	Cycles 2 to 4	5 (2.8, 6.8)	<1 (<0.1, 1.2)
FN-associated IV anti-infective use, % (95% CL)	Cycle 1	6 (4.4, 9.1)	1 (0.4, 2.5)
	Cycles 2 to 4	4 (2.5, 6.3)	<1 (0.1, 1.9)

CONCLUSIONS: Patients receiving moderately myelosuppresive chemotherapy with no growth factor support experienced two-thirds of neutropenic events in cycle 1. Patients receiving first and subsequent cycle pegfilgrastim were generally protected from experiencing neutropenic events.

233. Hematologic outcomes and costs in epoetin alfa (EPO) and darbepoetin alfa (DARB) treated cancer patients with anemia: results of the Dosing and Outcomes Study of Erythropoiesis Stimulating Therapies (D.O.S.E. Registry). Asli Memisoglu, ScD[1], Cyrus Peake, MS[1], Radha Vichare, MS[1], R. Scott McKenzie, MD[2], *Jamie Howell, PharmD, MS*[2], Catherine Tak Piech, MBA[2]; (1)Abt Associates–HERQuLES, Lexington, MA; (2)Ortho Biotech Clinical Affairs, LLC, Bridgewater, NJ.

PURPOSE: EPO and DARB, two erythropoietic stimulating therapies (ESTs), are FDA approved for the treatment of chemotherapy-related anemia. D.O.S.E. is an ongoing prospective, observational registry collecting data on real-world practice and outcomes associated with these ESTs in cancer patients.
METHODS: Data were drawn from hospital and community-based outpatient practices during 1/04–4/05. Adult patients were required to have diagnosis of a non-myeloid malignancy, baseline hemoglobin (Hb) <11g/dL, and received at least 2 doses of either EPO or DARB. Outcomes assessed included treatment duration; mean weekly and cumulative doses; Hb change from baseline at weeks 4, 8, 12; and proportion of patients receiving transfusions. Cost was based on 2004 wholesale acquisition cost.
RESULTS: 361 patients (149 EPO, 212 DARB) from 24 sites were identified. Baseline characteristics were similar between groups and reported for the entire 361 patients cohort: mean age 62.7 years, mean weight 74.6 kg, gender 65% female, and mean baseline Hb 10.0 g/dL. Breast and lung cancer were the most common malignancies in both groups. Both groups had identical mean treatment duration (56 days) and number of Hb measurements (8.5). The proportion of patients requiring blood transfusion (21%) was similar. The mean weekly doses were EPO 38,010 units and DARB 112 µg. The mean cumulative doses, or overall treatment doses, for EPO 348,910 units and DARB 1,124 µg were associated with a drug cost of $4,100 for EPO and $4,755 for DARB, a 16% difference. Mean Hb changes (g/dL) from baseline were similar at weeks 4 (0.8), 8 (0.9), and 12 (0.9).
CONCLUSIONS: Results of this prospective observational study suggest similar hematological outcomes with 16% higher drug cost in the DARB group compared to the EPO group. The similar number of Hb measurements suggest a comparable number of office visits for both treatment groups over the relatively brief treatment duration.

234. Greater area under the hemoglobin change curve is associated with improved outcomes in patients receiving epoetin alfa (EPO) or darbepoetin alfa (DARB) for chemotherapy-related anemia (CRA). Patrick Lefebvre, MA[1], Mei-Sheng Duh, MPH, Sc.D.[2], *R. Scott McKenzie, MD*[3], Samir H. Mody, PharmD, MBA[3], Richard C. Woodman, MD[3], Denise Williams, MD[4]; (1)Groupe d'Analyse, LtÉe., Montreal, QC, Canada; (2)Analysis Group, Inc, Boston, MA; (3)Ortho Biotech Clinical Affairs, LLC, Dallas, TX; (4)Johnson and Johnson Pharmaceutical Research and Development, Raritan, NJ.

PURPOSE: Previous research with erythropoiesis-stimulating therapies has shown area under the 16-week Hb change curve (Hb AUC_{16}) is a more sensitive and comprehensive efficacy measure versus traditional single time-point or threshold-based measurements such as hematopoietic response. To date, Hb AUC has not been validated within a randomized controlled trial of anemia treatments.
METHODS: Data were retrospectively analyzed from a randomized controlled clinical trial (n= 358) designed to compare the hematologic outcomes of EPO and DARB in solid tumor patients with CRA. Inclusion criteria were a baseline Hb ≤11g/dL and receiving chemotherapy. Hb AUC_{16} was calculated using sequential trapezoidal methodology based on Hb changes over 16 weeks of treatment and was stratified into quartiles to assess correlation with clinical and drug utilization outcomes. Trend tests were performed on the individual EPO and DARB groups, as well as the combined group, to determine if the following outcomes had significant linear trends across the Hb AUC_{16} quartiles: proportion of patients receiving transfusion, time to hematopoietic response (Hb rise ≥2 g/dL from baseline or Hb ≥12 g/dL during study), and average weekly EPO or DARB dose.
RESULTS: Mean Hb AUC_{16} values were higher for the EPO group versus the DARB group (EPO: 14.2g/dL; DARB: 7.9g/dL, p<0.001). Greater Hb AUC16 values had a strong linear association with decreasing proportions of patients transfused (p<0.0001), decreasing time to hematopoietic response (p<. 0001), and decreasing average weekly EPO or DARB doses (p<. 0001). These results were observed in the EPO and DARB groups separately, as well as in the two groups combined.
CONCLUSIONS: Hb AUC_{16} is associated with clinical outcomes and drug utilization benefits in patients with CRA receiving either EPO or DARB. These features should make it a preferred comprehensive efficacy measure in the assessment of comparative treatment responses.

235. Stability and compatibility of paclitaxel infusion under replicated clinical use conditions to facilitate dose-banding. *Asha Kattige, Ph.D*[1], Graham J. Sewell, Ph.D.[2]; (1)University of Bath, Bath, United Kingdom; (2)Kingston University, Kingston-upon-Thames, United Kingdom.

PURPOSE: To investigate the stability and compatibility of paclitaxel infusion at concentrations 0.3(mg/ml), 0.75(mg/ml) and 1.2(mg/ml), in Freeflex infusion bags containing 0.9% sodium chloride or 5% glucose under refrigerated storage and clinical use conditions to facilitate an outpatient chemotherapy dose-banding scheme.
METHODS: Dose-banding is widely used in UK and offers advantage of patient convenience but needs stability data to permit batch manufacturing. Stability and compatibility of paclitaxel infusion stored in Freeflex infusion bags was evaluated by incubating at 2-8°C or 25°C to represent refrigerated storage and clinical use conditions. Samples were withdrawn at selected time intervals and analysed for physical stability (visible and sub-visual particulates, pH, % weight loss) and chemical stability using a validated stability-indicating HPLC method.
RESULTS: Results indicated that in all cases, paclitaxel is chemically stable with variation in assay values within ± 5% but exhibited precipitation on prolonged storage at 2-8°C and 25°C. The stability of 0.3(mg/ml), 0.75(mg/ml) and 1.2(mg/ml) paclitaxel infusions at 2-8°C in 5% glucose was 28, 16 and 12 days respectively. There was a negligible change in pH and the variation over 28-day study period was less than 0.6 pH units. Similarly moisture diffusion across the infusion bag was minimal with less than 1% weight loss.
CONCLUSION: Stability timescale for various paclitaxel infusions varied and was a function of paclitaxel concentration in the infusion, diluents used and the storage temperature. In all cases, physical stability of the infusion was the limiting factor influencing the stability of the infusion. Maximum stability period of 28 days was observed for paclitaxel (0.3mg/ml) infusion prepared in 5% glucose and stored at 2-8°C. Given the increased popularity of the 90mg/m^2 weekly regimen in the UK, the 0.3(mg/ml) concentration would be appropriate for most patients and the 28-day shelf life would facilitate a dose-banding scheme.

236. Determination of paclitaxel in rabbit plasma using liquid chromatography tandem mass spectrometry: comparison of liquid liquid extraction (LLE) with solid phase extraction (SPE). *Armaghan Emami, Pharm.D., Ph.D.*[1], Noble Nemieboka, B.S.[2], Kenneth S. Bauer, Pharm.D., Ph.D.[1]; (1)Department of Pharmacy Practice and Science, School of Pharmacy, University of Maryland, Baltimore, MD; (2)University of Maryland Greenbaum Cancer Center, Baltimore, MD.

PURPOSE: Clinical application of a continuous low dose of paclitaxel as an anti-angiogenic agent has been recommended for treatment of cancer. Liquid chromatography tandem mass spectrometry (LC-MS/MS) has been used for the quantification of low concentration of paclitaxel in plasma samples. Both solid phase extraction (SPE) and liquid-liquid extraction (LLE) have been used as sample preparation methods. We have compared SPE and LLE as methods of sample extraction to quantify low concentration of paclitaxel based on the use of small sample volumes (200µl plasma).
METHODS: Rabbit plasma spiked with known amounts of paclitaxel was

extracted on an octadecyl C18/14% cartridge for SPE or with *tert*-butyl methyl ether (TBME) for LLE. Paclitaxel and the internal standard (docetaxel) were then detected using a QuatroMicro LC-MS/MS detector in positive ion mode using the mass transitions m/z 854.5♦286.1 and m/z 808.22♦182.22 respectively.
RESULTS: The calibration curve for paclitaxel was linear from 2-100ng/ml and 0.5-100ng/ml for SPE and LLE, respectively. The lower limit of quantitation (LLOQ) was 2ng/ml for SPE and 0.5ng/ml for LLE. The precision and accuracy of LLOQ were <19% and <15% for SPE and LLE, respectively.
CONCLUSION: The results indicated that LLE is a simpler, cheaper, more efficient and often faster procedure than the more commonly used SPE for detection of low concentrations of paclitaxel in plasma samples using LC-MS/MS.This assay was used to support a pharmacokinetics study of paclitaxel in rabbit samples. Additionally, this method could have clinical applicability in cases where small plasma volumes are a necessity.

237E. A large study of the older cancer patient in the community setting: initial report of a randomized controlled trial using pegfilgrastim to reduce neutropenic complications. *L. Balducci, MD*[1], J. Tam, PharmD, PhD[2], H. Al-Halawani, MD[3], S. Shahin, MS[4], J. Green, BA[4], R. Dansey, MD[4], W. Ershler, MD[5]; (1)HL Moffitt Cancer Center and Research Institute, Tampa, FL; (2)Geriatric Oncology Consortium (GOC), Baltimore, MD; (3)Cabrini Center for Cancer Care, Alexandria, LA; (4)Amgen Inc., Thousand Oaks, CA; (5)Institute for Advanced Studies in Aging, Washington, DC.

PURPOSE: Few randomized, controlled studies are conducted in patients ò 65 years. The Geriatric Oncology Consortium (GOC) was established to facilitate the study of older cancer patients. This study documents the feasibility of conducting community clinical trials in older patients and addresses neutropenia and its complications that may prevent optimal treatment.
METHODS: This large, prospective, open-label trial was conducted in patients ò 65 years receiving chemotherapy Q21 days for lung, breast, or ovarian cancer (solid tumor stratum), or NHL. Patients were randomized to either pegfilgrastim in first and subsequent cycles (Arm A) or no pegfilgrastim in cycle 1 with subsequent cycle use per physician discretion (Arm B). Endpoints included incidence of neutropenia (ANC<1x10^9/L) with or without fever (ò 38°C), chemotherapy dose delays and reductions, hospitalizations, antibiotic use. Results are presented only for patients with solid tumors.
RESULTS: The primary analysis set included 686 patients with solid tumors, 343 per arm. Median age was 72 years(range 65-88); 66% were female. Chemotherapy included carboplatin with paclitaxel (36%), etoposide (15%), or docetaxel (12%) and doxorubicin with cyclophosphamide (15%). Forty-two percent of patients in Arm B received pegfilgrastim in cycles 2-6, mostly for grade 3/4 neutropenia (62%). Overall febrile neutropenia incidence was significantly lower for patients in Arm A (4%) than for those in Arm B (10%)(p=0.0014). Patients in Arm A also had a lower incidence of neutropenia (30% vs 80%), chemotherapy dose reduction (7% vs 14%), hospitalization for neutropenia-related events (5% vs 9%), antiinfective use (12% vs 29%), and serious adverse events compared with patients in Arm B.
CONCLUSIONS: The study established the feasibility of community-based trials in this population and showed that pegfilgrastim use in first and subsequent cycles was associated with fewer neutropenia-related events compared with no cycle 1 use. This information may be useful to pharmacists when developing treatment guidelines for older patients.
Presented at the 41st Annual Meeting of the American Society of Clinical Oncology, Orlando, FL, May 13-17, 2005.

238E. Final results of a phase 3, randomized, open-label study of darbepoetin alfa 200 µg every 2 weeks versus epoetin alfa 40,000 U weekly in patients with chemotherapy-induced anemia. John Glaspy, MD[1], Russell Berg, BS[2], Dianne Tomita, MS[2], *Gregory Rossi, PhD*[2], Saroh Vadhan-Raj, MD[3]; (1)UCLA School of Medicine, Los Angeles, CA; (2)Amgen Inc., Thousand Oaks, CA; (3)University of Texas–MD Anderson Cancer Center, Houston, TX.

PURPOSE: This phase 3, noninferiority trial compared efficacy and safety of darbepoetin alfa (DA; Aranesp®) and epoetin alfa (EA).
METHODS: Eligible patients were adults with non-myeloid malignancy, >8-weeks planned chemotherapy, chemotherapy-induced anemia (CIA; hemoglobin≤11g/dL), and ECOG performance status 0-2. Patients were randomized 1:1 to DA 200mcg every-2-weeks (Q2W) or EA 40,000U weekly, stratified by screening hemoglobin (<10.0 and ≥10.0g/dL) and planned chemotherapy (platinum vs non-platinum). Patients were treated up to 16 weeks with identical dose-adjustment rules. Primary endpoint was RBC transfusion incidence (Kaplan-Meier estimate) from day 29 to end of treatment (EOT) (prespecified noninferiority margin of 11.5%).
RESULTS: Of 1220 patients randomized, 1209 received ≥1 dose of study drug. Most patients were women (66%) and white (83%). 49% were ≥65 years. 76% had stage 3 or 4 disease. 36% of patients had baseline hemoglobin<10g/dL. 42% were to receive platinum chemotherapy. Lung cancer (26%) was the most common tumor type. Between day 29 and EOT, 21% of DA patients received a RBC transfusion compared with 16% of EA patients, upper 95% confidence limit <11.5%. The two groups had similar adverse event profiles.

	DA (n=606)	EA (n=603)
Mean Change in FACT-An (95% CL)	7.1 (4.6, 9.7) (n=373)	6.5 (3.8, 9.1) (n=356)
Mean Change in FACT-F (95% CL)	4.2 (3.1, 5.3) (n=374)	3.5 (2.4, 4.7) (n=357)
Mean baseline hemoglobin (SD)	10.2 (0.9)g/dL	10.2 (0.9)g/dL
Mean week 17 hemoglobin (SD)	11.8 (1.5)g/dL (n=278)	11.9 (1.3)g/dL (n=245)
Patients achieving hemoglobin target (11-13g/dL), n (%)	463 (76%)	487 (81%)
Median time to target (Q1, Q3)	6 weeks (3, 13)	5 weeks (3, 9)
Patients maintaining target, n (%)	341 (74%) (n=438)	389 (80%) (n=470)
Mean Weekly Dose (SD)	114.7 (21.7)µg [229.4mcg Q2W]	42,714 (8,645)IU

CONCLUSIONS: Non-inferiority was demonstrated between DA 200 Q2W compared with EA 40,000 weekly in this large, randomized phase 3 study of efficacy and safety.
Presented at the 42nd Annual Meeting of the American Society of Clinical Oncology, Orlando, FL, May 13-17, 2005.

239. A single 6 milligram dose of rasburicase for the management of tumor lysis syndrome in adults. *Anne McDonnell, Pharm.D.*, Philip D. Hall, Pharm.D., Kristi Lenz, Pharm.D, Robert Hayslip, MD, Debra Frei-Lahr, MD; Medical University of South Carolina, Charleston, SC.

PURPOSE: Rasburicase is currently approved at a dose of 0.15 or 0.2 mg/kg daily for 5 days in pediatric cancer patients to lower plasma uric acid concentrations and to manage tumor lysis syndrome (TLS). There are reports of a single dose of rasburicase instead of the multiple doses, and there is limited information on rasburicase dosing in adults. Therefore, the objective of this study was to document the efficacy of a single 6 mg dose of rasburicase for managing TLS in adults.
METHODS: We retrospectively collected data on 11 adults with hematologic malignancies who received a single 6 mg dose of rasburicase. One patient received treatment at diagnosis and relapse. All patients received intravenous hydration with urinary alkalization and allopurinol. One subject did not receive allopurinol because of an allergy. Only patients at high-risk for TLS (e.g. large tumor burden, rising uric acid) or in TLS received rasburicase.
RESULTS: The 6 mg dose resulted in a median 0.07725 mg/kg dose (range: 0.01–0.136 mg/kg). A single 6 mg dose of rasburicase rapidly lowered the uric acid concentrations in 10 of the 11 patients. The median pre-rasburicase uric acid concentration was 11.7 mg/dL (range: 7.4–17.4 mg/dL) and fell to 2.4 mg/dL (range: 0.5–15.4 mg/dL) on the day after the rasburicase (p =0.022). In these 10 patients, uric acid concentrations remained low despite subsequent chemotherapy, and none required additional doses. The only patient who did not respond to the single 6 mg dose of rasburicase was a morbidly obese patient with a body mass index of 87. This patient received a subsequent dose of 12 mg and responded.
CONCLUSIONS: These results warrant further investigation of a single 6 mg dose of rasburicase in adults with TLS or at high-risk of developing TLS.

240E. Patterns of care and incidence of neutropenia-related complications during chemotherapy and the use of pegfilgrastim and filgrastim in community practice: results of the ACCEPT study. Luis T. Campos, MD[1], Mitchell H. Folbe, MD[2], Veena Charu, MD[3], *R. Dansey, MD*[4], Dave Delgado, PhD[4], Beiying Ding, PhD[4]; (1)Oncology Consultants, P.A., Houston, TX; (2)Medical Oncology, Troy, MI; (3)Pacific Cancer Medical Center, Inc., Anaheim, CA; (4)Amgen Inc., Thousand Oaks, CA.

PURPOSE: We conducted a retrospective cohort study to compare characteristics, patterns of care and neutropenia-related complications among patients receiving pegfilgrastim in 2003, with patients who received filgrastim in 2001.
METHODS: Consecutive medical records (n=829, filgrastim; n=1922, pegfilgrastim) were abstracted for adult chemotherapy patients from a random sample of 99 U.S. oncology practices to obtain data on characteristics, treatment details, and neutropenia-related complications.
RESULTS: The three most common tumor types were breast cancer (51%), lung cancer (19%), and non-Hodgkin's lymphoma (18%). There were no significant differences in age (mean 58 and 60 years for pegfilgrastim and filgrastim, respectively) or prior history of neutropenia or febrile neutropenia (4% and 5%, respectively). Pegfilgrastim was initiated in cycle 1 in 62% of patients, and in cycle 2 in 84%. Filgrastim was initiated in cycle 1 in 54% of patients, and in cycle 2 in 78%. Growth factor was initiated within 72 hours of chemotherapy in 86% of cycles for pegfilgrastim users but only 48% of cycles for filgrastim users. Among patients who received filgrastim in cycle 1, treatment was initiated >10 days after chemotherapy in 49% of patients vs. 6% of pegfilgrastim users. The incidence of neutropenia-related complications was greater in the cohort of patients who received filgrastim.

Neutropenia-related Complications	Pegfilgrastim (N=1922)	Filgrastim (N=829)	p-value for difference Febrile neutropenia
% (95% CL)	6% (5,7)	10% (8,12)	0.0004
Hospitalization for febrile Neutropenia	4% (3,4)	6% (4,8)	0.01
Anti-infective treatment for infection	24% (22,26)	32% (29,35)	<0.0001

CONCLUSIONS: Patients treated with pegfilgrastim were more likely to receive growth factor within 72 hours of chemotherapy, whereas with filgrastim, almost half of the use occurred later. Patients receiving pegfil-grastim had a lower incidence of neutropenia-related complications than patients treated with filgrastim in the year prior to pegfilgrastim introduction. Once-per-cycle dosing of pegfilgrastim provides added convenience to patients.
Presented at the 42nd Annual Meeting of the American Society of Clinical Oncology, Orlando, FL, May 13-17, 2005.

241E. Darbepoetin alfa for the treatment of anemia in patients with low-risk myelodysplastic syndrome. Janice Gabrilove, MD[1], Ronald Paquette, MD[2], Roger M. Lyons, MD[3], Chaudry Mushtaq, MD[4], Jan Montgomery, PharmD[4], Hung Lam, PhD[5], *Lyndah Dreiling, MD*[5]; (1)Mt Sinai School of Medicine, New York, NY; (2)UCLA Medical School-Hemat & Onc, Los Angeles, CA; (3)US Oncology-Hematology/Oncology Associates of South Texas, San Antonio, TX; (4)South Carolina Oncology Associates, Columbia, SC; (5)Amgen Inc., Thousand Oaks, CA.

PURPOSE: Most patients with myelodysplastic syndromes (MDS) develop clinically significant anemia during their disease course; this anemia can be treated with erythropoietic growth factors.
METHODS: Interim data from this phase 2, single-arm, open-label trial in low-risk MDS patients treated with darbepoetin alfa (DA) 500 µg every three weeks (Q3W) subcutaneously for 13 weeks are described. If hemoglobin changed <1.0 g/dL over baseline by week 6, dosing frequency was increased to Q2W at the same dose. Eligibility criteria included diagnosis of low or intermediate-1 risk MDS (IPSS classification), anemia (hemoglobin ≤11 g/dL), and absence of chronic myelomonocytic leukemia. The primary endpoint was the proportion of patients achieving an erythroid response (major [minor] erythroid response, ≥2.0-g/dL [≥1 to <2-g/dL] increase in hemoglobin from baseline or transfusion independence [50% reduction in transfusion requirements] for patients who were dependent at screening), provided as Kaplan-Meier estimates with 95% confidence limits.
RESULTS: Data from 100 patients (63 erythropoietin-naíve patients) were included in this interim analysis. Overall, patients had a mean (SD) age of 75.8 (8.3) years and a mean (SD) baseline hemoglobin of 9.9 (1.0) g/dL; 50% of patients were women. Overall, 43% (32, 54) of patients had a major erythroid response, and 41% (26, 57) of patients had a minor erythroid response. During weeks 1 to 13, 24% (15, 33) of patients required RBC transfusion. Mean (SD) average dose was 471.1 (46.2) µg/dose. Of the 57 erythropoietin-naíve patients evaluated for response, 51% (38, 65) had a major erythroid response. In addition, 37 patients who had previously received erythropoietic therapy were able to maintain hemoglobin levels on this less frequently-administered erythropoietic regimen.
CONCLUSIONS: This interim analysis provides initial data on the efficacy and safety data on the use of darbepoetin alfa to treat anemic MDS patients.
Presented at the MASCC/ISOO 17th International Symposium on Supportive Care in Cancer, Geneva, Sweden, June 30-July 2, 2005.

242. Evaluation of antiemetic agents used for chemotherapy-induced nausea and vomiting in a regional hospital. Jen-Seng Huang, MD[1], Chiung-Hui Tseng, Pharm.D.[2], Yu-Jen Chen, B.S.[3], Yao-Cheng Wu, B.S.[3], Shu-Ying Pai, B.S.[3], Yu-Chieh Chen, M.S.[3], Shin-Tarng Deng, M.S.[2], *Yow-Wen Hsieh, Ph.D.*[3]; (1)Department of Oncology, Chang-Gung Memorial Hospital, Keelung, Taiwan; (2)Department of Pharmacy, Chang-Gung Memorial Hospital, Linkou, Taiwan; (3)Department of Pharmacy, Chang-Gung Memorial Hospital, Keelung, Taiwan.

PURPOSE: This study evaluated the appropriate dosing and timing of antiemetic agents to patients receiving chemotherapy and the effective combination of antiemetics in a regional hospital (835 beds). The results of this study will be implemented into clinical practice in order to ensure that all patients with cancer in this hospital have access to the highest quality care.
METHODS: Patient information was collected through Hospital Information System at oncology outpatient department. Pharmacists recorded patients' basic information, current chemotherapy and antiemetic regimen. Two face to face interviews were conducted to evaluate symptoms associated with antiemetic agent induced nausea and vomiting.
RESULTS: Total 25 cases collected during study period at this moment. This evaluation is still ongoing. The emetogenic risk of chemotherapy used base on patients' treatment protocol can be classified to 7 patients received level 1, 7 received level 2, 5 received level 3, 4 received level 4 and 2 received level 5. The antiemetic agents prescribed as needed based for only 4 patients. Acute nausea and vomiting occurred in 8 patients and 1 patient experienced delayed nausea and vomiting. Only 13 patients (52%) received antiemetic agents according to National Comprehensive Cancer Network Nausea and Vomiting Treatment Guideline and 4 had acute nausea and vomiting. Of other 12 patients, 5 experienced nausea and vomiting.
CONCLUSION: Some discrepancies were found between treatment guideline and antiemetic agents used in our hospital. In order to let patients have better quality of care and eliminate the waste of medical resource, protocol should be established and another evaluation will be conducted after protocol is put into practice.

243. Evaluation of the incidence of carboplatin hypersensitivity reaction in cancer patients. *Marisa Navo, Pharm.D.*[1], Anuradha Kunthur, M.D.[1], Martina Badell, BA[2], Jubilee Brown, M.D.[1], Judith A. Smith, Pharm.D., BCOP[1]; (1)The University of Texas, M.D. Anderson Cancer Center, Houston, TX; (2)The University of Texas Health Science Center at Houston, Houston, TX.

PURPOSE: Although the reported incidence of carboplatin hypersensitivity is low, it is important to characterize because of its potentially fatal complications. Unfortunately, patient risk factors are not clearly defined. Most reported cases are in the ovarian cancer setting, suggesting a higher incidence in these patients. Recently, UT MD Anderson Cancer Center (UT MDACC) Pharmacy observed an increase in reported carboplatin hypersensitivity cases. The objectives of this retrospective chart review were to determine the incidence of carboplatin hypersensitivity in ovarian cancer patients in comparison to other oncology patients and to identify potential risk factors that may contribute to development of hypersensitivity reactions.
METHODS: All patients dispensed carboplatin between July 2002 and September 2003 were identified by the UT MDACC Division of Pharmacy dispensing records and retrospectively evaluated. All hospital records were reviewed for patient demographics, past medical history, and detailed carboplatin administration information. If patients experienced a hypersensitivity reaction, further information was gathered on symptoms, treatment, and outcome.
RESULTS: Of 1535 patients identified for review, 1333 were considered eligible. Overall, the incidence of carboplatin hypersensitivity was 2.5%. However, hypersensitivity reactions occurred more frequently in the ovarian cancer population (8.5%) when compared to other cancer sites. Possible risk factors include disease status, history of drug allergies, previous carboplatin exposure, and some investigational protocol combinations.
CONCLUSION: This study confirms the higher incidence of carboplatin hypersensitivity in ovarian cancer patients associated with previous exposure in the setting of recurrent disease. Also, some precaution is needed when using carboplatin in combination with investigational agents with synergistic/additive activity.

244E. Impact of 1st and subsequent cycle pegfilgrastim on neutropenic events in patients receiving myelosuppressive chemotherapy: preliminary results of FIRST, a prospective community-based study. Howard Ozer, MD[1], Beiying Ding, PhD[2], *R. Dansey, MD*[2]; (1)University of Oklahoma Cancer Center, Oklahoma City, OK; (2)Amgen Inc., Thousand Oaks, CA.

BACKGROUND: Most alterations to chemotherapy dose and schedule are due to neutropenic events, which mostly occur in the 1st cycle. The ANC registry has prospectively documented 1st cycle febrile neutropenia rates of 8% in patients receiving chemotherapy with community CSF support. We initiated a large, prospective community-based study in cancer patients receiving myelosuppressive chemotherapy to evaluate the impact of 1st and subsequent cycle pegfilgrastim (Neulasta®) on neutropenic events.
METHODS: This open-label, single-arm study is being conducted at 319 sites, with an enrollment of 2252 patients. Adult patients with cancers other than leukemia or MDS are eligible, including patients with major co-morbid illnesses who are not generally eligible for clinical trials. Patients receive pegfilgrastim 6 mg ~24 hours post- chemotherapy in each cycle. Endpoints include neutropenic complications and chemotherapy dose reductions and delays. Point estimates and 95% CL are provided.
RESULTS: 1st cycle data from 874 patients at 201 sites are shown. 76% of patients were women, most had breast cancer (51%). The mean (SD) age was 58.6 (12.9). 48% of pts had early stage (I-II) disease, 21% received prior chemotherapy, 15% received prior radiotherapy, and 26% had significant co-morbidities. Serious adverse events were consistent with those observed in patients receiving myelosuppressive chemotherapy.

	N=874 % (95% CL)
Febrile neutropenia in cycle 1	2 (1,4)
Neutropenia-related IV antibiotics use in cycle 1	2 (1,3)
Neutropenic hospitalizations in cycle 1	2 (1,3)
Reported cycle 2 dose reductions (all reasons)	6 (5,8)
Neutropenia-related	2 (1,3)
Reported cycle 2 dose delays (all reasons)	5 (4,7)
Neutropenia-related	<1 (0,1)

CONCLUSIONS: Patients treated in community practice receiving pegfil-

grastim in first and subsequent cycles of myelosuppressive chemotherapy experience a low incidence of both neutropenic complications and alterations in chemotherapy dose and schedule.
Presented at the 42nd Annual Meeting of the American Society of Clinical Oncology, Orlando, FL, May 14-17, 2005.

245. In vitro interaction between topotecan (TPT) and paclitaxel (PAC) in three human ovarian cancer cell lines. *David L. DeRemer, Pharm.D.*, Cynthia A. Mattingly, B.S., Val R. Adams, Pharm.D. BCOP FCCP; University of Kentucky College of Pharmacy, Lexington, KY.

BACKGROUND: TPT and PAC are both active agents in the treatment of ovarian cancer and there is interest in using the agents together. Previous in vitro data evaluating the combination has not been reported in ovarian cancer cell lines; however, the combination has been evaluated in lung, colorectal, breast, teratoma and glioma cell lines. Most of these studies have demonstrated synergy for the combination; however, in some cell lines antagonism was reported. Interestingly, PAC upregulates cellular topoisomerase I concentrations in colon cancer cells, which may improve TPT efficacy. Clinical data has started to emerge with concurrent PAC and TPT in ovarian cancer; however, studies evaluating the most synergistic method of administering this combination of drugs in ovarian cancer have not been published. To provide rationale for future clinical trials, the effects of combining TPT and PAC in differing sequences as well as differing dosing ratios were evaluated in this study. We hypothesized that exposing ovarian cancer cells to PAC prior to TOP would be synergistic.
PURPOSE: To determine the in vitro drug sensitivity of three human ovarian cell lines after simultaneous or sequential treatment with topotecan and paclitaxel.
METHODS: Concurrent administration of both agents and the sequences of TOP -> PAC and PAC -> TOP were evaluated in three human ovarian cancer cell lines: NCI PA-1, CAOV-3, and SKOV-3. Cellular effects were determined by SRB assay and the isobologram and combination index (CI) method of Chou-Talalay was used to evaluate interactions between drugs.
RESULTS: Treating ovarian cancer cell lines with PAC->TPT produced both synergistic and antagonistic results that varied with concentration and cell line. Concurrent exposure and TPT->PAC produced variable results; however, all concurrent exposure experiments in PA-1 and CAOV-3 cells demonstrated antagonism.
CONCLUSIONS: Concurrent PAC and TPT to treat ovarian cancer is not likely optimizing patient outcome.

246. A cost-effective analysis of palonosetron in combination with 3-day corticosteroid for the prevention of chemotherapy-induced nausea and vomiting (CINV) in a private practice office. *Siu-Fun Wong, PharmD*, Julie Ugai, PharmD, Ryan Quist, PhD; Western University of Health Sciences, College of Pharmacy and Hematology Oncology Medical Group of Orange County, Inc., Pomona, CA.

PURPOSE: Palonosetron was approved for the prevention of acute and delayed CINV but corticosteroids were not routinely prescribed in the pivotal trials. This study evaluated the cost-effectiveness of adding 3-day corticosteroid to palonosetron for the prevention of CINV.
METHODS: A prospective single-center observational study for adult cancer patients receiving moderate to severe emetogenic potential antineoplastic chemotherapy was conducted. Subjects prescribed palonosetron 0.25 mg IV plus dexamethasone 10 mg IV on day 1 followed by 4-8 mg PO qd-bid x 2 days were included. Patients with concurrent radiation therapy to upper GI, pre-existing nausea and/or vomiting (N/V), concurrent medical condition(s) causing N/V, or ongoing antiemetic(s) were excluded. Chemotherapy regimen,antiemetic treatment, and subject demographic information were collected by chart review and personal interview after informed consent. Efficacy, rescue medication use, and tolerability were assessed at baseline and during the acute and delayed phase of CINV up to 120 hours after chemotherapy. Subject satisfaction questionnaire was administered at post-chemo visit.
RESULTS: Nine females and 1 male with mean age of 59.9 year were studied. Average number of emetogenic risk factor was 3.4. Complete emetogenic response improved from 70% to 100% at baseline (p=0.157), 60% to 80% during acute phase (p=0.564) and 20% to 60% during delayed phase (p=0.025). Fatigue was the most common side effect. All 8 patients responded to the satisfaction questionnaire preferred the study drug administration and 5 subjects felt better CINV control. The cost analysis revealed that palonosetron plus corticosteroid decrease drug costs for acute and delayed CINV by 30% and 90%, respectively, 45% increase in drug reimbursement, and 18% increase in infusion reimbursement.
CONCLUSIONS: Addition of 3-day corticosteroid to palonosetron appears cost effective to both the practice and the patient. A larger study is warranted to confirm the result of this study.

247. Evaluation of voriconazole use in bone marrow transplant patients in a community hospital. *Donna R. Burgess, R.Ph.*[1], Debra A. Garza, R.Ph., MBA[2], David S. Burgess, PharmD, FCCP[3]; (1)University of Texas at Austin College of Pharmacy and Methodist Hospital, Department of Pharmacy, San Antonio, TX; (2)University of Texas at Austin College of Pharmacy and Methodist Hospital, Department of Pharmacy, San Antonio, TX; (3)University of Texas at Austin College of Pharmacy and University of TX Health Sci. Ctr., San Antonio, TX.

PURPOSE: Invasive fungal infections have become the leading infectious cause of death in bone marrow transplant patients. The prevention and treatment of these infections due to newer antifungal agents is being debated. The objective of this study was to evaluate the use of voriconazole and associated fungal infections in the adult BMT patients in our community hospital.
METHODS: A retrospective review of all BMT patients admitted between Jan 2004–May 2005 who received voriconazole was performed. Data collected included demographic and clinical data (age, sex, HLA matching, underlying illness, conditioning regimen, GVHD prophylaxis, acute and chronic GVHD, corticosteriod use, fungal infection, antifungal therapy, mortality).
RESULTS: Overall, 29 patients (20 male, 9 female) with an average age (SD) of 45.9 ± 11.9 yrs were evaluated. The majority (52%) of these patients had undergone a matched-related peripheral stem cell transplant. Fluconazole was used in 78% of the patients as the initial antifungal prophylaxis agent after transplant. However, voriconazole was used as the initial antifungal agent in 6 patients (22%). Of these 6 patients, 3 had a history of a previous invasive fungal infection and 3 had refactory cancer that received intensive chemotherapy. Overall, 27 patients (93%) developed moderate-severe acute GVHD (grades II-IV) which required high-dose corticosteriods. Once this occurred, antifungal prophylaxis was changed to voriconazole in 71% of the patients. The overall mortality in this evaluation was 52%. However, only 4/29 (14%) died of invasive fungal infections due to either aspergillosis or zygomycosis. None of these patients received voriconazole as initial antifungal prophylaxis.
CONCLUSIONS: In our hospital, voriconazole use was limited to BMT patients that were at high risk for serious invasive fungal infections. Further studies are needed to determine the most appropriate choices of fungal prophylaxis in this patient population.

248E. Polymorphism in the hypoxia-inducible factor 1a gene may confer susceptibility to androgen-independent prostate cancer. *Cindy H. Chau, PharmD, PhD*, Matthew G. Permenter, BS, Seth M. Steinberg, PhD, Avi S. Retter, MD, William L. Dahut, MD, Douglas K. Price, PhD, William D. Figg, PharmD, MBA; National Cancer Institute, Bethesda, MD.

The hypoxia-inducible factor 1a (HIF-1a) plays a major role in cancer progression. The role of this transcription factor in prostate cancer development and its transition to a metastatic and androgen refractory state remains to be elucidated. Previous reports have identified the existence of single nucleotide polymorphisms (SNPs) in the oxygen-dependent degradation domain of the HIF-1 gene in several cancers including androgen-independent prostate cancer (AIPC). Studies in prostate cancer however, are variable and limited in the number of cases assessed.
PURPOSE: Herein we further investigate these SNPs, specifically C1772T (which results in an amino acid change from proline 582 to serine) and G1790A (alanine 588 to threonine) to determine the association of these polymorphisms with metastatic AIPC.
METHODS: The frequency of these polymorphisms was evaluated in a population of individuals with metastatic AIPC compared to a set of healthy control subjects using nested PCR amplification of genomic DNA and bi-directional DNA sequencing.
RESULTS: The distribution of HIF-1a genotypes for C1772T in 196 AIPC patients was 161 C/C (82.1%), 29 C/T (14.8%), and 6 T/T (3.1%). The genotype distribution in 196 controls was 179 C/C (91.3%), 14 C/T (7.1%), and 3 T/T (1.5%). Our results demonstrate a significant difference in genotype distribution between AIPC patients and control subjects only for the C1772T polymorphism (p=0.024). The association of the incidence of the polymorphism with overall survival was determined to be not statistically significant (p=0.93).
CONCLUSIONS: These results suggest that the C1772T polymorphism in HIF-1a may confer susceptibility to AIPC and contribute to the progression of this disease. Given the high vascular nature of prostate cancer and the recent development of anti-angiogenic therapies as a potential therapeutic treatment modality, it remains to be determined whether this polymorphism may also be able to predict patient response to this type of therapy.
Published in Proc Amer Assoc Cancer Res 2005;46:4144.

Pediatrics

249. Evaluation of hydrocortisone in neonates with pressor resistant hypotension. *Varsha Bhatt-Mehta, M.S., Pharm.D.*, Charles F Baker, M.D., John Barks, M.D., Delia Vazquez, M.D., Robert E. Schumacher, M.D.; University of Michigan, Ann Arbor, MI.

PURPOSE: Evaluate the safety and efficacy of a protocol of intravenous hydrocortisone (IVHC) for the treatment of pressor resistant hypotension in neonates.
METHODS: Records of 220 infants (2001-04) receiving IVHC were reviewed. 84 infants on IVHC according to protocol (use IVHC if MAP was less than gestational age (GA) despite a combined inotrope(dopamine +dobutamine (I) dose of 20 µg/kg/min) were included in the study. Baseline cortisol (BC) level was drawn before IVHC. Maintenance doses were guided by BC. Data on MAP and I doses at baseline, 6, 12, and 24 hrs after HC, BC levels, concomitant drugs and potential adverse effects of HC (hyperglycemia requiring insulin, gastrointestinal perforations (GP), necrotizing enterocolitis (NEC), intraventricular hemorrhage (IVH), periventricular leukomalacia (PVL)and positive blood cultures during and after treatment). Appropriate statistical tests were used to compare baseline MAP and I dose to MAP changes at 6, 12, and 24 hrs, to analyze the variance between the different time points and correlate of gestational age (GA) and birth weight (BW) to BC level.
RESULTS: 84 infants (GA 33 ± 6.2 (median 36) weeks; BW 2.39 ± 1.3 (median 2.8) kg) were included. BC levels were 0.5µg/dl to 27.3 µg/dl (mean 6.2 ± 6.4). Change in MAP from baseline was statistically significant at 6, 12 and 24 hrs (P<0.0001 for all). The reduction in total I dose from baseline was significant at 12hrs (P=0.002) and 24 hrs (P<0.0001). There were no cases of GP or PVL observed (upper 95% CL = 0.07,3 cases each of IVH and NEC (diagnosed prior to treatment IVHC), 10 positive blood cultures, and 27 cases of hyperglycemia. Concomitant medications included antihypertensives, indomethacin,and ranitidine.
CONCLUSION: HC improved MAP within 6 hr of initiation and reduced or eliminated the I need by 12 to 24 hours. No clinically significant adverse effects were observed.

250. Candesartan cilexetil effectively reduces blood pressure in hypertensive children. *Amy M. Franks, Pharm.D.*, Stephanie F. Gardner, Pharm.D., Ed.D., Cindy D. Stowe, Pharm.D., Thomas G. Wells, M.D.; University of Arkansas for Medical Sciences, Little Rock, AR.

PURPOSE: To determine the safety and efficacy of the angiotensin II receptor antagonist candesartan cilexetil in the treatment of pediatric hypertension.
METHODS: Hypertensive pediatric subjects were eligible for study participation if untreated systolic and/or diastolic blood pressure (BP) exceeded the 95th percentile for gender/age/height. Subjects underwent a 7-day washout period prior to initiating weight-based doses of candesartan cilexetil (2-8 mg daily). The dose of candesartan cilexetil was doubled after 7 days of therapy if inadequate antihypertensive response was determined by home BP monitoring (HBPM). Three methods of BP measurement were compared before and after 2 weeks of treatment with a stable dose of candesartan cilexetil: casual clinic measurement, 24-hour continuous ambulatory BP monitoring (ABPM), and HBPM. Self-reported adverse effects and clinical laboratory analyses were used to determine safety.
RESULTS: Eleven subjects (mean age 14.2 years) received a final median daily dose of 8 mg (0.13 mg/kg/) candesartan cilexetil. Study treatment resulted in significant reductions in systolic (-6.0%, p=0.03) and diastolic (-10.8%, p<0.01) BP as measured by ABPM. Significant reductions in systolic (-7.4%, p=0.03) and diastolic (-5.9%, p=0.01) BP were also observed with casual clinic measurement. Similarly, significant reductions in mean arterial pressure were found using both the ABPM (-8.6%, p<0.01) and casual (-6.7%, p=0.01) measurement. No statistically significant changes in systolic BP, diastolic BP, or mean arterial pressure were found using HBPM. Percent nocturnal systolic or diastolic dipping did not change with candesartan cilexetil treatment. Clinical laboratory measures remained unchanged during treatment, and subjects reported nonspecific mild adverse effects.
CONCLUSION: Candesartan cilexetil safely and effectively reduced BP as demonstrated by ABPM and casual clinic measurements.

251E. Efficacy and safety of procedural sedation by a pediatric sedation team using propofol. *Sasko D. Stojanovski, PharmD*[1], Marc S. Leder, MD[2], Milap C. Nahata, Pharm.D., FCCP[3]; (1)College of Pharmacy, Ohio State University, Columbus, OH; (2)Department of Pediatric Emergency Medicine, Columbus Children's Hospital, Columbus, OH; (3)Colleges of Pharmacy and Medicine, Ohio State University, Columbus, OH.

PURPOSE: To determine the effectiveness and safety of propofol sedation in pediatric patients undergoing various outpatient procedures as performed by a Pediatric Sedation Team (PST).
METHODS: A retrospective review of the medical records from April 2003 to November 2004 of the PASS Team (Pediatric Analgesia and Sedation Service) was conducted for pediatric patients who received propofol for outpatient procedures at our Children's Hospital. Patient demographics, procedure type, total propofol dose, vital signs, and complications related to propofol procedural sedation were obtained for each patient.
RESULTS: One hundred eighty-eight separate procedures were preformed in 105 patients. The mean age was 4.5 ± 3.3, (range 0.67-17) years; 66% were male. Eighty-six percent of the cases were for radiology procedures (MRI, Nuclear Medicine, fluoroscopy) and 14% were performed in the PICU. The mean total propofol dose was 9 ± 5.5 mg/kg (n=145). Propofol mean onset time was 4.3 ± 5.1 minutes and peak effect occurred at 10.7 ± 8.7 minutes. The mean length of stay was 91.8 ± 36.1 (33-225) minutes and mean sedation duration 61.5 ± 28.6 (11-155) minutes. The mean baseline systolic and diastolic blood pressures were 110 ± 16 and 64 ± 14 mmHg, mean systolic blood pressure was lowered by 24 ± 21 and mean diastolic blood pressure 22 ± 18 mmHg. Seventy-three percent of procedures had no complications during sedation; however, hypotension (<30% drop in BP) occurred in 21% and O_2 saturation <90% in 6%. One procedure was stopped due to desaturation.
CONCLUSIONS: Propofol use by a PST comprised of Pediatric Emergency Medicine Physicians and Intensivists with advanced pediatric airway skills was an effective means of procedural sedation for various outpatient procedures. Complications such as desaturations and hypotension were recognized and appropriately treated such that only one case needed to be aborted secondary to desaturation. No patient required endotracheal intubation. The incidence of hypotension was higher than previously reported; however, questions remain about of its clinical significance.
Presented at the Annual Meeting of the Pediatric Academic Society, Washington, D.C., May 14-17, 2005.

252. A descriptive analysis of compounding pharmacy practices. *Angela K. Treadway, Pharm.D., BCPS*[1], Deeatra Craddock, Pharm.D.[2]; (1)Texas Tech Health Sciences Center School of Pharmacy/North Texas Veterans Health System, Dallas, TX; (2)Texas Tech Health Sciences Center School of Pharmacy/Community Pharmacy-Denton, TX, Dallas, TX.

PURPOSE: Extemporaneous compounding of pharmaceutical products is a critical part of pediatric therapeutics. We prospectively surveyed pharmacies to describe compounding practices.
METHODS: Blinded surveys were mailed to 522 institutional and community pharmacies. A total of 109 (21%) were returned for analyses.
RESULTS: Eighty-three percent of responding pharmacies were from urban communities located in the Midwest, Northeast, South, and West geographical regions. Half (54%) of the pharmacies were institutional, with less than 10% of all prescriptions requiring extemporaneous compounding. One-third (30%) of pharmacies did not have formal compounding policies and procedures that are essential for quality control. Using caffeine citrate as an example, 65% of pharmacies reported compounding caffeine citrate for apnea of prematurity with in the last 12 months. Cost containment (41%) was the primary reason for compounding the commercially available caffeine. Whereas the most common reasons for compounding products in general were product availability (69%) and unsuitable route/formulation (21%); cost was <0.1%. Three-fourths of respondents used either formulation "recipes" from pharmacy compounding organizations, published literature or both. When evaluating product content and stability, 40% assured compounding accuracy using double check "mixing and making" procedures by technicians and/or pharmacists. In addition, 43% of compounding pharmacies depend on published literature related to the formulation ërecipe' used for expiration dating. Only 9% of pharmacies validated active ingredient content using a quantitative analytical technique, 3% validated stability using quantitative stability testing, and 5% utilized microbiologic testing to assure sterility. When queried whether samples of compounded prescriptions could be obtained for external validation testing, less than half (45%) of respondent pharmacies agreed.
CONCLUSIONS: Despite increasing availability of published literature, 30% of responding pharmacies did not have policies and procedures and few pharmacies conduct internal product validation. Standardization of compounding practices is essential to assure quality prescription products for care of infants and children.

253E. Measured growth parameters in girls with ADHD receiving MAS XR. Thomas J. Spencer, MD[1], Stephen V. Faraone, PhD[2], *Jill A. Morgan, PharmD, BCPS*[3], David A. Mays, PharmD, MBA, BCPS[4]; (1)Harvard University and Massachusetts General Hospital, Boston, MA; (2)Department of Psychiatry, Syracuse, NY; (3)University of Maryland, Baltimore, MD; (4)Shire Pharmaceuticals Inc., Wayne, PA.

OBJECTIVE: The objective of this study was to compare, following long-term MAS XR exposure, the actual growth (height and weight) observed in girls with ADHD to the published CDC norms for the respective age groups.
METHODS: In this multicenter, 24-month, open-label study of the safety of MAS XR, long-term growth data were collected for girls (6–12 years of age) who met DSM-IV TR® criteria for a diagnosis of ADHD. Participants were recruited from 2 short-term, double-blind studies of MAS XR. Patients were stratified into cohorts by recorded age at entry into the study (the CDC 50th percentile was estimated based on age at entry into study and estimated age at study conclusion). Mean and actual heights and weights were plotted for age cohorts, as well as for all patients, at each visit over the 24-month period. Mean changes from study entry for maximal gain in actual height and weight were calculated. The last visit of the double-blind treatment phase for girls

previously enrolled in the 2 acute studies was the baseline visit for the long-term study. Growth measures were collected at baseline, monthly from 12 to 24 months, and at early termination, if applicable.
RESULTS: A total of 55 girls with ADHD completed this long-term extension study. After 24 months, average growth rate was 3.61 inches and average weight increase was 8.3 lb. In the majority of cases this growth tracked above or on par with the 50th percentile CDC growth charts. Actual growth, measured in height and weight over time, showed consistent measurable increases over the 24-month period.
CONCLUSIONS: In this 24-month study, consistent, measurable growth increases were observed in girls who received MAS XR for ADHD, and the mean increases in actual height and weight were in accordance with the estimated CDC 50th percentile.
Presented at the Annual Meeting of the American Academy of Child and Adolescent Psychiatry, Toronto, ON, Canada, October 18-23, 2005.

254. Successful rate of conventional intravenous indomethacin for the treatment of patent ductus arteriosus in premature infants. *Liza Li, Pharm.D.*[1], Michael J. Gonyeau, B.S., Pharm.D., BCPS[1], Tola Dawodu, RPh, Pharm.D.[2], Eric Eichenwald, MD[2]; (1)Northeastern University School of Pharmacy, Boston, MA; (2)Brigham and Women's Hospital, Boston, MA.

PURPOSE: Premature infants in a neonatal intensive care unit with patent ductus arteriosus (PDA) treated with intravenous indomethacin were evaluated to assess the rate of permanent PDA closure, specifically in premature infants ≤26, 27-28, and ≥29 weeks gestational age, and rate of adverse effects.
METHODS: A retrospective medical chart review was performed. A computer generated list of medical record numbers of premature infants born between January 1 and December 31, 2004 that received indomethacin for treatment of patent ductus arteriosus. Data collected included postnatal information, PDA treatment (indomethacin dosing and surgical ligation); electrolytes, urine output (ml/kg/hr), and serum creatinine levels, and results of abdominal imaging were collected to assess adverse effects.
RESULTS: A total of 72 medical charts were reviewed. Permanent closure of ductus arteriosus occurred in 52/72 (72%) infants by the end of the indomethacin treatment. There was an increasing trend for permanent PDA closure with increasing gestational age from ≤26, 27-28, and ≥29 weeks (56% vs. 79% vs. 80%, respectively, p≤0.1) and as a result a decreasing trend for surgical ligation (33% vs. 14% vs. 10%, respectively, p≤0.1). Most infants required more than one course to permanently close a ductus arteriosus. There were only 2/72 (3%) infants that experienced oliguria (<1ml/kg/h) and 1 discontinued indomethacin treatment due to this adverse effect. There was a slight trend toward increased risk of electrolyte imbalance in repeated or prolong courses. The risk of necrotizing enterocolitis was the same for first course and repeated courses.
CONCLUSIONS: Gestational age may have a role in predicting permanent duct closure with indomethacin treatment. However, most will need repeated or prolong course(s) to permanently close the duct, which may increase the risk of electrolyte adverse effects. Future prospective studies are warranted to evaluate different factors associated with permanent closure of PDA and indomethacin therapy.

255. Effect of heliox on continuous nebulization of albuterol in pediatric mechanically ventilated models. *Sandra S. Garner, Pharm.D.*, Donald B. Wiest, Pharm.D., Charles E. Stevens, R.R.T., David M. Habib, M.D.; Medical University of South Carolina, Charleston, SC.

PURPOSE: Heliox, a mixture of helium and oxygen, has been used to nebulize medications with mixed results. Heliox's low density may improve drug delivery through narrow ventilator tubing and airways but may also reduce drug exiting the nebulizer. This study evaluated the effect of heliox on albuterol delivery by continuous nebulization in pediatric mechanically ventilated models.
METHODS: Models of a 10kg infant and 30kg child receiving PRVC ventilation with humidification were used. Infant settings were: endotracheal tube (ETT)=4.0mm, VT=150ml, PEEP=2cm H_2O, and rate=20bpm with child settings of: ETT=6.0mm, VT=450ml, PEEP=2cm H_2O, and rate=16bpm. Albuterol 10mg/hr was nebulized for 1 hour at 3L/min using the EZflow® continuous nebulizer with ventilator settings adjusted to maintain a constant tidal volume. Albuterol was collected on a filter which was rinsed with resulting concentrations measured by HPLC. Five trials for various heliox (50/50, 60/40, and 70/30) and nitrogen/oxygen mixtures were conducted in the infant model. With the child model, five trials of 70/30 heliox and nitrogen/oxygen were conducted. Data are reported as mean ± S.D. with significant differences determined by one- or two-way ANOVA (alpha=0.05) and Bonferroni's method of multiple comparison.
RESULTS: By two-way ANOVA (r^2 = 0.88), percentage albuterol delivery with the 70/30 mixtures was significantly less in the infant vs. the child model (2.1 ± 0.6 vs. 7.6 ± 2.1%, p<0.0001). There was significantly decreased albuterol delivery with 70/30 heliox vs. 70/30 nitrogen/oxygen (4.3 ± 2.4 vs. 5.4 ± 3.8%, p=0.05). A significant interaction was found between gas mixture and model (p=0.02). There was no difference in percentage albuterol delivery among the heliox mixtures in the infant model: 70/30: 2.3 ± 0.8%, 60/40: 2.4 ± 0.6%, and 50/50: 3.3 ± 0.7% (one-way ANOVA, p=0.19).
CONCLUSION: These results suggest heliox decreases albuterol delivery administered by continuous nebulization. Further study is needed to determine the mechanism of reduced delivery.

256. Dosage and effectiveness of intrapleural doxycycline for pediatric post-cardiotomy pleural effusions. *David S. Hoff, Pharm.D.*, David B. Gremmels, M.D., Karen Hall, B.S.Pharm., Francis X. Moga, M.D.; Children's Hospitals and Clinics of Minnesota, Minneapolis, MN.

PURPOSE: The use of doxycycline for recalcitrant post-cardiotomy pleural effusion in adults is well described. However, the dosage and effectiveness of doxycycline in the pediatric population are not standardized. This study reports on the effectiveness of a standardized protocol for the management of pleural effusions in pediatrics.
METHODS: A retrospective chart review was conducted of all patients at our institution who received doxycycline pleurodesis between December 21, 2001 and May 23, 2005. Doxycycline indication, dosing, effectiveness and adverse effects were documented.
RESULTS: Twelve patients received a total of 18 doses of doxycycline. All patients had significant underlying heart disease requiring surgical repair and cardiopulmonary bypass. The mean patient age and weight was 0.95 years (14 days-2.5 years) and 6.8 kg (2.7-16 kg), respectively. The mean dose was 130 mg (19.1 mg/kg/dose). Each dose was infused into a previously placed chest tube over 5 minutes. The tube was then clamped for a mean duration of 5.7 hours before being unclamped and connected to 20 cm of wall suction. Seventy-two percent of the doses achieved 0 ml/hr chest tube output by 96 hours. Four patients (22%) with prolonged post therapy effusion greater than 96 hours had elevated central venous pressures. These included two patients with post Fontan physiology, one patient with a thrombosed superior vena cava and one patient with repaired total anomalous pulmonary venous return. The most common untoward effects were increased blood pressure (4/18), increased heart rate (3/18) and fever (2/18). Additional pain medications were necessary in all patients.
CONCLUSION: Intrapleural doxycycline infusion is effective for persistent post-cardiotomy pleural effusion in pediatric patients. The protocol was well tolerated.

257E. Assessing parents preferences for the avoidance of undesirable anesthesia side effects in their children undergoing surgical procedures. *Deborah Wagner, PharmD*, Joe M. Yap, MD, Celia D'Errico, DO, Kathy Bradley, CRNA; University of Michigan Health Systems, Ann Arbor, MI.

PURPOSE: Undesirable anesthesia side effects in children can lead to serious and sometimes life threatening events. The purpose of this study is to assess parental preferences for the avoidance of anesthesia side effects in their children undergoing surgery using a Willingness to Pay (WTP)model.
METHODS: After Institutional Review Board approval, 150 surveys were distributed to parents of children undergoing surgical procedures. All surveys contained an informed consent cover letter, were distributed randomly and collected in a blinded envelope to a return box. There was no selection bias for age, race, ethnicity, marital status, and were unlinkable in any manner to either the child or the parent. Children whose parents were surveyed were between the ages of 2-12 years old and participation was totally voluntary. The survey described 7 of the most commonly occurring side effects; nausea, vomiting, shivering, somnolence/sedation, sore throat, pain, or none. Parents were asked to rank order from 1=the most unwanted to 7=least troublesome and to allocate a percent of an imaginable $100 to each of the side effects. Demographic information was also collected.
RESULTS: A total of 150 surveys were distributed of which 142 were returned. Of the 142 returned, 133 were complete and 9 were partially complete. Descriptive statistics were used to analyze the data. Parental preferences ranked vomiting as the least desirable side effect with pain being next. The corresponding dollar value in terms of WTP were greater for pain then vomiting. There was no statistical difference between the rankings of vomiting and pain.
CONCLUSION: The results are consistent with results from previous studies in the adult paptient population where vomiting is identified as the most undesirable side effect of anesthesia. Understanding parental preferences for avoiding anesthesia side effects in their children may ultimately allow practioners to further tailor therapy amongst pediatric patients.
Presented at the Annual Meeting of the Society for Pediatric Anesthesia, Miami, FL, February 24-27, 2005.

Pharmacoeconomics/Outcomes

258. Is paclitaxel cost-effective for the adjuvant chemotherapy in early-stage breast cancer? *Supon Limwattananon, MPHM, PhD*[1], Chulaporn Limwattananon, MPharm, MSc, PhD[1], Savitree Maoleekulpairoj, MD[2],

Nopadol Soparatanapaisal, MD[3]; (1)Faculty of Pharmaceutical Sciences, Khon Kaen University, Khon Kaen, Thailand; (2)Health Systems Research Institute, Nonthaburi, Thailand; (3)Faculty of Medicine, Mahidol University, Bangkok, Thailand.

An economic evaluation, in Thailand, of paclitaxel added subsequently to doxorubicin plus cyclophosphamide (AC) adjuvant therapy for early breast cancer (EBC) in women who have axillary lymph nodes positive is presented. An incremental cost-effectiveness ratio (ICER) representing ratio of the differences in total cost and effectiveness between two competing alternatives (AC alone vs. paclitaxel following AC) was the primary measure in this study. Health care cost associated with the evaluated chemotherapy was compared under Thai health care context. Most of the total cost (77.9%) for paclitaxel arm was attributed to an administration of the adjuvant medication. For the cost of non-paclitaxel arm, the initial adjuvant fraction (39.0%) was less than the downstream fraction (60.7%) due to disease recurrence treatment, routine follow up, and terminal care. Data on the relative efficacy of paclitaxel were derived from a randomized controlled trial by Cancer and Leukemia Group B (CALGB 9344), in which paclitaxel increased disease-free survival (DFS) by 17%. Based on Markov simulation for 15 years, paclitaxel extended patient's life by 0.47 years, on average, which is equivalent to 0.30 quality-adjusted life years (QALY). Such an increased effectiveness was off set by the adjuvant cost net of recurrence, follow-up, and terminal care by 221,433 Baht (or $5,678; 39 Baht = $1). This means an additional year of perfect health gained by paclitaxel is achieved through an incremental cost of $18,926. Such an incremental cost-effectiveness ratio (ICER) in this reference case analysis is beyond the cost-effectiveness threshold of 3 times of the national income per capita ($2,190 for Thailand) recommended by World Health Organization. For paclitaxel to become close to cost-effective, our sensitivity analysis suggested that an improvement in DFS to 28% (as in the case of women with estrogen receptor negative) would introduce the lowest ICER of $10,102 per QALY.

259. A US pharmacoeconomic model of parenteral parecoxib versus opioid and ketorolac analgesia following major surgery. *Mason W. Russell, MAPE*[1], Jeffrey D. Miller, MS[1], Peter J. Neumann, ScD[2], Joseph Menzin, PhD[1], Mark E. Boye, PhD[3], Dale A. Rublee, PhD[4]; (1)Boston Health Economics, Inc., Waltham, MA; (2)Harvard School of Public Health, Boston, MA; (3)Pfizer Inc, Ann Arbor, MI; (4)Pfizer Inc, New York, NY.

PURPOSE: To estimate the clinical and economic consequences of parecoxib sodium versus alternative parenteral postsurgical pain management strategies in hospital inpatients undergoing selected major surgeries.
METHODS: We developed a US model of postsurgical pain management to assess comparative clinical and economic outcomes in patients receiving alternative parenteral analgesic regimens (parecoxib, ketorolac, and opioids). Model parameters were derived from clinical trial data, a large inpatient billing database, and published literature. The model tracks cohorts defined by age and gender over the 3-day period following major abdominal, orthopedic, or gynecologic surgery. Parecoxib and ketorolac regimens include adjunctive opioids. The model estimates occurrences of opioid-related symptoms ("clinically meaningful events" or CMEs), time in a postanesthesia care unit (PACU) or special care unit (SCU), various pain intensity metrics, and direct medical costs. Model outcomes include differences by treatment regimen (parecoxib versus comparator) in CMEs, PACU/SCU time, pain intensity scores, direct medical costs, and incremental cost-effectiveness ratios.
RESULTS: Hospitalization costs in the 3 days following surgery were $44 per patient lower among parecoxib- versus opioid-treated patients, and $41 per patient higher among parecoxib- versus ketorolac-treated patients. Patients receiving parecoxib spent 13 minutes less time, on average, in PACUs and SCUs than opioid-treated patients, and 3 minutes longer than ketorolac-treated patients. Total CMEs were approximately 26% lower among parecoxib- versus opioid-treated patients; inadequate data precluded estimating CMEs for ketorolac patients. Pain intensity scores were uniformly lower for parecoxib-treated patients versus comparators. Incremental cost-effectiveness analysis suggests that parecoxib therapy is more effective and less costly than opioid therapy.
CONCLUSIONS: Results from this model suggest that the opioid-sparing properties of parecoxib translate into better clinical outcomes, reduced healthcare resource utilization, and lower costs versus an opioid-only pain management strategy. Parecoxib also appears to confer superior pain management at relatively small incremental costs relative to ketorolac.

260E. Annual costs of pain medications in patients with diabetic peripheral neuropathy. Stephen Able, PhD[1], Rebecca Robinson, MS[1], Kimberly Sterling, PharmD[1], *Jeff Hille, MPH*[2], Robert Obenchain, PhD[1], Martha Davis, PhD[1], Ralph Swindle, PhD[1]; (1)Eli Lilly and Company, Indianapolis, IN; (2)Eli Lilly and Company, San Francisco, CA.

INTRODUCTION: Prevalence-based estimates of the direct cost of diabetic peripheral neuropathy pain (DPNP) in the US are extremely limited. To better understand such costs, a retrospective claims analysis was conducted.
METHODS: Data were from the PharMetrics Patient-Centric Database. A representative sample of adult patients with a diagnosis of diabetic neuropathy and any 2002 pharmacy claim for a pain medication was used. Claimants with a diagnosis of schizophrenia, bipolar, psychoses, or depression were excluded. Average wholesale price for prescriptions were from First Databank.
RESULTS: Preliminary analysis was conducted on 1444 patients. Medications prevalent in patients included narcotics (60.4%); antidepressants (39.3%), including TCAs (20.6%) and SSRIs (18.8%); NSAIDS (45.3%), including Cox-2 inhibitors (21.6%), and anticonvulsants (26.4%), including gabapentin (21.1%). The largest shares of total cost were for anticonvulsants (27.0%), antidepressants (23.0%), and narcotics (20.7%). Over 60% of patients had claims in more than one of the 13 pain medication categories studied, 35% in 3 or more. Total per treated member per month (PTMPM) costs for pain medications was $71.67. PTMPM for patients on monotherapy was $22.36, for those on multiple therapies $103.60. No dominant patterns of combination therapies were evident.
CONCLUSIONS: In 2002, there was nothing indicated for the treatment of DPNP. Patients received an assortment of pain medications with a majority receiving multiple therapies. Most costs arise from those on multiple therapies. These data provide a payer perspective of annual costs to the system. Data are limited in that pain medications may or may not be directly tied to only DPNP
Presented at the Annual Meeting of the American Psychiatric Association, Atlanta, GA, May 21, 2005.

261. Evaluation of a pharmacist incentive program for therapeutic conversion of calcium channel blockers at a VA medical center. *Steven T. Boyd, PharmD, BCPS, CDE*[1], Samuel Bottaro, R.Ph., MS, DPh[2], Dennis Mostek, PharmD[2], Paul Bierman, PharmD[2], Jerome Alexander, R.Ph.[2]; (1)Creighton University, Omaha, NE; (2)Omaha VA Medical Center, Omaha, NE.

PURPOSE: To evaluate the cost-savings generated through a pharmacist incentive program targeting conversion of non-formulary amlodipine to formulary felodipine.
METHODS: The Omaha VA Pharmacy Administration implemented a two-phase non-formulary calcium channel blocker drug conversion program involving pharmacy, cardiology, and pharmacy and therapeutics committee (P&T). Staff pharmacists (22) and clinical pharmacists (12) performed the protocol conversion of amlodipine to felodipine. Phase-One targeted active amlodipine utilizers for treatment of hypertension and angina without a diagnosis of heart failure. Patients were automatically converted to felodipine using equivalent doses. Phase-Two involved collaboration between a cardiologist and pharmacist for utilizers with heart failure and/or other cardiac conditions. Patients converted were notified of the program via telephone and letters with a drug picture chart. Individual pharmacists received an incentive award for percentage of patients switched to felodipine: Gold > 98% = $2,000; Silver > 95% = $1,500; Bronze > 89% = $1,100.
RESULTS: Baseline amlodipine treated patients included 980(21%) of all calcium channel blocker treated patients. Total cost of amlodipine use was $395,092 annually. The incentive project is expected to reduce amlodipine treated patients to 80 (1.71%) costing $32,252 annually. Felopidine baseline costs only increased from $121,746 to $164,901. It is anticipated pharmacists will be paid a total of $68,000 for reaching gold level. The VA medical center is expected to have a 1st year cost-savings of $251,645 for this incentive conversion project and a cost-containment of $319,645 for the subsequent years.
CONCLUSION: An incentive program for pharmacists in cooperation with appropriate physician groups and pharmacy administration demonstrated significant cost-savings and future cost-containment. Future programs will be investigated.

262. Modeling the costs and outcomes of solifenacin vs. behavioral therapy or no therapy for treatment of overactive bladder in primary care. *Nancy Neil, PhD*[1], Sharon Block, B.S.[1], Kristine Ogden, B.S.[1], Les Noe, RPh, MPA[1], Libby Black, PharmD[2], Todd E. Williamson, Ph.D.[3]; (1)Ovation Research Group, Highland Park, IL; (2)GlaxoSmithKline, Research Triangle Park, NC; (3)Sanofi-Aventis, Bridgewater, NJ.

INTRODUCTION: The modeling objective was to estimate the clinical and economic impact of treating overactive bladder (OAB) with solifenacin (SOL), behavioral therapy (BT), or no therapy (NT).
METHODS: A Markov model was used to simulate primary care management of OAB. Estimates of OAB prevalence, treatment patterns, resource use, effectiveness (continence), persistence, and incidence/costs of co-morbid conditions were drawn from published literature. The model simulates three phases of care: *Diagnosis*–assumes 20% of prevalent cases seek evaluation and treatment for OAB; cases not seeking treatment (NST) remain in the model. *Treatment*–assumes three, four-week cycles. Treatment-seeking patients

receive SOL 5mg, BT, or NT. Treated patients experiencing sub-optimal results may proceed to increased dose (SOL arm only), SOL 5mg + BT, or may discontinue therapy. Patients non-persistent with therapy remain symptomatic and off treatment for the duration of the model. *Follow-up*–treatment costs, and the incidence/costs of treatment associated with expected co-morbid events are modeled throughout a simulated 12-month period.
RESULTS: More patients treated with initial SOL 5mg achieved continence (65%), compared to BT (34%), NT (0%), or NST (0%). Per-patient treatment of comorbid events was less costly with initial SOL 5mg compared to BT, NT and NST ($1492 annually vs. $1687, $1865 and $1858, respectively). Compared to BT, SOL was dominant (more effective, less costly). The additional cost of gaining each additional continent patient with SOL, relative to NT and NST, was $1114 and $1641, respectively. Results of sensitivity analyses will be presented.
CONCLUSIONS: For patients with OAB initiating therapy in primary care, first-line treatment with low-dose solifenacin is more effective (achievement of continence) and less costly compared to behavioral therapy. Initial solifenacin 5mg lowers the overall cost of care by reducing costs associated with management of comorbid conditions. Further studies are needed to compare solifenacin with other pharmacotherapies for OAB.

263. Potential 30-day cost savings from acute coronary syndrome treatment improvements. *Robert W. Klein, PhD*[1], Robert L. Ohsfeldt, PhD[2], Lee J Smolen, MS[1], Patrick L. McCollam, PharmD[3]; (1)Medical Decision Modeling, Indianapolis, IN; (2)University of Iowa, Iowa City, IA; (3)Lilly Research Laboratories, Indianapolis, IN.

OBJECTIVES: This research uses a decision tree model of acute coronary syndrome (ACS) to determine the magnitudes of cost drivers and clinical events affected by a hypothetical new treatment at 30-days.
METHODS: The model was built using TreeAge Pro Healthcare and parameterized to replicate the Clopidogrel in Unstable angina to prevent Recurrent ischemic Events (CURE) trial. The model reports results at 30-days for clopidogrel plus aspirin vs. a hypothetical alternative. Reductions in risk for four events are analyzed: myocardial infarction (MI), percutaneous coronary intervention (PCI), cardiovascular death and stroke. Modeled risks and costs of coronary artery bypass grafting (CABG) surgery and bleeding complications are not modified. In the sensitivity analysis, inputs for costs used Erlang distributions.
RESULTS: The effects on costs of reducing relative risks of each event (and all 4 together) by 10% and 20% are evaluated. Cost offsets are highest for PCI ($195, $389; 3.9%, 7.9% of total costs). All other 30-day offsets are less than 2.0%. Total savings for a 20% reduction in all 4 events are ($260, $522; 5.3%, 10.6%) at 30-days. Point estimates of all event costs were replaced with distributions. When 1000 Monte Carlo simulations of the model with 20% reductions to all risks were run the minimum difference in cost was $89, the maximum $2100, (standard deviation $287). Only 131/1000 observations had <$50 savings, while 438/1000 saved >$500. Concurrent 20% reductions in 1000 patients avoid 25 PCIs, 5 MIs, 4 deaths, and 1 stroke. Thus the number needed to treat to avoid one event would be 29.
CONCLUSIONS: In this short-term model, PCI influences cost more than MI, stroke, or other cardiovascular death but all are clinically important. Knowing the relationship between event costs and risk reductions can help estimate the potential cost impact of new treatments.

264. Potential unrecognized costs of clopidogrel pretreatment in acute coronary syndrome. *Paul P. Dobesh, Pharm.D.*[1], Patrick L. McCollam, PharmD[2]; (1)University of Nebraska Medical Center, Omaha, NE; (2)Lilly Research Laboratories, Indianapolis, IN.

PURPOSE: The American College of Cardiology and American Heart Association (ACC/AHA) recommend clopidogrel plus aspirin in patients undergoing percutaneous coronary intervention (PCI) for acute coronary syndromes (ACS). Clinical trial data support a clopidogrel loading dose several hours before PCI and continued daily with aspirin thereafter to reduce ischemic endpoints. The ACC/AHA also recommends that patients needing coronary artery bypass graft (CABG) surgery have their clopidogrel withheld for 5-7 days to prevent significant bleeding. Literature also suggests the CABG rate exceeds the ischemic event rate averted by clopidogrel in these patients. Since the need for CABG cannot be predicted at the needed time of clopidogrel loading, some patients may incur additional hospitalization awaiting CABG and therefore unrecognized costs due to clopidogrel administration.
METHODS: A spreadsheet model was created to estimate cost of clopidogrel therapy incurred by patients needing same-stay CABG. Based on a literature review, the model included a range of inputs for institutional annual PCI volume (500-2000/year), proportion of patients with ACS requiring same-stay CABG (5-20%), and cost/day of hospital stay ($750). This allowed calculation of number of patients awaiting clopidogrel elimination for CABG, total number of hospital days needed for these patients (assuming 5 days/patient), and potential cost incurred by the institution. Sensitivity analysis was conducted utilizing a range of hospital daily cost ($500-1000).
RESULTS: The potential cost of early clopidogrel administration ranges from $93,750 for an institution performing 500 PCI/year and a 5% CABG rate to $1,500,000 for an institution performing 2000 PCI/year and a 20% CABG rate. Sensitivity analysis for cost/day of hospitalization was $62,500-$2,000,000.
CONCLUSIONS: Administration of clopidogrel to ACS patients who may eventually require non-urgent same-stay CABG may be associated with unrecognized costs as well as impeding institutional efficiency when the waiting time for these patients is considered.

265E. Avoiding adverse cardiovascular outcomes with prompt blood pressure control: an economic analysis based on the Valsartan Antihypertensive Long-term Use Evaluation (VALUE) trial. *Paul Radensky, MD, JD*[1], Simon Tang, MPH[2], Kamlesh Thakker, PhD, MBA[3]; (1)McDermott Will & Emery LLP, Miami, FL; (2)Pfizer Inc US Outcomes Research, New York, NY; (3)Pfizer Inc US Medical, New York, NY.

PURPOSE: Improved outcomes in hypertensive patients are usually ascribed to gradual, long-term blood pressure (BP) control. However, results from VALUE demonstrate significant reductions in cardiovascular (CV) events in high CV risk patients, associated with BP lowering over the short term (3 months). This analysis examined the cost-effectiveness of antihypertensive therapy, based on CV event rate reduction in the first 3 months of the VALUE trial.
METHODS: An economic model was developed to determine costs per event avoided for stroke and all-cause mortality in the 0-3 month period of the VALUE trial (the only discrete outcomes showing significant differences between regimens in the early treatment period). Drug utilization was determined from the VALUE publication (Julius et al. *Lancet*, 2004;363: 2022); drug costs were from public sources reflecting retail pharmacy pricing. Stroke and all-cause mortality event rates were determined from the published paper using Kaplan-Meier graphs and reported odds ratios (OR) with 95% confidence intervals (CI), for valsartan vs amlodipine: stroke 1.94 (1.10-3.42); all-cause mortality 2.84 (1.51-5.34). Sensitivity analyses were conducted based on the upper and lower bounds of the CI for the OR and ± 20% on event rates.
RESULTS: Over 3 months, amlodipine-based treatment reduced mean systolic BP 3.8 mmHg more than valsartan-based treatment, leading to reduction of 36 strokes and 53 deaths per 15,000 patients. Drug cost is $9.67 higher per patient for amlodipine vs. valsartan. Cost per stroke averted is $4,003 (range $2,282-$26,698); cost per all-cause death avoided is $2,742 (range $1,821-$6,582).
CONCLUSIONS: All antihypertensive regimens may not be equally efficacious at rapidly reducing BP. Among patients at high CV risk prompt BP reduction with amlodipine-based therapy, as seen in VALUE, can reduce stroke and all-cause mortality within 3 months. These results reinforce the cost-effectiveness of optimal antihypertensive therapy for early and aggressive BP lowering to reduce CV events.
Published in Am J Hypertens 2005;18(suppl):72A.

266E. Hospitalized community-acquired pneumonia: a three-year review of patient factors associated with prolonged length of stay. *Daryl D. DePestel, Pharm.D.*[1], Richard W. Dettloff, Pharm.D.[2], Tom A. Wolfe, Pharm.D.[3], Kevin Townsend, Pharm.D.[4], Bonnie A. DeLor, Pharm.D.[5], Martin Ginnamore, Pharm.D.[6]; (1)University of Michigan Health System and College of Pharmacy, Ann Arbor, MI; (2)Pfizer, Rockford, MI; (3)Pfizer, Westerville, OH; (4)Pfizer, Chelsea, MI; (5)Pfizer, Hartland, MI; (6)Pfizer, Dublin, OH.

OBJECTIVES: The primary objective of this analysis was to identify factors associated with prolonged length of stay (LOS) in patients with hospitalized community acquired pneumonia (CAP).
METHODS: Data were collected retrospectively on 1861 randomly selected patients with a discharge ICD-9 diagnosis of CAP who were admitted between October 2000 and April 2003 to 29 hospitals in the Great Lakes region. A standardized electronic database was used to collect demographic and clinical data. Logistic regression analysis was used to adjust for potential confounding variables and to identify patient factors associated with a LOS greater than 4 days (cohort median). Pneumonia Severity Index Score (PSI) defined risk class. Antibiotic selection was evaluated relative to standard guidelines (Infectious Diseases Society of America).
RESULTS: Patient factors associated with a LOS greater than 4 days included admission during the 2001-2002 season (OR, 1.35; 95% CI, 1.06-1.72), increasing age (OR, 1.01; 95% CI, 1.00-1.02), Risk Class III (OR, 1.50; 95% CI, 1.10-2.06), Risk Class IV (OR, 1.67; 95% CI, 1.20-2.32), Risk Class V (OR, 3.01; 95% CI, 2.0-4.76), ICU admission for pneumonia (OR, 2.11; 95% CI, 1.31-3.40), gram-negative sputum culture (OR, 2.15; 95% CI, 1.37-3.38), gram-positive blood culture (OR, 2.01; 95% CI, 1.28-3.17), increasing hours to antibiotic administration (OR, 1.02; 95% CI, 1.01-1.04), modification of empiric antibiotic regimen (OR, 1.45; 95% CI, 1.17-1.81) and intravenous to oral antibiotic conversion (OR, 2.01; 95% CI, 1.63-2.48). Administration of

antibiotic regimens consistent with IDSA guidelines was associated with reduced odds for a longer LOS (OR, 0.50; 95% CI, 0.33-0.77).
CONCLUSIONS: Several factors were associated with a hospital LOS greater than 4 days. Guideline-compliant antibiotic use was associated with reduced odds for a long LOS. These findings may facilitate further research and the development of targeted management strategies to control LOS and ultimately resource consumption.
Published in Value in Health 2005;8(3):311.

267. Use of typical antipsychotics in depot and oral formulations in the usual care of schizophrenia patients. *Haya Ascher-Svanum, PhD*[1], Baojin Zhu, PhD[1], Douglas Faries, PhD[1], Lizheng Shi, PhD[2], Bill Montgomery, B. Pharm[1], Steve Marder, MD[3]; (1)Eli Lilly and Company, Indianapolis, IN; (2)Department of Health Systems Management Tulane University, SL-29, New Orleans, LA; (3)UCLA, Veteran Affairs Great Los Angeles Healthcare System, Los Angeles, CA.

PURPOSE: To prospectively assess and compare the use of typical antipsychotics (fluphenazine and haloperidol) in depot versus oral formulations in the usual care of patients with schizophrenia.
METHODS: We used data from a large prospective naturalistic non-randomized multi-site study of schizophrenia in the United States, conducted 7/1997-9/2003. The analytical sample included initiators on haloperidol and fluphenazine in oral or depot formulations who received the medication for at least 60 days and had medication information for at least one year post initiation (N=299). Medication use patterns included dose, frequency, the association between dose and adjunctive use of antiparkinsonian agents, and the association between dose and illness severity as assessed by the PANSS at enrollment. Medication effectiveness during the 1-year post initiation was defined as time to all-cause medication discontinuation, which was measured by the number of days to first medication gap larger than 30 consecutive days. Trained examiners systematically abstracted medication information from patients' medical records, using a form developed for the study.
RESULTS: Modal dose and frequency was 25 mg per bi-weekly injection of fluphenazine depot (N=47), and 100 mg per monthly injection of haloperidol depot (N=50). Mean oral dose was 12 mg/day for fluphenazine (N=93), and 10.7 mg/day for haloperidol (N=109). Higher depot doses were associated with greater adjunctive use of antiparkinsonian agents (p=0.0424) and higher scores on the PANSS Positive subscale at enrollment (p=0.0503). During the 1-year post medication initiation, patients treated with depot were twice as likely to stay on the medication compared to patients treated with oral formulations (Odds Ratio=2.1, p=0.0021).
CONCLUSION: Higher doses of depot antipsychotics appear to be associated with greater use of adjunctive antiparkinsonian agents and greater illness severity. Patients treated with depot typical antipsychotics were twice as likely to stay on their medication as patients treated with typical antipsychotics in oral formulations.

268. Evaluation of cost savings from a pharmacist-directed IV to PO conversion program in a 200-bed community hospital. *Renee Medders, BS*, Thomas H. Cobb, Pharm.D; CMMC, Jackson, MS.

PURPOSE: This study was designed to evaluate the financial benefits of a Pharmacist directed IV to PO conversion program.
METHODS: A study of pharmacy initiated IV to PO conversions from Feb 1, 2005 thru April 30, 2005 to evaluate cost savings, appropriate renal dosing, and conversion back to IV therapy. Hospital Pharmacists were delegated the authority to convert dosage forms from IV to PO for patients receiving IV medications who met specific criteria approved by the hospital's medical staff. Post conversion, medical charts of each patient were reviewed for evaluation of the outcome of the switch.
RESULTS: Conversions were initiated in the critical care, telemetry, and med-surg units. Over the 3-month period 188 conversions were made resulting in a cost savings of $3,975.76, resulting in a yearly savings of $15,903.04. Of the 188 conversions, the 3 most common were Prevacid (33.28%), Reglan (29.49%), and Pepcid (12.19%). The top 3 in terms of cost savings were Prevacid (36.78%), Levaquin (16.6%) and Diflucan (12.6%). Of the 188 conversions, 11 were converted back to IV, 6/11 were Prevacid, 2/11 were Levaquin, and 1 each were Zithromax, Flagyl, and Reglan. Of the 11 patients, 5 were started on TPN during the course of their hospital stay and their oral meds were converted back to IV. At the time of conversion, 11 of the 188 required dosage adjustment based on renal function. Levaquin and Reglan accounted for 10 and 1 of the 11 respectively.
CONCLUSIONS: Pharmacist directed IV to PO conversion programs can reduce cost to community hospitals without affecting quality of care.

269. An economic claims analysis of combined ipratropium bromide and albuterol versus individual components in chronic obstructive pulmonary disease patients. *John M. York, Pharm.D.*[1], J. Smeeding, R.Ph., MBA[2], R. Brook, M.S., MBA[3], L. Wong, Pharm.D.[4], F. Hoehler, Ph.D.[4], Gerald L.. Klein, M.D.[5]; (1)Akita Biomedical Consulting, San Clementa, CA; (2)University of Texas at Austin, Austin, TX; (3)The JeSTARx Group, Dallas, TX; (4)DEY Laboratories, LP, Napa, CA; (5)University of the Pacific, Stockton, CA.

PURPOSE: To compare the ipratropium and albuterol combination product (IAC) for nebulization versus individual generic components (DSA) on health care resources and compliance in COPD patients.
METHODS: This retrospective managed care claims analysis compared IAC and DSA in COPD patients (aged ≥ 40 years with ≥ 15 months of plan eligibility). Per-member-per-month (PMPM) claims (total, medical, inpatient, pharmacy, and emergency department [ED] expenditures) for 12 months were analyzed. Compliance was evaluated by reviewing frequency of interruptions and discontinuations. Statistics included Student *t*-tests, χ^2, and Wilcoxon ranked sum tests. Multiple regression analyses were performed to assess impact age, sex, staging, date of treatment, and baseline costs levels upon unadjusted mean observations for Total PMPM and any subgroup where statistical significance was found. Adjusted observations were presented as least square means.
RESULTS: Analysis involved 1531 subjects:468 IAC and 1063 DSA. PMPM comparisons included: total (IAC $1840.36, DSA $2046.73; p=0.22), medical (IAC $549.59, DSA $570.70; p=0.65), inpatient (IAC $874.97, DSA $1105.80; p=0.10), pharmacy (IAC $415.80; DSA $370.22; p=0.07), and ED (IAC $36.67, DSA $52.84; p=0.03). ED visit frequencies were 0.93 for IAC and 1.33 for DSA (p<0.001). IAC had fewer therapy interruptions: 0.78 versus 0.85 (p=0.003). IAC was lower by $206.37 for Total PMPM (NS) and $16.17 for ED PMPM (p=0.003). Multiple regression found that IAC was lower by $204.15 (NS) for total expenditures and $21.41 (p<0.05) for ED costs. A significant interaction was found for group and age in patients older or younger than 65 years.
CONCLUSIONS: Overall, IAC total expenditures were no greater than with DSA. IAC was associated with significantly lower ED resource used and fewer therapy interruptions. Multiple regression analysis supported unadjusted mean values for unadjusted total and ED expenditures.

270. Clopidogrel loading dose and cardiovascular outcomes in acute coronary syndrome patients who undergo percutaneous coronary intervention. *Cheng Wang, MD, PhD*[1], Jianming He, MS[1], Jay P. Bae, PhD[2], Patrick L. McCollam, PharmD[2], Brian T. Griffin, MBA[1]; (1)Solucient Inc, Berkeley Heights, NJ; (2)Eli Lilly & Company, Indianapolis, IN.

PURPOSE: The 2002 AHA/ACC guideline recommends acute coronary syndrome patients who undergo percutaneous coronary intervention (ASC-PCI) be given 300mg loading dose (LD) of clopidogrel, but higher LD has emerged in practice. A recent trial involving 255 patients found 600 mg of clopidogrel had better outcomes than 300mg (Patti et al, 2005). The current study investigates whether patients treated with higher clopidogrel LD experience better outcomes in the usual care setting.
METHODS: We followed 6,282 ACS-PCI patients in a national hospital database with time-stamp information (1/2003–9/2004) for 60 days upon discharge. Using the time-stamp, LD was measured as total dose within 24-hour window of peri-PCI procedure, and myocardial infarction (MI) was captured from post-procedure lab tests. Patients receiving >300mg are grouped into high LD (HLD) (nH=1,465) and =300 mg, the low LD group (LLD) (nL=4,152). Primary endpoints (i.e., death, stroke, repeat revascularization, and MI) plus bleeding and re-admission were monitored. Logistic regression tested effects of LD on events with controls for risk.
RESULTS: LD ranged from 75mg to 1275mg. The HLD group did not experience better outcome. While 28.49% of LLD experienced an event, the rate was 44.23% for the HLD (p<0.0001). MI rate was higher for HLD at 42.18% compared to 25.91% of LLD (p<0.0001). Bleeding, readmission, and mortality were similar (p=NS). Risk-adjusted logistic regression also found no evidence for better outcome in patients given HLD of clopidogrel.
CONCLUSIONS: Using time-stamp data, this large study retrospectively investigated effects of HLD clopidogrel in usual care setting. Patients receiving HLD did not experience better outcome. If providers tend to select HLD to treat high-risk patients in practice, an underlying dose-outcome bias would exist in the data. It is unclear how much of the bias is mitigated by higher dosing in the usual care setting. More research is needed.

271. Resource utilization of adults admitted to a tertiary hospital with community acquired pneumonia (CAP) caused by Streptococcus pneumoniae (SP). Heather K. Sun, Pharm.D., David P. Nicolau, Pharm.D., FCCP, *Joseph L. Kuti, Pharm.D.*; Center for Anti-Infective Research and Development, Hartford Hospital, Hartford, CT.

PURPOSE: While the clinical outcomes of CAP are well described, the breakdown of resources utilized during treatment is not well elucidated. We performed a retrospective review of patients admitted with CAP due to SP over a 4-year period in a large tertiary hospital to determine where treatment resources are consumed.
METHODS: The medical records of 543 adults with respiratory/blood cultures positive for SP were reviewed. Charge data were collected from detailed

medical bills and broken out by the following departments: non-ICU bed, ICU bed, Pharmacy, Antibiotics, Laboratory, Radiology, Respiratory, Rehabilitation, and Other. Charges were converted to costs using department specific cost to charge ratios and inflated to 2003. Patients with penicillin resistant (R) or intermediate (I) SP were matched to susceptible (S) cases by age, ICU stay, Pneumonia Severity Index (PSI) and admit year. Resource consumption as a percent of total costs was analyzed.
RESULTS: 166 patients were included. Penicillin susceptibility was 74% S, 10% I, and 16% R. Empiric antibiotic therapy was considered appropriate in 88% of patients. Over 50% were admitted with PSI IV or V, and 27% were treated in the ICU. Infection-related mortality was 10.7% and mean length of stay was 8.8 ± 7.9 days. Median (25th-75th%) total costs were $8,654 (5,457-16,027). Mean (SD) utilization by department was non-ICU bed: 46% (22), ICU bed: 9% (17), Pharmacy: 10% (4), Laboratory: 10% (4), Radiology: 5% (6), Respiratory: 5% (5), Rehabilitation: 1% (1), and Other: 14% (9). Antibiotics made up 50% (19) of pharmacy costs.
CONCLUSIONS: Hospital bed costs accounted for over half of resource consumption in the treatment of SP CAP, followed distantly by Pharmacy and Laboratory costs. These data confirm that the largest reductions in costs associated with SP CAP can be achieved by reducing hospital length of stay.

272E. Association between health services costs and effectiveness of depression treatment. *Greg E. Simon, MD, MPH*[1], Rezaul Khandker, MD[2]; (1)Center for Health Studies, Group Health Cooperative, Seattle, WA; (2)Wyeth Research, Collegeville, PA.

PURPOSE: This study examined whether remission of depression was associated with decreased health services costs.
METHODS: Pooled data from 7 longitudinal studies of patients beginning depression treatment were used to examine the relationship between clinical outcome of acute-phase treatment and health services costs over the subsequent 6 months. Clinical outcomes were assessed by structured telephone interviews. Health services costs were assessed using health plan accounting records.
RESULTS: Of 1816 patients entering treatment and meeting criteria for major depressive episode, 29% had persistent major depression 3-4 months later, 37% were improved but did not meet criteria for remission, and 34% achieved remission of depression. Those with persistent depression had higher baseline depression scores and higher health services costs before beginning treatment. After adjustment for baseline differences, mean health services costs over the 6 months following acute-phase treatment were $2106 (95% CI: $1684 to $2545) for those achieving remission, $2333 (95% CI: $1940 to $2754) for those improved but not remitted, and $2955 (95% CI: $2452 to $3509) for those with persistent major depression. Average costs for depression treatment (antidepressant prescriptions, outpatient visits, mental health inpatient care) ranged from $431 in the remission group to $599 in the persistent depression group.
CONCLUSIONS: Clinical outcome of acute phase depression treatment predicts subsequent health services costs, and persistence of depression is associated with 40% higher costs compared to full remission. The excess costs associated with persistence of depression are nearly twice as great as spending on depression treatment.
Presented at the Annual Meeting of the Academy of Managed Care Pharmacy, Nashville, TN, October 5-8, 2005.

273E. Early therapy with nesiritide in hospitilized patients with acute decompensated heart failure associated with reduced costs: a Markov analysis. *Glen T. Schumock, Pharm.D, MBA*[1], Robert J. DiDomenico, PharmD[1], Juan C. Blackburn, MD, MBA, MPH[1], Surrey M. Walton, PhD[1], Daniel E. Hilleman, PharmD[2]; (1)University of Illinois at Chicago, Chicago, IL; (2)Creighton University Medical Center, Omaha, NE.

INTRODUCTION: Heart failure (HF) is a common clinical syndrome associated with morbidity, mortality, and a significant economic burden to patients, providers, and society. Acute decompensated heart failure (ADHF) leads to frequent hospital admissions, which account for up to 70% of the cost of HF. Nesiritide may reduce downstream resource utilization and improve patient outcomes when used early in the treatment course.
OBJECTIVE: The purpose of this study was to evaluate the costs and patient outcomes of nesiritide, given within 24 hours of hospitalization, versus standard therapy for the treatment of ADHF.
METHODS: A Markov model of ADHF was developed using TreeAge-Pro Healthcare software. The model incorporates complications of therapy (atrial fibrillation and renal failure), location of inpatient care (intensive care unit, inpatient ward, or emergency department only), and hospital readmissions. Three stages of disease were included within each cycle of the model: well (survive ADHF hospitalization without suffering ADHF readmission), sick (survive ADHF hospitalization but suffer ADHF readmission), and death. Transition probabilities were calculated from previous published clinical trials. Estimates of hospital costs were obtained from a pilot study conducted at Creighton University Medical Center. The model was run over 6 cycles of one month each. The analysis was conducted from the hospital perspective.
RESULTS: Over 6 months, the total hospital costs (including all readmissions) for a patient treated with nesiritide or standard therapy were $9,787.65 and $10,914.28, respectively (2004 US dollars), a net decrease of $1,126.63 favoring nesiritide. Cost differences were largely attributable to a lower probability of readmission for patients receiving nesiritide. Survival at 6 months also favored nesiritide, with net gain of 0.081 years per patient over standard therapy.
CONCLUSIONS: Our model predicts that nesiritide, given within 24 hours of hospitalization for ADHF, reduces overall costs and may improve survival over 6 months compared to standard therapy.
Presented at the 9th Annual Scientific Meeting of the Heart Failure Society of America, Boca Raton, FL, September 18-21, 2005.

274E. Impact of extended spectrum b-lactamase (ESBL) producing bacteria on initial antibiotic outcomes: a case controlled study. *Su Young Lee, PharmD*, Joseph L. Kuti, PharmD, David P. Nicolau, PharmD; Center for Anti-Infective Research and Development, Hartford Hospital, Hartford, CT.

BACKGROUND: While carbapenems are recommended for extended-spectrum b-lactamase (ESBL) infections, few case controlled studies are available to support or refute the use of other antibiotic classes against ESBL infection.
METHODS: This retrospective study compared the outcomes of 21 cases receiving various antibiotics for non-urinary ESBL infections with 32 controls, matched on pathogen species, age, infection site, ICU stay, and date of hospitalization, receiving the same antibiotic for non-ESBL strains. Multiple logistic regression was used to identify independent predictors for mortality, success, and ESBL presence.
RESULTS: Independent risk factors for ESBL infection were prior antibiotic history and extended hospital stay prior to infection. No variables were independently associated with mortality except a trend with ESBL presence (OR 5.7, p=0.08). However, cases were more likely to have clinical failure (OR 8.4, p=0.014), and those receiving non-carbapenem antibiotics had lower success rates compared with their controls (39% vs. 79%, p=0.013), while all receiving a carbapenem had success.
CONCLUSION: When non-carbapenem antibiotic classes were utilized for ESBL infections outside the urinary tract, therapy was more likely to result in a clinical failure, and required changes in antibiotic regimen. Moreover, ESBL infection increased hospital length of stay and additional antimicrobial therapy. As result, considerable effort should be provided to optimize the detection of and treatment of non-urinary ESBL infections.
Presented at the Interscience Conference on Antimicrobial Agents and Chemotherapy, New Orleans, LA, September 21-24, 2005.

275E. Assessing antidepressant use patterns and costs associated with switching products. *Denise Kruzikas, PhD*[1], Rezaul Khandker, MD[2], Trent McLaughlin, PhD[1], Michael Tedeschi, RPh, MBA[2]; (1)NDCHealth, Yardley, PA; (2)Wyeth Research, Collegeville, PA.

PURPOSE: This study examines patterns of antidepressant use including drug switching and related resource utilization.
METHODS: Using retrospective claims of managed care enrollees in a national database (PharMetrics), this study follows newly diagnosed depression patients (age 18+) with newly prescribed antidepressants. We identified the proportion of switchers from commonly prescribed SSRIs (fluoxetine, citalopram, sertraline, and paroxetine) to an SNRI (venlafaxine), and vice-versa. We then aggregated healthcare costs for a 1-year period following diagnosis for various switcher groups. Multivariate regression analyses determined predictors of switching and factors influencing overall and depression-related costs.
RESULTS: Of the 48,950 patients in the study population, 89% were treated with SSRIs and 11% with SNRIs. Between 12% and 15% switched antidepressants; 29% of SSRI switchers switched to an SNRI. Increased likelihood of switching was associated with female gender, Medicaid coverage, prior anxiolytic use, treatment by a psychiatrist or psychologist, and paroxetine as the index medication. Compared with SSRI non-switchers, costs for SSRI switchers were 36% higher for all causes and 58% higher for depression-related causes. Compared with SNRI non-switchers, costs for SNRI switchers were 27% higher for all causes and 5% higher for depression-related causes. More costly patients are switching from SSRI to SNRI than vice versa. Among SSRI patients switching to SNRI, costs increased with the number of switches. Multivariate analyses confirmed that switching was associated with higher overall and depression-related costs.
CONCLUSIONS: Depressed patients frequently switch antidepressants. Switchers incur significantly higher overall and depression-related costs, and in general, more costly SSRI patients switch antidepressants.
Presented at the Annual Meeting of the Academy of Managed Care Pharmacy, Nashville, TN, October 5-8, 2005.

276. Clinical and financial outcomes of a therapeutic interchange program for erythropoietic growth factors in adult hemodialysis patients. *Rima A.*

Mohammad, Pharm.D., James G. Stevenson, Pharm.D., Bruce A. Mueller, Pharm.D., Burgunda V. Sweet, Pharm.D., Rachel L. Perlman, M.D.; University of Michigan Hospitals and Health Systems, Ann Arbor, MI.

PURPOSE: Data suggesting therapeutic equivalence of darbepoetin and epoetin and the high economic impact that erythropoietic growth factors (EGFs) have on hospital expenses, has led to interest in implementing therapeutic interchange programs. The objectives of this study were to determine the clinical impact on Hgb levels and post-discharge epoetin dose requirements and the economic impact of a darbepoetin for epoetin therapeutic interchange in hospitalized chronic HD patients, compared to an epoetin-only historical control group.
METHODS: A retrospective review was conducted. The control group consisted of chronic HD patients treated before the therapeutic interchange program was implemented and the interchange group included patients after implementation. Approximately 40 HD patients were identified in each group. Parameters collected, spanning the time periods of 2 months before, during, and after hospitalization, include demographics, Hgb levels, EGF dosing, iron therapy, iron studies, nature of HD, diagnosis for hospitalization, hospital length of stay, surgical interventions, and transfusions. Descriptive and parametric statistics were utilized to measure differences between the two groups.
RESULTS: There were no differences between groups in baseline demographics, baseline HD, hospital information, and EGF dose requirements. Hemoglobin levels decreased in both groups but the difference between them was not statistically significant (p=0.07). The total EGF cost before and after hospitalization was similar in both groups. There was a statistically significant difference between groups in the total EGF cost during hospitalization (p<0.05).
CONCLUSIONS: No differences were seen in hemoglobin levels or EGF dose requirements between pre- and post-interchange groups. For the post-interchange group, there was a statistically significant reduction in cost of EGF during hospitalization.

277E. Economic analysis of pegfilgrastim in patients receiving cancer chemotherapy. *Leon E. Cosler, R.Ph., Ph.D.*[1], Adi Eldar-Lissai, MBA, Ph.D.Candidate[2], David A. Dale, MD[3], Jeffrey Crawford, MD[4], Gary H. Lyman, MD, MPH[2]; (1)Albany College of Pharmacy, Albany, NY; (2)University of Rochester School of Medicine and Dentistry, Rochester, NY 14642, Rochester, NY; (3)University of Washington School of Medicine, Seattle, WA; (4)Duke University Medical Center, Durham, NC.

INTRODUCTION: Randomized controlled trials (RCTs) have demonstrated that prophylactic granulocyte colony-stimulating factor (pG-CSF) including filgrastim and pegfilgrastim are capable of reducing the risk of febrile neutropenia (FN) in patients receiving cancer chemotherapy. A meta-analysis of the 14 RCTs of pG-CSF has confirmed significant reductions in FN and infection-related mortality (IRM) along with improved chemotherapy dose intensity.
METHODS: An economic analysis of pegfilgrastim prophylaxis was conducted based on risk and efficacy estimates from the meta-analysis and direct US cost estimates for hospitalization and outpatient care. Expected costs along with estimates of incremental cost savings and cost-effectiveness (CE; $/life saved) were generated. Threshold and sensitivity analyses on all variables and Monte Carlo simulation based on lognormal hospital cost distributions were performed to assess the robustness of the model.
RESULTS: Under baseline conditions, a net cost savings with pegfilgrastim of $578 was estimated. A net cost savings was observed for an FN risk >16.4%, daily cost of hospitalization >$1,282 and a relative risk reduction >72%. Cost savings thresholds are found to decrease further with increasing IRM, longer hospital lengths of stay or cost/day and greater estimated efficacy. In Monte Carlo simulation, lower costs were observed with pegfilgrastim in two-thirds of patients with an average cost savings with pegfilgrastim [± 95% CL] of $600 [-1000, 3600]. Further distribution analysis based on Monte Carlo simulation along with a cost-effectiveness analysis based on the reduction in IRM will be presented.
CONCLUSIONS: Incorporation of risk and efficacy estimates from a recent meta-analysis along with updated cost estimates into clinically relevant models demonstrates that pegfilgrastim reduces overall costs associated with moderately myelosuppressive chemotherapy. Further increases in healthcare costs or the use of validated FN risk models for targeted therapy will further increase the estimated cost savings.
Published in J Clin Oncol 2005;23(16S):538s.

278. A cost-benefit analysis of an outpatient, pharmacy-managed medication assistance program for indigent patients. *Effie L. Gillespie, Pharm.D.*[1], Nickole N. Henyan, Pharm.D.[1], Stephen Sander, Pharm.D.[1], Gregory C. Gousse, R.Ph., M.S., FASHP[2], Craig I. Coleman, Pharm.D.[1]; (1)University of Connecticut School of Pharmacy, Storrs, CT and Hartford Hospital, Hartford CT, Hartford, CT; (2)Hartford Hospital, Hartford CT, Hartford, CT.

PURPOSE: Pharmacy-managed medication assistance programs (MAPs) have the potential to recoup losses incurred by the pharmacy department, but whether this offsets the personnel cost of the program has not been well established. The purpose of this study was to conduct a cost-benefit analysis of our pharmacy-managed MAP.
METHODS: Patients were enrolled into the MAP at our institution by healthcare professional referral. Patients were assisted in identifying pharmaceutical manufacturers' providing free drug and completing applications. The program's benefit was defined as value of drug procured using average wholesale price (AWP) in 2005 US. Costs to the pharmacy consisted of personnel cost (time administering program X wage rate $18.02/hour). Net benefit was calculated as the value of drug procured minus personnel costs. Threshold sensitivity analysis and Monte Carlo simulation were performed by varying drug value, personnel time and wage rate.
RESULTS: Over the 24-month period (May 2003 through April 2005), 143 patients were enrolled into the program with 328 medication shipments received. The total benefit for all drugs was $83,504. An average of 4 hours/week was spent administering the program, resulting in personnel costs of $7,496. The program yielded a net benefit of $76,008. Upon sensitivity analysis, the breakeven point was reached when drug value was reduced to $7,496, personnel time increased to 4,634 hours (44 hours/week) or the wage rate increased to $200/hour. When value of drug procured, personnel time and wage rate were simultaneously varied within plausible ranges derived from the literature ($68,175 to $171,584, 2 hours to 40 hours/week and $13.65 to $43.60/hour, respectively), Monte Carlo simulation demonstrated there was a 96.1% chance of the program being cost-beneficial.
CONCLUSIONS: This study illustrates that our pharmacy-managed, MAP for indigent inpatients was cost-beneficial. Our conclusions were found to be robust to changes in drug value, personnel time and wage rate.

279E. Sedative agents with a rapid recovery profile improve practice efficiency for colonoscopy: results of a Monte Carlo cost simulation model. *John Vargo, MD, MPH*[1], Thomas Bramley, PhD, RPh[2], Kellie Meyer, PharmD, MPH[2], Brian Nightengale, PhD[2]; (1)The Cleveland Clinic Foundation, Cleveland, OH; (2)Applied Health Outcomes, Palm Harbor, FL.

PURPOSE: Sedation with propofol is popular due to its rapid onset of action and recovery profile compared with the traditional combination of an opioid and benzodiazepine for use during endoscopic procedures. There are few data regarding the impact of sedation with rapid-recovery agents on the efficiency of an endoscopy unit.
METHODS: A model was constructed to assess the ability of rapid-recovery agents, (propofol and AQUAVAN® Injection (GPI 15715), an investigational agent that is a water-soluble prodrug of propofol) to increase practice efficiency and determine break-even costs for such agents based on current reimbursement levels for colonoscopy. Reimbursement inputs were obtained from the Centers for Medicare & Medicaid Services (CMS) and reflect facility services, physician services, and operating costs. Costs of sedation agents for colonoscopies completed in hospital outpatient clinics and ambulatory surgical centers (ASCs) were obtained from Red Book. Recovery profiles of the sedation agents were obtained from published literature examining time to discharge. Sensitivity analyses were performed to measure the robustness of model results to changes in base-case inputs. Using a Monte Carlo simulation, inputs were varied simultaneously and randomly for 1,000 iterations to determine a range of cost estimates.
RESULTS: In the time to complete 1 colonoscopy with midazolam/meperidine, 1.76 and 1.91 colonoscopies are completed with propofol and AQUAVAN, respectively. The break-even cost for rapid-recovery agents was $71.53 in a hospital outpatient clinic and $61.48 in an ASC. Monte Carlo simulation indicated the break-even cost of a rapid-recovery agent was most sensitive to operating costs and time to complete colonoscopies.
CONCLUSIONS: Rapid-recovery agents, such as propofol and AQUAVAN, create practice efficiency through earlier discharge, which allows completion of more colonoscopies during a specified time period. Our model suggests that propofol-mediated sedation for colonoscopy can improve practice efficiency in various practice settings. Supported by funding from Guilford Pharmaceuticals Inc.
Presented at the Digestive Disease Week of the American Gastroenterological Association, Chicago, IL, May 14-19, 2005.

280. Incidence and potential economic impact of hyponatremia in hospitalized patients. *John Long, MD, PhD, MBA*, John P. Proach, MS; Triage HealthCom, LLC, Lawrenceville, NJ.

PURPOSE: This study determined the economic impact of hyponatremia in hospitalized patients and evaluated potential opportunities for cost savings.
METHODS: Several data sources were reviewed to obtain claims, admissions, cost, and discharge data from a consortium of 176 hospitals nationwide.
RESULTS: Hyponatremia was found as a secondary diagnosis or coexisting condition in 16,791 cases. The most common DRGs that included a diagnosis of hyponatremia were congestive heart failure (CHF, n=13,778), syndrome of

inappropriate secretion of antidiuretic hormone (SIADH, n=1355), and transurethral resection of the prostate (TURP syndrome, n=193). Hyponatremia was identified in 73% (7398/10,073) of complicated CHF cases and in 25% (6380/25,038) of uncomplicated CHF cases. In a typical hospital with 190 cases of uncomplicated CHF annually, mean cost of an uncomplicated CHF case was $6247, whereas mean reimbursement was $3667, suggesting a $2580 loss per case (total annual loss of $490,200). If complicated CHF cases were also considered, the typical hospital's annual loss was estimated at $2,883,096. Of the estimated 228,400 TURP cases nationwide (based on 11,435 surgeries in the surveyed hospitals), hyponatremia was projected in 2% (4569 cases). Furthermore, up to 4000 cases of SIADH were estimated nationwide. Endocrine disorders such as SIADH cost between $12,305 and $24,745 each and are reimbursed at only $3861 each. New therapies that provide safe and predictable correction of serum sodium levels may mitigate the economic impact of hyponatremia associated with these underlying conditions by reducing the length of stay (LOS), physician attending time, or requirement for frequent laboratory testing. For example, if LOS is reduced by 8 hours, hospital costs for a complicated CHF case may be reduced by $2128.
CONCLUSIONS: The incidence and economic burden of hyponatremia is potentially high among patients with complicated CHF, TURP syndrome, and SIADH. Safe and effective treatment of hyponatremia may help relieve this burden.

281. Trends in the prevalence of community acquired MRSA in a Medicaid population. *Michael Dickson, BS, PhD*[1], Jerry Gibson, MD[2], George Kotchmar, MD[1], Dixie Roberts, BS[2]; (1)University of South Carolina, Columbia, SC; (2)South Carolina Department of Health and Environmental Control, Columbia, SC.

PURPOSE: There is small but growing evidence that MRSA infections, previously limited to hospitals, also are community acquired especially among certain population segments. CA-MRSA has been attributed to a new virulent strain causing outbreaks in community settings and severe invasive disease in people without previous risk factors. The purpose of this study is to analyze trends in the prevalence of CA-MRSA in a Medicaid population.
METHODS: This study used a retrospective cohort study design. South Carolina Medicaid recipients in the first six months of 2001 and 2003 were included if they had a qualifying ambulatory diagnosis (Qdx) for skin abscesses most likely caused by Staphylococcus aureus (ICD9-CM of 680, 681, 682). Healthcare utilization and costs were followed for six months from the first Qdx (index date). Services included ambulatory, hospital, nursing home, and drugs. Pre-index-date data includes 12 months of claims for controlling selection bias and confounding. Subjects were marked CA-MRSA if they had no nursing home or inpatient hospital use in 12 months prior to their index date. We hypothesized that demographics, pre-index date cost of care, chronic disease score, and qualifying category (disabled or not) would be associated with being a CA-MRSA case.
RESULTS: The typical subject in both years was a black female from an urban location. The rate of ambulatory-diagnoses MRSA increased from 1.76% in 2001 to 2.01% in 2003. In 2001, 72.7% of the ambulatory-diagnoses cases of MRSA cases were CA-MRSA with similar results for 2003. The odds of being a CA-MRSA case were 0.993 for age, and 1.303 for being disabled. An OLS regression on log(total cost), post-index-date was significant ($p<0.05$) for age, race, urban location, pre-period cost of care, being disabled, and being CA-MRSA ($R2 = 0.56$).
CONCLUSIONS: CA-MRSA is increasing in the SC Medicaid population, especially among the disabled population.

282. Bleeding criteria discrepancies in the identification of bleeding events in patients receiving glycoprotein (GP) 2b-3a inhibitors for percutaneous coronary intervention (PCI). *Marianne McCollum, Ph.D., R.Ph.*[1], Sallie K. Young, PharmD[2], Kathleen A. Stringer, PharmD[1], Ann K. Wittkowsky, PharmD[3], Sarah A. Spinler, PharmD[4]; (1)University of Colorado School of Pharmacy, Denver, CO; (2)Penn State Milton S. Hershey Medical Center, Hershey, PA; (3)University of Washington, Seattle, WA; (4)Philadelphia College of Pharmacy, University of the Sciences in Philadelphia, Philadelphia, PA.

PURPOSE: Appropriate assessment of hemorrhagic complications associated with anticoagulants is important for making both patient-specific clinical and population-level (e.g., formulary) decisions. Presently, there is no uniformly accepted standard definition for bleeding; clinical trials have used a variety of definitions making it difficult to interpret data across studies. This study evaluated agreement between two sets of criteria for bleeding events associated with GP 2b-3a use in patients undergoing PCI.
METHODS: Medical records of consecutive PCI patients receiving GP 2b-3a inhibitors at two university-affiliated hospitals were reviewed concurrently to document bleeding. Patients with active bleeding disorders were excluded. Bleeding criteria were prospectively defined: Thrombolysis in Myocardial Infarction (TIMI) criteria and investigator criteria (INV). TIMI bleeding was defined as intracranial hemorrhage, drop in hemoglobin (Hgb) of > 5 g/dL from baseline, spontaneous and observed hematuria or hematemesis, or observed blood loss associated with a decrease in Hgb > 3 g/dL or in Hgb ≥ 4 g/dL in the absence of clinical bleeding. INV bleeding was defined as intracranial, retroperitoneal, intraocular or clinically overt bleeding associated with a decrease in Hgb ≥ 3 g/dL from baseline or any clinically overt bleeding (e.g., groin oozing/hematoma). The degree of agreement between TIMI and INV criteria was assessed using the kappa statistic.
RESULTS: Records from 423 post-PCI patients were reviewed; 229 patients experienced a bleed by INV criteria, 23 patients met the TIMI criteria for bleeding. The kappa statistic was 0.09, indicating poor agreement between the TIMI and INV criteria.
CONCLUSIONS: Use of GP 2b-3a inhibitors in PCI procedures was associated with 10 times as many bleeding events when defined by INV criteria. Use of TIMI versus INV criteria to assess bleeding could potentially underestimate clinically significant bleeding and adversely affect conclusions from clinical trials and economic evaluations estimating the impact of bleeding in patients undergoing PCI.

283E. Cost-effectiveness of intensive statin therapy in patients with acute coronary syndrome. *Tracy Mayne, Ph.D.*[1], Michael Koren, MD[2], Sanford Schwartz, MD[3], Michael Drummond, Ph.D.[4]; (1)Pfizer Pharmaceuticals, New York, NY; (2)Jacksonville Center for Clinical Research, Jacksonville, IN; (3)University of Pennsylvania, Merion Stn, PR; (4)University of York, York, United Kingdom.

PURPOSE: The objective of this study was to assess the cost-effectiveness of intensive therapy in patients hospitalized with acute coronary syndrome (ACS).
METHODS: We performed incremental cost-effectiveness analyses for various economic endpoints using data from PROVE-IT, the first head-to-head outcomes RCT comparing a moderately intensive statin therapy regimen versus an intensive statin therapy regimen in subjects presenting with ACS. Wholesale acquisition cost (WAC) was used to estimate the cost of statin medication. The costs of cardiovascular hospitalizations were estimated using average U.S hospital costs (Radensky et al., 2001, updated to 2004 using the CPI medical care component inflator). Medicare payments were used to estimate costs of physician services for cardiovascular procedures, ER and outpatient visits and for the costs of skilled nursing facility care. Analyses of various likely scenarios were performed.
RESULTS: Compared with moderate LDL–C lowering statin therapy, intensive LDL–C lowering statin therapy was associated with reduced cardiovascular hospitalizations and related physician services and corresponding cost savings. Using PROVE-IT event rates, intensive therapy saved $5,404,229 over the course of the two year mean study follow–up period:

Scenario Comparison	Moderate Rx	Intensive Rx	Difference Trial based
	$34,637,250	$29,233,021	-$5,404,229
Managed care	$32,931,008	$29,233,021	-$3,697,987
Generic moderate	$32,057,079	$29,233,021	-$2,824,058
Free moderate	$31,224,766	$29,233,021	-$1,991,745

Thus, intense LDL–C lowering statin therapy was both more clinically effective and less expensive than moderate LDL–C lowering.

CONCLUSIONS: As observed in PROVE-IT, the clinical benefits of intensive LDL–C lowering statin treatment compared to a moderate statin regimen in ACS patients resulted in both fewer clinical outcomes and lower overall health care expenditures considering either branded or generic drug prices and thus is both clinically and cost-effective.
Presented at the 54th Annual Scientific Session of the American College of Cardiology, Orlando, FL, March 6-9, 2005.

284. Cost analysis of patients with acute heart failure (HF): characteristics and outcomes of high vs. low cost groups. *Joseph Dasta, MSc*[1], Tien M. Ng, PharmD[2], Amy Durtschi, PhD[3], David Feldman, MD, PhD[4], Trent McLaughlin, PhD[5]; (1)College of Pharmacy, The Ohio State University, Columbus, OH; (2)University of Southern California, Los Angeles, CA; (3)Abbott Laboratories, Chicago, IL; (4)College of Medicine, The Ohio State University, Columbus, OH; (5)NDCHealth, Phoenix, AZ.

PURPOSE: The purpose of this study is to compare the patient characteristics and outcomes associated with varying degrees of costs in treating patients with acute HF.
METHODS: All inpatient admissions in 2003 from NDCHealth's Hospital Patient Level database of 350 geographically diverse hospitals were reviewed for a primary discharge diagnosis of HF (ICD-9-CM: 428.xx). Admissions were stratified into quartiles based on total hospital costs. Parenteral drugs used (inotrope: dobutamine, dopamine, milrinone, IV nitroglycerin, nesiritide, IV furosemide), clinical outcomes and costs of these groups were compared using chi-square or ANOVA.
RESULTS: Of the 2,515,872 inpatient admissions during 2003, 131,057 (5.2%) had a primary discharge diagnosis of HF. Table 1. Information on the four cohorts

	Quartile I	Quartile II	Quartile III	Quartile IV
N	32,717	32,792	32,815	32,733
Mean Cost	$37,992	$10689	$5913	$3026
Mean Age, years	72	72	73	72
IV Inotropes, %	20.3	10.4	6.6	3.6
IV Nitroglycerin, %	7.9	5.5	4.7	2.9
IV Furosemide, %	81.8	83.2	83.9	80.0
Nesiritide, %	11.8	8.5	6.1	3.0
Admitted to ICU/CCU, %	50.7	40.3	29.9	21.3
Mechanical Ventilation (MV), %	10.2	3.3	1.3	0.5
Admitted via ED, %	72.0	76.9	76.3	69.8
Mean Total LOS, days	11.2	6.1	4.9	3.4
Mortality Rate	6.8	3.6	2.9	4.1

All items are statistically significant (P<0.05) ED = Emergency Department, LOS = length of stay Cost = charge x cost to charge ratio

CONCLUSIONS: Costs of treating patients with acute HF rise in relation to prolonged LOS, and care requiring ICU admission, MV, IV vasodilators, and IV inotropes. Additional therapeutic interventions are needed to improve cost-effective care and patient outcomes.

285. A large administrative hospital database for health outcomes research: sedative use in the real-world setting. *AnneMarie Sesti, PharmD*[1], Judi Jacobi, PharmD, FCCP, BC[2], Trent McLaughlin, PhD[3], Joseph Dasta, MSc[4]; (1)NDCHealth, Deerfield, IL; (2)Methodist Hospital/Clarian Health, Indianapolis, IN; (3)NDCHealth, Phoenix, AZ; (4)College of Pharmacy, The Ohio State University, Columbus, OH.

PURPOSE: It is important to evaluate drug use in naturalistic settings particularly with newly released drugs. This project describes hospital-based database research evaluating charges and outcomes of sedatives.
METHODS: NDCHealth's 350 geographically-diverse hospital database was used. The data are from billing claims and charge masters of ~3 million inpatient admissions annually providing itemized usage and charge data. A two-phase analysis was conducted from 7/03-6/04 for intravenous sedatives–dexmedetomidine (Dex), diazepam (D), lorazepam (L), midazolam (M) and propofol (P). Phase I: description of demographics and individual sedative usage. Phase II: comparison of combination sedative characteristics; cardiac surgeries represented the largest cohort where Dex was used [ICD-9 35.xx (valves) and 36.xx (bypass)]. Primary outcomes were LOS, charges and mortality analyzed with univariate statistics.
RESULTS:

Phase 1–Descriptive Results (Individual Medications)

	Dexmedetomidine	Diazepam	Lorazepam	Midazolam	Propofol
Drug Administrations	7,774	349,328	1,900,709	1,621,800	1,149,352
Patient Admissions	2,944	108,703	322,731	952,712	615,330
Male	64%	51%	51%	48%	50%
Mean LOS (days)	2.6	3.2	5.9	1.7	1.9
Primary ICD-9 Medical-Surgical Categories	Cardiac	Cardiac	Misc.	GI	Ortho
Mean Patient Charges ($)	121,983	53,268	63,144	44,665	48,438

There was variability in the demographics and outcomes across the drug groups. Dex was rarely used alone (5% of patients) whereas the most common drug combination in the cardiac segment was M + P (32%).

Phase 2–Comparative Results In Cardiac Surgery Patients Receiving Sedative Combinations

		M+P	M+P+Dex
Patient Admissions	N	9,996	356
LOS–Days**	Mean (SD)	9.4 (6.6)	8.8 (6.7)
Patient Charges*	Mean (SD)	$106,468 ($85,033)	$88,678 ($55,932)
Mortality*	N (%)	311 (3%)	3 (1%)

Univariate Statistics–*p<0.05, **p<0.0001

CONCLUSIONS: Outcomes research analyses are feasible with an inpatient claims database and can reveal outcome differences that require further investigation.

Pharmacoepidemiology

286. Patent ductus arteriosus prevention in very low birth weight neonates: using a cumulative meta-analysis to build a practice guideline and clinical pathway. *Tuan T. Dinh, MSc, RPh*, Carla K. Findlater, PharmD; Perinatology Program, Dept. of Newborn and Developmental Paediatrics, Sunnybrook and Women's College Health Sciences Centre, Toronto, ON, Canada.

PURPOSE: Controversy exists regarding prophylactic indomethacin's (PI) utility in preterm neonates, based on non-significant results from an adequately-powered, randomized controlled trial (RCT) primarily examining neurodevelopmental benefit (TIPP, N= 1202). Consequently, some neonatal intensive care units (NICU) have abandoned routine PI. However, other benefits may still be obtained for non-neurological outcomes. We performed a cumulative meta-analysis to validate continued PI usage in our NICU and to generate a practice guideline and clinical pathway.
METHODS: Cumulative Meta-Analysis and Guideline Sixty articles were screened using the MEDLINE MeSH terms: Patent Ductus Arteriosus (PDA), RCT, Newborn. Sixteen studies (N=2545) were selected (kappa =1.0) meeting the inclusion criteria : RCT , indomethacin at < 24hr age, methodological quality score > 5/10 . Primary outcomes were: PDA, mortality, ligation, renal failure (RF), necrotising enterocolitis (NEC). Cumulative meta-analysis was performed using the random effects model. Subgroup analysis was performed on different dosing regimens. Guideline recommendations were generated.
CLINICAL PATHWAY Guideline quality assurance was completed from June-September 2002 (195 admitted infants). Forty-one eligible neonates were monitored until discharge. Reasons for guideline deviations were obtained from prescribers through a questionnaire.
RESULTS: Cumulative meta-analysis of PI historically exhibited significant relative risk (RR) reductions in PDA and surgical ligation rates of 73 % and 60% by 1985 and 1999 respectively. No other outcomes showed benefit from PI. RF revealed a RR increase of 56% by 1988 . Increased NEC risk was never demonstrated. Subgroup analysis suggested that prolonged, low dose regimens were optimal. Initiation of a PI guideline for neonates < 27 wk achieved a 35% implementation rate. The questionnaire response rate was 38%. Ninety-six percent of reasons for guideline non-acceptance were clinical judgement-related rather than bias towards the neurodevelopmental evidence. However, 69% of respondents stated confusion regarding continued PI use and requested further information.
CONCLUSIONS : Further prescriber education regarding PI utility is needed.

287. Geographic variation in the prescription of mood-stabilizers and atypical antipsychotics for treatment of bipolar spectrum disorder by U.S. physicians. *Larry W. Segars, Pharm.D., BCPS*, Anthony Rene, Ph.D., M.P.H.; University of North Texas Health Science Center-School of Public Health, Fort Worth, TX.

PURPOSE: To assess potential geographic variation in use of mood-stabilizers and atypical antipsychotics for treatment of bipolar spectrum disorder by U.S. physicians.
METHODS: This study utilized the Centers for Disease Control & Prevention's 2002 multi-stage National Ambulatory Medical Care Survey (NAMCS). U.S. office visits associated with bipolar spectrum disorder were identified from the dataset using DSM-IV diagnosis codes. Medications typically associated with the title mood stabilizer and all available atypical antipsychotic treatments were captured by use of the FDA drug classification code for both trade and generic names. The dependent variable was use of one of these medications to treat bipolar spectrum disorder with independent variables assessed, via univariate and multivariate analyses, including region of country, age group, gender, ethnicity, race, physician specialty, and payment type.
RESULTS: The 2002 NAMCS randomly sampled a weighted national estimate of 889,980,491 U.S. physician office visits. A weighted estimate of 1,201,673 office visits were associated with a diagnosis of bipolar spectrum disorder. No regional variation in the prescription of either the mood stabilizers or atypical antipsychotics was found. Additionally, no statistically significant associations were found in any univariate or multi-variable analyses of each of the independent variables and two dependent variables. Furthermore, there was no difference in the prescription of either of these two groups of medications by age group, sex, race, ethnicity, and pay type or by prescriber specialty. Finally, no confounding or effect modification was discovered between any of the variables.
CONCLUSION: Although geographic variation has been demonstrated in the use of various psychiatric medications for other psychiatric illnesses, this study demonstrated via use of the 2002 NAMCS dataset that there is no statistically significant regional variation in the prescription of either the mood stabilizers or the atypical antipsychotics for the treatment of the bipolar spectrum disorders.

288. Comparing models for estimating anticholinergic burden from medications using serum anticholinergic activity as the gold standard. *Ryan M. Carnahan, Pharm.D., M.S.*[1], Brian C. Lund, Pharm.D., M.S.[2], Paul J. Perry, Ph.D.[3], Kennith R. Culp, Ph.D.[4], Bruce G. Pollock, MD, PhD[5]; (1)University of Oklahoma College of Pharmacy, Tulsa, OK; (2)Laureate Psychiatric Research Center, Tulsa, OK; (3)University of Iowa Colleges of Pharmacy and Medicine, Iowa City, IA; (4)University of Iowa College of Nursing, Iowa City, IA; (5)University of Pittsburgh, Pittsburgh, PA.

BACKGROUND: A validated tool for measuring anticholinergic drug burden would be tremendously useful in both research and clinical practice. For many epidemiologic and clinical applications, a scale based solely on a patient's drug regimen, without relying on any direct physiological measures, would be particularly useful. One such scale, the Anticholinergic Drug Scale (ADS), was found to be significantly associated with serum anticholinergic activity (SAA) in a sample of 96 subjects. However, improvements in the scale need to be explored.

METHODS: Subjects included 300 nursing home residents participating in a cross-sectional study of delirium. Medications taken within one day prior to the blood draw for measurement of SAA were rated for anticholinergic properties using the ADS. Linear regression was used to determine the best model for predicting SAA. The ADS has traditionally assigned each drug a weighted score of 0-3, corresponding to no known, potential, clinically significant and marked anticholinergic activity. In order to improve on this arbitrary weighting strategy, the first modification was to empirically derive weights using regression parameter estimates. The second modification was to adjust for dose, where total daily doses were weighted from 1-4 based upon the proportion of the maximum recommended daily dose received and factored into the total score.
RESULTS: Though scores in all models were significantly associated with SAA, the model using the empirically derived estimates explained the most variance (r-square = 0.0926, t=5.51, p<0.0001). This model suggested a weighting strategy of 0, 1, 3, 4 as an improvement over the original 0, 1, 2, 3 strategy.
CONCLUSION: Future studies utilizing the ADS should examine both the traditional and empirically derived scoring methods to help determine most valid method. Much of the variance in SAA remains unexplained by ADS scores.

289. Prevalence of cardiovascular risk factors among people with and without diabetes and CHD. *Marianne McCollum, R.Ph., Ph.D., BCPS*, Samuel L. Ellis, PharmD, Elaine H. Morrato, MPH, Vahram Ghushchyan, MA, Patrick W. Sullivan, PhD; University of Colorado School of Pharmacy, Denver, CO.

PURPOSE: The National Cholesterol Education Program, Adult Treatment Panel III (NCEP ATP III) included diabetes mellitus (DM) as a risk factor (RF) for major coronary events equivalent to existing coronary heart disease (CHD). The purpose of this study is to determine the prevalence of additional CHD RFs for people with and without DM and CHD.
METHODS: Nationally representative 2000 and 2002 Medical Expenditure Panel Survey (MEPS) data for respondents 18 years or older were used. MEPS, sponsored by the Agency for Healthcare Research and Quality, yields results representative of adults in the general population. DM and CHD were determined by ICD-9-CM codes or self-reported DM, CHD, angina, heart attack, stroke, or other heart disease. Six additional RFs assessed were hypertension, high cholesterol, smoking, age ≥45 years (men), ≥55 years (women), obesity and physical inactivity in four subgroups: CHD-, DM-; CHD-, DM+; CHD+, DM-, CHD+, DM+.
RESULTS: The CHD-, DM+ group had significantly higher mean RF counts than did the CHD-, DM- group and the CHD+, DM- group (2.6 versus 1.4 and 2.4, respectively; both p<0.01). The CHD+, DM+ group had the highest mean RF count at 3.4. Proportions of each subgroup with >2 RFs were: CHD-, DM-: 39.5%; CHD-, DM+: 81.9%; CHD+, DM-: 74.9%; CHD+, DM+: 95.1%.

	CHD–	CHD+
DM–	1.4	2.4
DM+	2.6	3.4

Mean Risk Factor Count

CONCLUSIONS: The presence of diabetes, with or without existing CHD, is associated with a high prevalence of multiple cardiac RFs in the general population, putting people with diabetes at higher risk for major coronary events. The prevalence of cardiac risk factors reported demonstrates the extensiveness of this public health issue. It is important that clinical pharmacists practicing in diabetes care clinics treat modifiable risk factors in patients with diabetes aggressively with lifestyle modifications and pharmacotherapy consistent with NCEP ATP III recommendations.

290E. Comparison of patients with primary vs secondary heart failure from a database of 2.5 million hospital admissions: implications for patient diagnosis, treatment, and reimbursement policies. *Joseph F. Dasta, MSc*[1], David Feldman, MD[2], Amy Durtschi, PhD[3], Trent McLaughlin, PhD[4], Robert Padley, MD[3]; (1)College of Pharmacy, The Ohio State University, Columbus, OH; (2)College of Medicine, The Ohio State University, Columbus, OH; (3)Abbott Laboratories, Chicago, IL; (4)NDCHealth, Phoenix, AZ.

INTRODUCTION: There is no coding algorithm to distinguish primary (PCHF) versus secondary (SCHF) discharge diagnoses of congestive heart failure (CHF). We compared characteristics and outcomes of patients hospitalized with PCHF vs. SCHF discharge diagnoses to evaluate the differences between these categories.
METHODS: All admissions in 2003 from 350 hospitals were reviewed for a CHF diagnosis. Data were compared using chi-square or *t*-tests, where appropriate. Level of significance was 0.05.
RESULTS: Of the 2,515,872 admissions during 2003, 498,713 (19.8%) had a primary or secondary diagnosis of CHF. Surprisingly, 73.7% of these admissions had SCHF. These patients were more likely to be transferred from other facilities (10.0% vs. 4.4%*), discharged to a skilled nursing facility (17.6% vs. 11.1%), and have a higher in-hospital mortality rate (8.0% vs. 4.3%*), than primary CHF patients. The PCHF admissions had more patients over 75 years (54.5% vs. 50.6%*), males (46.7% vs. 43.8%*), emergency department admissions (73.7% vs. 63.1%*), and discharges to home vs. other locales (10.0% vs. 4.4%*). Differences in length of stay were also observed (PCHF 6.4 + 16.0) vs SCHF 9.5 + 31.8) days consistent with total hospital costs which were significantly higher in SCHF patients; $20,084 ± 36,191vs $14,395 ± 28,622. The use of IV furosemide (82.2% vs. 65.7%*) and nesiritide (7.4% vs. 1.9%*) were significantly higher in PCHF admissions. However, usage of inotropes (PCHF: 10.2% vs. 9.7% for SCHF) and vasodilators (5.2% vs. 5.6%) were not significantly different.
CONCLUSIONS: Most heart failure patients are admitted with CHF as a secondary diagnosis. These patients tend to incur higher cost, have longer length of stay, and have higher mortality rates than those with a primary CHF diagnosis. These data have patient care, policy, and reimbursement implications regarding assessment of risk for CHF at admission and diagnosis assignment at discharge.
Published in Circulation 2005;111:e345.

Pharmacogenomics

291. Association of the CYP1B1*3 allele with survival in patients with prostate cancer receiving docetaxel. *Tristan M. Sissung, M.S.*[1], Romano Danesi, PhD[2], Douglas K. Price, PhD[3], Seth M. Steinberg, PhD[4], Ronald De Wit, M.D., PhD[5], Michael C. Cox, PharmD[1], William Dahut, MD[6], William Figg Sr., PharmD[1], Alex Sparreboom, PhD[1]; (1)Clinical Pharmacology Research Core, Medical Oncology Clinical Research Unit, National Cancer Institute, Bethesda, MD; (2)Department of Oncology, Transplants and Advanced Technologies in Medicine, University of Pisa, Pisa, Italy; (3)Clinical Pharmacology Research Core, Cancer Therapeutics Branch, National Cancer Institute, Bethesda, MD; (4)Clinical Pharmacology Research Core, Biostatistics and Data Management Section, National Cancer Institute, Bethesda, MD; (5)Erasmus Medical Center–Daniel den Hoed Cancer Center, Rotterdam, Netherlands; (6)Clinical Pharmacology Research Core, Cancer Therapeutics Branch, National Cancer Institute, Bethesda, MD.

Docetaxel is a microtubule stabilizing agent that has been approved for use in the treatment of several human malignancies. There is evidence from preclinical studies that the cellular response to docetaxel is indirectly linked to expression of the enzyme cytochrome P450 1B1 (CYP1B1). We hypothesized that certain polymorphic variants in the CYP1B1 gene that increase protein expression and/or catalytic efficiency could affect the clinical efficacy of docetaxel treatment. To this end, we conducted CYP1B1 genotyping studies in 25 men with prostate cancer receiving docetaxel as a single-agent. Our results show that patients who are wild type or heterozygous for the CYP1B1 4326C>G variant (L432V; CYP1B1*3) have a significantly longer overall survival as compared to patients homozygous for the CYP1B1*3 allele (15.7 vs 7.3 months; P = .012). We have also found that the systemic clearance of docetaxel is unaltered by CYP1B1 genotype status (P = .39), indicating that effects of CYP1B1*3 on clinical response are not related to altered systemic metabolism of docetaxel by CYP1B1. This pilot study provides evidence that CYP1B1*3 may be a potentially important genetic marker for estimating overall survival in patients with prostate cancer treated with docetaxel and warrants independent verification. This link is likely associated with CYP1B1*3 genotype-dependent estrogen metabolism, as the catechol estrogens and their subsequent metabolites are known to bind tubulin and thereby may interfere with the primary mechanism of action of docetaxel.

292. Genetic variation in endothelial nitric oxide synthase (NOS3) and risk of coronary heart disease in Caucasians: an atherosclerosis risk in communities (ARIC) study. *Craig R. Lee, Pharm.D.*[1], Kari E. North, Ph.D.[1], Molly S. Bray, Ph.D.[2], Christy L. Avery, B.S.[1], M. J. Mosher, Ph.D.[1], David J. Couper, Ph.D.[1], Gerardo Heiss, M.D., Ph.D.[1], Darryl C. Zeldin, M.D.[3]; (1)UNC-Chapel Hill, Chapel Hill, NC; (2)Baylor University, Houston, TX; (3)National Institute of Environmental Health Sciences, Research Triangle Park, NC.

PURPOSE: We previously reported that cigarette smoking modified the association between the *E298D* polymorphism in *NOS3* and coronary heart disease (CHD) risk in the ARIC study. Using a larger sample size, we sought to complete a more comprehensive analysis characterizing potential associations between genetic variation in *NOS3*, smoking history and risk of CHD events.
METHODS: Using a case-cohort design, 2065 (70% Caucasian) participants of the biethnic, multicenter ARIC study (all 1085 incident CHD cases occurring from 1987-98; 980 noncases from a cohort representative sample) were genotyped for the reduced function *E298D* and *T-786C NOS3* polymorphisms. Multiplicative scale interaction testing evaluated the influence of baseline smoking status (yes/no) and history (≥/<20 pack-years) on associations between genotype and CHD risk by multivariable proportional hazards regression. All analyses were race-stratified.

RESULTS: In Caucasians, the *D298* allele was present in 53.3% and 52.8% of CHD cases and noncases, respectively (p=0.862). Association between the *E298D* polymorphism and CHD risk was significantly modified by baseline smoking status [adjusted hazard rate ratio (aHRR) (95% CI)]: *E/E* nonsmoker, 1 (referent); *E/E* smoker, 1.19 (0.77-1.83); *E/D* or *D/D* nonsmoker, 0.83 (0.61-1.13); *E/D* or *D/D* smoker, 2.07 (1.39-3.07) (interaction p=0.013). The *C-786* allele was present in 62.7% and 57.7% of CHD cases and noncases, respectively (p=0.079). Significantly increased CHD risk was observed in ≥20 pack-year smokers with the *C-786* allele relative to ≥20 pack-year smokers carrying two *T-786* alleles (aHRR 1.52, 95% CI 1.01-2.27, p=0.042). Moreover, ≥20 pack-year smokers with the phase reconstructed haplotype containing both the *C-786* and *D298* alleles demonstrated increased CHD risk relative to ≥20 pack-year smokers without the haplotype (aHRR 1.62, 95% CI 1.11-2.37, p=0.013). Similar analysis demonstrated no significant associations in African-Americans.
CONCLUSIONS: A complex interplay between genetic variation in *NOS3*, smoking history and CHD risk appears to exist in Caucasians. Future evaluation is warranted.

293. Genetic variation in cyclooxygenase-1 (PTGS1) and risk of ischemic stroke: an atherosclerosis risk in communities (ARIC) study. *Craig R. Lee, Pharm.D.*[1], Kari E. North, Ph.D.[1], Molly S. Bray, Ph.D.[2], David J. Couper, Ph.D.[1], Gerardo Heiss, M.D., Ph.D.[1], Darryl C. Zeldin, M.D.[3]; (1)UNC-Chapel Hill, Chapel Hill, NC; (2)Baylor University, Houston, TX; (3)National Institute of Environmental Health Sciences, Research Triangle Park, NC.

PURPOSE: Cyclooxygenase-1 activity significantly contributes to endothelial and platelet function, and may be important in ischemic stroke risk. We sought to determine if genetic variation in *PTGS1* was associated with ischemic stroke risk.
METHODS: Using a case-cohort design, 1336 participants (69% Caucasian) of the biethnic, multicenter ARIC study (all 300 incident ischemic stroke cases occurring from 1987-98; 1036 noncases from a cohort representative sample) were genotyped for eight polymorphisms in *PTGS1*. Genotype frequencies were compared across case status by chi-square. Associations between genotype and risk of incident stroke events were evaluated by proportional hazards regression with covariate adjustment. All analyses were race-stratified.
RESULTS: In Caucasians, the *A-1006* allele in the *PTGS1* proximal promoter was significantly more common in stroke cases versus noncases (18.2% versus 10.9%, p=0.013). After adjusting for age, gender, and study center, the *A-1006* allele was associated with significantly increased risk of incident stroke relative to *G-1006* homozygotes (adjusted hazard rate ratio (aHRR) 1.77, 95% CI 1.07-2.92, p=0.027). A similar association was observed when also adjusting for diabetes, hypertension, and smoking status (aHRR 1.69, 95% CI 0.98-2.92, p=0.058), although this did not attain statistical significance. Due to its pharmacological effect, baseline aspirin use was hypothesized to be a potential effect modifier of this association. Although aspirin use was associated with a significantly lower stroke risk in Caucasians (aHRR 0.51, 95% CI 0.31-0.84, p=0.008), it did not significantly modify the associations described with the *G-1006A* polymorphism. In African-Americans, the rare *S230* allele in exon 7 was present in 2.6% and 1.0% of stroke cases and noncases, respectively (p=0.197), and was associated with increased stroke risk relative to *G230* homozygotes (aHRR 13.1 95% CI 1.77-97.5, p=0.012).
CONCLUSIONS: An association between genetic variation in *PTGS1* and ischemic stroke risk appears to exist. Future confirmatory studies in larger populations are warranted.

294. Leptin and leptin receptor gene polymorphisms and increases in body mass index (BMI) from olanzapine treatment in persons with schizophrenia. *Vicki L. Ellingrod, Pharm.D., BCPP*, Jeffrey R. Bishop, Pharm.D., Jessica Moline, B.S., Del D. Miller, Pharm.D., M.D.; University of Iowa College of Pharmacy, Iowa City, IA.

PURPOSE: The objective of the current investigation was to determine the relationship between polymorphisms of the leptin system (leptin gene and leptin receptor) and olanzapine-induced weight gain in persons with schizophrenia.
METHODS: Thirty-seven subjects who were part of an open label, six week, fixed dose trial of olanzapine response and adverse effects were assessed for weight gain at baseline and study completion. These subjects were subsequently genotyped for the -1548 G/A polymorphism of the leptin gene and the Q223R polymorphism of the leptin receptor. The relationship between alleles at each locus, allele-olanzapine blood level interactions, and percent change in body mass index (BMI) from baseline were conducted.
RESULTS: Genotypes and alleles for each locus were not individually associated with olanzapine-induced weight gain in this study population. Changes in BMI from baseline increased significantly as olanzapine blood levels increased in persons carrying at least one G allele at both candidate loci compared to those who did not have a G allele at each (interaction term p=0.04). For persons with this allelic combination, there was a significant linear relationship between olanzapine blood levels and percent change in BMI after six weeks of treatment (p=0.0098). After controlling for baseline BMI and age, the relationship between percent change in BMI and olanzapine blood levels was still significant (p=0.0029) in persons with at least one G allele at each locus.
CONCLUSIONS: This study suggests that genetic variability in the leptin gene and leptin receptor may predispose some individuals to excessive weight gain from increased exposure to olanzapine. Confirmation of these results may allow us to institute gene-guided monitoring parameters in persons treated with olanzapine to avoid or minimize weight-related morbidity.

295. Association of genetic variants in ABCB1 **and** CYP3A4/5 **with the pharmacokinetics of erlotinib.** *Charity D. Scripture, Pharm.D., M.S.*[1], Tristan M. Sissung, M.S.[1], Matthew G. Permenter, B.S.[2], Douglas K. Price, Ph.D.[2], Sandra M. Swain, M.D.[3], Alex Sparreboom, Ph.D.[1], William D. Figg, PharmD[1]; (1)Clinical Pharmacology Research Core, Center for Cancer Research, National Cancer Institute, Bethesda, MD; (2)Molecular Pharmacology Section, Center for Cancer Research, National Cancer Institute, Bethesda, MD; (3)Cancer Therapeutics Branch, Center for Cancer Research, National Cancer Institute, Bethesda, MD.

PURPOSE: Erlotinib is an orally available, small molecule inhibitor of epidermal growth factor receptor (EGFR) tyrosine kinase. Wide interpatient variability in the pharmacokinetics (PK) of erlotinib has been reported. Cytochrome P450 3A is involved in the metabolism of erlotinib. Extensive overlap has been observed between CYP3A substrates and P-glycoprotein (encoded for by *ABCB1*). Variants in the *CYP3A* and *ABCB1* genes have been described with altered functionality in vitro. The aim of this study was to retrospectively evaluate the functional consequence of select *CYP3A4*, *CYP3A5*, and *ABCB1* variants on erlotinib PK in 13 female patients with metastatic breast cancer.
METHODS: Patients were treated with erlotinib at a dose of 150 mg/day and PK analysis was performed as described by Tan et al. (JCO 2004; 22:3080). All patients were genotyped by direct nucleotide sequencing for a single-nucleotide polymorphisms (SNPs) in *ABCB1* in exon 21 (2677G>A/T; Ala893Ser or Thr; *ABCB1**7), which is associated with altered PK of the orally administered, P-glycoprotein substrate fexofenadine. In addition, the most common SNPs in both *CYP3A4* (-392A>G; *CYP3A4*1B*) and *CYP3A5* (22893G>A; *CYP3A5*3C*) were examined.
RESULTS: There were 3 carriers of the *CYP3A4*1B* allele. Twelve of the patients were carriers of the *CYP3A5*3C* allele, 10 were homozygous variant. Twelve patients were carriers of the *ABCB1*7* allele, 3 of which were homozygous variant. None of the tested variants were associated with a significant difference in the area under the plasma-concentration time curve (AUC) of erlotinib (*ABCB1*7*, p=0.77; *CYP3A4*1B*, p=0.46; *CYP3A5*3C*; p=0.63).
CONCLUSIONS: It is concluded that functional variants in the *CYP3A4/5* and *ABCB1* genes are not significantly associated with the AUC of erlotinib in this study. Additional genetic variants or haplotypes of importance to erlotinib pharmacokinetics may yet be discovered. However, given the limited sample size, evaluation in a larger patient population is necessary to confirm these findings.

296E. Genetic predisposition to oral absorption of imatinib: correlation of a variant allele in ABCG2 with transport activity. *Erin R. Lepper, MChem*[1], Allan T. Van Oosterom, MD, PhD[2], Ernst A. de Bruijn, PhD[2], William D. Figg, PharmD[3], Jaap Verweij, MD, PhD[4], Alex Sparreboom, PhD[3], Kees Nooter, PhD[4]; (1)SAIC-Frederick, Inc., Bethesda, MD; (2)Catholic University of Leuven, Leuven, Belgium; (3)Clinical Pharmacology Research Core, Center for Cancer Research, National Cancer Institute, Bethesda, MD; (4)Erasmus University Medical Center, Rotterdam, Netherlands.

BACKGROUND: Imatinib mesylate (Gleevec, STI-571), an inhibitor for Bcr-abl tyrosine kinase, is currently being used in the treatment of chronic myeloid leukemia and gastrointestinal stromal cell tumors. Interindividual pharmacokinetic variability of imatinib in humans is very substantial, but currently unexplained. Imatinib has recently been shown to be a substrate for ABCG2, a transporter protein that is highly expressed in the intestines and liver, suggesting a major role in drug disposition. A single nucleotide polymorphism (SNP) has been identified in the *ABCG2* gene resulting in a non-synonymous mutation (421C>A; Q141K) that causes impaired ability to transport substrates in vitro. We sought to determine whether patients possessing the mutation would have higher exposure to imatinib.
METHODS: Patients were treated with oral imatinib at a dose of 100-1000 mg/day. At steady-state, a series of blood samples were drawn to provide a full pharmacokinetic profile over one dosing interval. Imatinib concentrations in plasma were determined by LC/MS/MS. Pharmacokinetic parameters were calculated by non-compartmental analysis using WinNonlin, and were normalized to total drug dose. Genotyping was carried out using direct sequencing.

RESULTS: Of 36 white cancer patients evaluated (23 males, 13 females; median age, 59 years), 32 were wild-type and four were heterozygous for the ABCG2 421C>A SNP (allele frequency, 0.056). Systemic exposure to imatinib, assessed using the area under the curve, was approximately 3-fold higher in patients that were heterozygous for the tested SNP compared to patients with the wild-type sequence [mean (± SE), 391 ± 255 versus 136 ± 17.9 ng.h/mL; P = 0.011, *t*-test].
CONCLUSIONS: This pilot study indicates a genetic predisposition to the oral absorption of imatinib, suggesting that patients with decreased ABCG2 activity due to *ABCG2* 421C>A may be at an increased risk for imatinib-induced toxicity. This observation warrants confirmation in a larger patient population involving different ethnic groups.
Presented at the Annual Meeting of the American Society of Clinical Oncology, Orlando, FL, May 13-17, 2005.

297E. Association between the polymorphic GRM3 gene and negative symptom improvement during olanzapine treatment. *Jeffrey R. Bishop, Pharm.D.*, Vicki L. Ellingrod, Pharm.D., Jessica Moline, B.S., Del D. Miller, Pharm.D., M.D.; University of Iowa College of Pharmacy, Iowa City, IA.

PURPOSE: The excitatory neurotransmitter glutamate has become an important area of focus for schizophrenia researchers. Polymorphisms in the type-three metabotropic glutamate receptor gene (GRM3) have been associated with the pathogenesis of schizophrenia. The purpose of this study was to determine whether a pharmacogenetic relationship exists between six polymorphisms of GRM3 and clinical improvement during olanzapine treatment in persons with schizophrenia.
METHODS: Forty-two subjects meeting DSM-IV criteria for schizophrenia started olanzapine and were titrated to a fixed dose of 7.5-20 mg/day for 6 weeks. The Brief Psychiatric Rating Scale (BPRS) total score and the Scale for Assessment of Negative Symptoms (SANS) were completed at baseline and then weekly to assess psychopathology. Six polymorphisms in the type-three metabotropic glutamate receptor were assessed for their relationship to percent change in BPRS and SANS scores from baseline.
RESULTS: The principle finding of this study is that GRM3 polymorphisms were collectively significant predictors of negative symptom improvement in persons with schizophrenia treated with the atypical antipsychotic olanzapine. After controlling for baseline SANS scores, the genotypes as a whole were significant predictors of negative symptom improvement, accounting for approximately 28% of the variance in scores (F=16.30, df=29, p<0.001). The single nucleotide polymorphism SNP1 (rs274622), located in a conserved regulatory region of the GRM3 promoter, had the most significant influence on SANS scores, but the effects of this locus could not be fully separated from the other polymorphisms. The mean decrease in SANS scores was 21% vs. 51% for SNP1 T/T+T/C and SNP1C/C subjects, respectively.
CONCLUSIONS: These data suggest that polymorphisms in the GRM3 gene may be useful as predictors of negative symptom improvement in persons with schizophrenia treated with olanzapine.
Presented at the Annual Meeting of the Pharmacogenetics in Psychiatry, New York, NY, April 14-16, 2005.

298. Vitamin K reductase genotype and warfarin dose requirements. *Kathryn Momary, Pharm.D.*[1], Nancy L. Shapiro, PharmD[1], Edith A. Nutescu, PharmD[1], Cathy M. Helgason, MD[2], Larisa Cavallari, Pharm.D., BCPS[1]; (1)University of Illinois at Chicago, College of Pharmacy, Chicago, IL; (2)University of Illinois at Chicago, Chicago, IL.

PURPOSE: There is substantial inter-patient variability in the dose of warfarin necessary to achieve optimal anticoagulation. Cytochrome P450 gene polymorphisms, which have been linked to warfarin sensitivity, are uncommon among African Americans. Vitamin K reductase (NQO1) is involved in vitamin K recycling, the target of warfarin therapy. The objective of this study was to determine whether a common polymorphism (Pro187Ser) in the gene encoding NQO1 influences warfarin dose requirements in African Americans.
METHODS: Genetic samples and information on vitamin K intake and warfarin adherence were collected from 58 African Americans on a stable dose of warfarin, defined as the same dose for 3 consecutive clinic visits. Demographic data and INR values were also collected. Patients taking drugs known to interact with warfarin were excluded from study participation. NQO1 genotype was determined by PCR and RFLP methods. Warfarin doses were compared between NQO1 codon 187 Pro allele homozygotes and Ser allele carriers.
RESULTS: Thirty-four patients (59%) were 187Pro allele homozygotes and 24 patients (41%) were Ser allele carriers. Demographic characteristics, INR, vitamin K intake, and warfarin adherence were similar between genotype groups. The median (range) warfarin dose was 7.3 (3.2-14.3) mg/day in 187Pro allele homozygotes and 6.2 (2.0-14.3) mg/day in Ser allele carriers; p=NS.
CONCLUSIONS: Warfarin doses did not vary by NQO1 genotype among patients in our study. Our data do not support a role for the NQO1 gene in determining warfarin sensitivity in African Americans.

Pharmacokinetics/Pharmacodynamics/Drug Metabolism/Drug Delivery

300. Pharmacokinetics of mycophenolic acid and its phenolic-glucuronide and acyl-glucuronide metabolites in stable lung transplant recipients on cyclosporine or tacrolimus. *Lillian S. L. Ting, BSc.(Chem), MSc.(Pharm)student*[1], Nilufar Partovi, BSc(Pharm), PharmD[2], Robert D. Levy, MD, FRCPC[3], K. Wayne Riggs, BSc(Pharm), PhD[1], Mary H. H. Ensom, BS(Pharm), PharmD, FCCP[4]; (1)University of British Columbia, Vancouver, BC, Canada; (2)University of British Columbia and Vancouver General Hospital, Vancouver, BC, Canada; (3)University of British Columbia, St. Paul's Hospital and BC Transplant Society, Vancouver, BC, Canada; (4)University of British Columbia and Children's & Women's Health Centre of British Columbia, Vancouver, BC, Canada.

PURPOSE: To characterize the pharmacokinetics (PK) of mycophenolic acid (MPA) and its glucuronidated metabolites, MPAG (phenolic-glucuronide) and AcMPAG (acyl-glucuronide), in stable lung transplant recipients on cyclosporine (CsA) or tacrolimus (TAC).
METHODS: Following written informed consent and upon administration of a steady-state morning mycophenolate mofetil (MMF) dose, blood samples were collected at 0,0.3,0.6,1,1.5,2,4,6,8,10, and 12 hours. Total MPA, MPAG, AcMPAG, and free MPA (fMPA) concentrations were measured by a validated high-performance liquid chromatography method with ultraviolet detection and PK parameters calculated by non-compartmental analysis (WinNonlin 4.1).
RESULTS: Patients were: 11 males and 10 females, mean(± standard deviation, SD) 4.6 ± 4.2 years post-transplant, age 48.1 ± 14.2yr and weight 71.0 ± 17.5kg. All were on prednisone, with 11 on cyclosporine and 10 on tacrolimus. Mean albumin concentration was 3.8 ± 0.5g/dL and serum creatinine 1.4 ± 0.5 mg%. MMF dosage ranged from 1.5 to 3 grams daily. Mean(± SD) MPA PK parameters in CSA and TRL groups were: area-under-the-curve0-12h (AUC) 23.45 ± 13.55 and 34.16 ± 19.85µg*hr/mL; dose-normalized AUC 19.25 ± 11.23 and 28.00 ± 15.43µg*hr/mL; maximal concentration (C_{max}) 8.64 ± 5.96 and 6.97 ± 3.54µg/mL; time to C_{max} 1.6 ± 1.6 and 1.84 ± 2.89h; and minimum concentration 0.53 ± 0.35 and 0.97 ± 0.50µg/mL, respectively. Mean(± SD) AUC ratios of MPAG:MPA were 29.31 ± 13.18 and 15.08 ± 5.82 (p=0.006); and AcMPAG:MPA were 2.35 ± 4.18 and 0.45 ± 0.72, respectively, for CSA and TRL groups. Mean fMPA was 7.0 ± 5.1%.
CONCLUSIONS: Large inter-patient variability was observed in MPA PK parameters and metabolic ratios in lung transplant recipients. Concomitant medications (CsA and TAC) alone cannot explain the variability observed. Population PK and pharmacogenetic studies are underway to identify other factors that contribute to the variability. These results will help optimize treatment strategies for the lung transplant population.

301E. Intragastric acid control in nonsteroidal anti-inflammatory drug (NSAID) users: comparison of esomeprazole, lansoprazole, and pantoprazole. Jay L. Goldstein, MD[1], Philip B. Miner Jr., MD[2], Paul K. Schlesinger, MD[1], Sherry Liu, PhD[3], *D. Douglas Stogsdill, PharmD*[3], Debra G. Silberg, MD[3]; (1)University of Illinois at Chicago, Chicago, IL; (2)Oklahoma Foundation for Digestive Research, University of Oklahoma Health Sciences Center, Oklahoma City, OK; (3)AstraZeneca LP, Wilmington, DE.

PURPOSE: To compare esomeprazole, lansoprazole, and pantoprazole for control of intragastric pH in patients taking COX-2–selective or nonselective (ns) NSAIDs.
METHODS: In this multicenter, randomized, open-label, 3-way crossover study of esomeprazole 40 mg, lansoprazole 30 mg, and pantoprazole 40 mg once daily, the 24-hour intragastric pH profile at steady state was evaluated in adult *Helicobacter pylori*-negative patients. Eligible patients had to have a condition that required prescription-strength, daily dosages of a COX-2–selective or ns-NSAID for ≥1 month before entry and throughout the study. Patients were randomized to 1 of 6 treatment sequences and took each study drug on 5 consecutive mornings in the clinic under observation. On day 5, patients underwent a catheter-based 24-hour pH study. A washout period of ≥10 days preceded each treatment period. The percentage of time that gastric pH was >4 was calculated and hours per 24 hours was based on the calculated percentage. Only valid pH data from patients who completed all treatment periods were included in analyses. RESULTS: Valid pH data were available for a mean of 23.3 hours per 24-hour period in 77 patients. Esomeprazole 40 mg maintained intragastric pH >4 for a significantly greater proportion of a 24-hour period (74.3%) compared with lansoprazole (66.4%; *P*=.0003) or pantoprazole (60.7%; *P*<.0001). Mean hours that pH was >4 were 17.8, 15.9, and 14.6 after taking esomeprazole, lansoprazole, and pantoprazole, respectively. Subanalyses of data from patients taking either COX-2–selective NSAIDs (n=38) or ns-NSAIDs (n=39) showed similar results, and time with pH >4 was significantly greater (*P*<.05) with esomeprazole than with either comparator.

CONCLUSIONS: In patients taking either COX-2–selective or ns-NSAIDs, oral esomeprazole 40 mg once daily provides significantly greater control of intragastric acid at steady state than daily oral doses of either lansoprazole 30 mg or pantoprazole 40 mg.
Published in Gastroenterology 2005;128(suppl 2):A-241.

302E. Safety and laxative effects of sodium phosphate (NaP) tablets in healthy volunteers. *Martin Rose, M.D., J.D.*[1], Nancy Ettinger[1], Jeffrey Arcara[1], William G. Kramer, Ph.D.[2], Kelli Walker, PharmD, MS[1]; (1)InKine Pharmaceutical Co., Inc., Blue Bell, PA; (2)Kramer Consulting LLC, North Potomac, MD.

PURPOSE: To assess the safety and laxative effects of one week of therapy with NaP tablets and polyethylene glycol (PEG, Miralax®).
METHODS: Thirty-one healthy volunteers were randomized to receive 8 NaP tablets (1.5 g/tablet), 12 NaP tablets, or PEG 17g each morning for 7 days. NaP tablets were taken four q15min with 8oz of any beverage. PEG was dissolved in 8oz water. Patients kept a diary of their bowel movements (BMs) (eg. time, consistency, ease of passage) and GI symptoms (eg. cramps, flatus, rectal irritation). Subjects who met criteria for excess laxative effects had mandatory dosage reductions. Serum electrolytes were measured at baseline and 4 times during treatment.
RESULTS: NaP was associated with a significantly greater increase in mean daily BMs than PEG at day 1 and 7. Changes in stool consistency score were significantly greater with NaP after day 1 and 7. Subjects randomized to NaP required at least one dose reduction, compared to none randomized to PEG. The time to first soft or liquid BM was significantly shorter with NaP. No subject was discontinued for an adverse event; one subject (PEG group) was lost to follow-up after vomiting on day 2. Changes from baseline in electrolytes did not differ significantly among groups following completion of dosing.

Change from Baseline in BMs per Day (Mean ± SD)	NaP 8 tabs	NaP 12 tabs	PEG
Day 1	1.97 ± 1.53*	3.29 ± 2.40*	-0.18 ± 0.68
Last treatment day (day 7)	1.15 ± 0.76*	1.56 ± 0.96*	0.13 ± 0.44

*p<0.05 compared to PEG

CONCLUSION: NaP tablets taken for one week were well-tolerated by volunteers and produced significantly greater and more prompt laxative effects than PEG. Changes from baseline in electrolytes did not differ significantly among treatment groups at end of dosing. NaP tablets show promise as a treatment for constipation. Lower doses should be considered in future studies.
Published in Amer J Gastroenterol 2003;98:s290.

303. Pharmacokinetics of prazosin tablet in Korean healthy volunteers. Hyesun Gwak, Pharm.D., Ph.D., *Yunhee Kwon, BS*, Ahyoung Choi, BS; College of Pharmacy, Ewha Womans University, Seoul, South Korea.

PURPOSE: This study was aimed to determine the pharmacokinetics of Prazosin tablet in 16 healthy Korean volunteers after administration of one single dose of 2-mg prazosin hydrochloride
METHODS: Sixteen healthy volunteers (8 males and 8 females) aged between 19 and 55 years were selected. Blood samples (7 mL) were collected at predetermined time after the oral administration of prazosin hydrochloride. After addition of internal standard (IS, terazosin hydrochloride) and alkalization of the plasma, the drug and IS were extracted into *tert*-butylmethylether. The organic phase was back-extracted into 0.05% phosphoric acid and 50 µL of the acid solution was injected into a reverse-phase C18 column with a mobile phase consisting of water : acetonitrile : triethylamine = 75 : 25 : 0.1 (pH 5.0). The samples were detected utilizing a fluorescence detector.
RESULTS: Prazosin and IS showed good resolutions and an excellent linear relationship was (r^2 = 1) was obtained between the peak area ratios and the corresponding concentrations in the ranges of 0.5-50 ng/mL. Intra- and inter-day precision (within 9.59%) and accuracy (average value ranged from 102.15-114.23%) were acceptable for all quality control samples including the lower limit of quantification of 0.5 ng/mL. From the plasma prazosin concentration vs. time curves, the mean AUC was 108.4 ± 74.2 ng•h/mL and C_{max} of 23.1 ng/mL reached 2.1 h after administration. The mean biological half-life of prazosin was 2.5 ± ; 0.6 h. Female showed higher AUC (80.0 ± 15.2 vs 136.8 ± 98.5 ng•h/mL), C_{max} (17.8 ± 4.2 vs 28.3 ± 22.4 ng/mL) and prolonged half-life (2.0 ± 0.7 vs 2.8 ± 0.3 h) even though they were not statistically significant.
CONCLUSIONS: The results from the validation of the method in human plasma indicate that the method is accurate and precise. Also, it was found that females had higher AUC and C_{max} and prolonged half-life.

304E. Application of theoretical PK/PD modeling for optimization of linezolid therapy. *Julia Z. Zack, PharmD*, Alan Forrest, PharmD, Sanela Bilic, PharmD, MBA, Pam Kelchlin, BS, Patrick F. Smith, PharmD; SUNY at Buffalo, Buffalo, NY.

Our aim was to use a PD model, derived from kill-curve experiments, linked with simulation of human PK, to predict the impact of differing dosage regimens on timecourse of MRSA CFU. Two clinical MRSA isolates (MIC 2 & 4 mg/L) were investigated. PD kill-curve experiments, with serial sampling over 24 h, at a range of LZD exposures, were fit by a PD mixture model (capacity limited replication, 1st order elimination, effect of LZD as a Hill-type model inhibiting replication). Both strains were described as having 2 subpopulations: a predominant 'sensitive,' ED50 (concentration for 1/2 maximal effect) of 0.4 & 0.6 x MIC and the 'resistant', ED50 at 3 & 5 x MIC for each organism. This PD model and LZD PK parameters from our previous population analysis were used to predict PD responses to 4 dosing regimens: 600mg PO q12h without (BID) or with (fBID) a frontload (1st dose of 900mg) and 600mg PO q8h without (TID) or with (fTID) a frontload (1st dose of 1200mg). All modeling & simulations were performed using ADAPT II. One measure of drug activity was AUC(0-96h) of bacterial CFU/mL. For MIC=2 mg/L, compared to no drug, the AUC for the BID regimen was reduced by 87%, fBID was -93%, TID was -99.6% & fTID was -100%. For MIC=4 mg/L, BID was-73%, fBID was -80%, TID was -98.8% & fTID was -100%. Based on these simulations, the usual LZD BID regimen may not provide adequate activity at MIC>= 4 mg/L. If tolerable, and when warranted, a TID regimen may offer a substantial benefit over BID. With a 'slow' rate of kill and shallow concentration-effect curve, LZD is predicted to show only modest benefit for the loading doses. Further studies are necessary to verify these results.
Presented at the 45th Interscience Conference on Antimicrobial Agents and Chemotherapy, New Orleans, LA, September 21-24, 2005.

305. Retrospective evaluation of the modification of diet in renal disease (MDRD) equation for estimation of aminoglycoside pharmacokinetics. *Kazumi Morita, Pharm.D.*[1], Kelly M. Smith, Pharm.D.[2], Susanne E. Liewer, Pharm.D., B.C.O.P[1], George A. Davis, Pharm.D.[3], Donald G. Perrier, Ph.D.[2]; (1)University of Kentucky Chandler Medical Center, Lexington, KY; (2)University of Kentucky College of Pharmacy, Lexington, KY; (3)Sanofi Aventis, Lexington, KY.

PURPOSE: The MDRD equation has been shown to be more accurate and precise than the Cockcroft-Gault (CCG) equation for estimating renal function in certain populations. However, there are no studies using the MDRD equation to predict aminoglycoside pharmacokinetic parameters. Therefore, the performance of the CCG and MDRD equations for predicting aminoglycoside pharmacokinetic parameters was compared.
METHODS: Medical records were reviewed to identify 100 patients who received once-daily aminoglycoside therapy between July and December 2003. The inclusion criteria for this study were: 1) stable and reliable serum creatinine, 2) two serum drug concentrations following a given dose, and 3) all data necessary for the CCG and MDRD equations.
The aminoglycoside elimination rate constant (k) was estimated from renal function calculated by each method. For the CCG equation, k was predicted from k = (0.00293 x Clcr) + 0.014. For the MDRD equation, this equation for k was modified resulting in k = (0.00358 x GFR) + 0.014 using a correction factor (GFR = 0.82 x Clcr) to adjust for the tubular secretion of creatinine. The actual k was calculated from two serum aminoglycoside concentrations following a given dose. Correlations between the actual and estimated k were determined. The bias and precision of each equation were also determined.
RESULTS: Ninety-nine (99) patients were enrolled. The actual k was 0.180 ± 0.077 hr^{-1}. The estimated k using the CCG, MDRD, and simplified MDRD was 0.282 ± 0.105 hr^{-1}, 0.304 ± 0.110 hr^{-1}, and 0.360 ± 0.127 hr^{-1}, respectively, all of which were significantly higher than the actual k (p<0.001). All equations also were biased and lacked precision in predicting the actual k.
CONCLUSIONS: CCG and MDRD equations were not good predictors of the aminoglycoside k in our study population based on the currently available relationships.

306. Population pharmacokinetics: simulations and individual dosage optimization of alpha-1-antitrypsin replacement therapy. *Dolors Soy, Ph.D.*[1], Cristian De la Roza, M.D.[2], Beatriz Lara, M.D.[2], Sara Vila, M.D.[2], Cristina Esquinas, R.N.[2], Antoni Torres, M.D.[2], Jose Ribas, Ph.D.[1], Marc Miravitlles, M.D.[2]; (1)Pharmacy Service. Hospital Clinic Barcelona., Spain; (2)Pneumology Unit. Hospital Clinic Barcelona., Spain.

BACKGROUND: Severe alpha-1-antitrypsin (AAT) deficiency treatment is costly and inconvenient. Long-life intravenous exogenous-AAT (E-AAT) doses of 60mg/kg/7days are recommended to keep total serum AAT concentrations (T-AAT) around the protective value of 0.5 g/L.
PURPOSE: To evaluate whether other than weekly intervals of E-AAT administration are effective in maintaining steady-state T-AAT above 0.5g/L and, to optimize individual dosage regimens to achieve the recommended target.
METHODS: Six patients were included. Their mean baseline T-AAT was 0.23 g/L. Mean trough E-AAT values of at least 0.27 g/L were needed to attain the

T-AAT threshold. Simulations: A two-compartment pharmacokinetic (PK) model with intravenous infusion and first order elimination was applied to simulate several sets of 1000 E-AAT vs time profiles (NONMEM-V). The doses tested were: 50 and 60mg/kg/7days, 100 and 120mg/kg/14days, 150 and 180mg/kg/21days and 250mg/kg/28days. Mean (90% CI) E-AAT were computed for each schedule using S-Plus5. Optimization: Later, by using the individual baseline T-AAT and the Bayesian approach under the previous population PK model, a rational individual optimal dosage was estimated. To validate this dosage schedule, serial T-AAT were obtained and determined by nephelometry.
RESULTS: Simulations: In weekly administrations, 50mg/kg appear to be enough for obtaining protective trough concentrations. Both, 120 and 100mg/kg fortnightly administered may be suitable. E-AAT infusions of 180mg/kg/21 days require individual drug monitoring. Longer intervals are inappropriate. Optimization: Individual optimal E-AAT dosage regimens at 7, 14 and 21 days were established. In one case, weekly administrations were needed (phenotype: YYBarcelona) and two patients declined to change their previous schedule every 21 days. Bi-weekly E-AAT infusions were chosen for the rest and trough T-AAT result in protective values in all cases.
CONCLUSIONS: By using population PK data and a few individual samples, it is feasible to optimize the maintenance AAT dosing with extended interdose intervals to 14 or 21 days.

307E. Population pharmacokinetic/pharmacodynamic model of GPI 15715 and GPI-derived propofol in sedation. *Ekaterina Gibiansky, Associate, Director, DMPK*[1], Leonid Gibiansky, PhD[2]; (1)Guilford Pharmaceuticals Inc., Baltimore, MD; (2)Metrum Research Group, Avon, CT.

OBJECTIVES: Data from AQUAVAN® Injection (GPI 15715) dose-ranging study were used to build a population PK model of GPI 15715 and GPI-derived propofol and a PK/PD model relating propofol concentrations to the observed Modified Observer's Assessment of Alertness/Sedation (MOAA/S) scores.
METHODS: Fentanyl IV bolus was given to 164 patients 5 min prior to receiving an initial dose of IV AQUAVAN. Supplemental bolus doses of AQUAVAN were given if needed. A linear 5-compartment model described the PK of GPI 15715 (compartments 1, 2), propofol (compartments 4, 5), and a GPI 15715/ propofol concentration delay (compartment 3). PK/PD models were developed using MOAA/S data and individual propofol concentration predictions. Probabilistic model described probabilities of being at each MOAA/S level. Continuous model described the expected MOAA/S scores. Predictive check simulations were used to assess the predictive abilities of the models.
RESULTS: Lean body weight (LBW) was the best predictor of GPI 15715 and propofol concentrations. GPI 15715 and propofol central volumes, and GPI 15715 clearance increased by 1.8%, 2.5%, and 1.4% per kg of LBW, respectively. Predicted propofol C_{max}(at 4-5 min post-dose) were proportional to LBW-0.45. There was no effect of fentanyl dose or exposure, age, or gender on GPI 15715 and propofol PK. Individual predictions of MOAA/S scores were similar for probabilistic and continuous PK/PD models. Older patients (> 65 years) were estimated to have approximately 25% stronger effect at the same propofol concentrations. The models could not detect any additive effect of fentanyl on MOAA/S scores. Gender did not influence MOAA/S scores.
CONCLUSIONS: Lean body weight was the only predictor of propofol exposure. Dose reduction of about 25% is needed for patients over 65 years of age. Supported by Guilford Pharmaceuticals Inc.
Presented at the Annual Meeting of the American Society of Anesthesiologists, New Orleans, LA, October 22-26, 2005.

308. Intraperitoneal administration of clindamycin in continous ambulatory peritoneal dialysis patients. Min Jung Chang, MS.[1], Wan Gyoon Shin, Pharm.D, Ph.D[2], Sang Eun Lee, MS.Candidate[1], Jee Hyun Suh, MS.Candidate[1], *Miae Kim[1], M.S. candidate*; (1)Graduate School of Pharmacy, Seoul National University, Seoul; (2)Graduate School of Pharmacy, Seoul National University, Seoul, South Korea.

PURPOSE: This study evaluated the pharmacokinetic data of Intraperitoneal(IP) clindamycin in Continous Ambulatory Peritoneal Dialysis(CAPD) patients to prove that the adequate therapeutic concentration of clindamycin is maintained in the dialysate and plasma after intraperitoneal administration.
METHODS: Data was evaluated by single-dose, open-labelled study. Five noninfected volunteer CAPD patients received a single dose of IP clindamycin 600mg(300mg/L). Blood and dialysate samples were collected prior to drug administration, 0, 0.5, 1, 1.5, 2, 3, 6, 12, 24 hours after drug administration. Unless a patient was anuric, urine was collected for 24 hours. Clindamycin concentrations were assayed by high-performance liquid chromatography. Pharmacokinetic parameters were calculated by noncompatmental methods.
RESULTS: T_{max} in the dialysate was 3 hours and C_{max} in the dialysate was 10.121μg/mL. Time over therapeutic concentration in the dialysate and plasma was from 0.5 to 6 hours and from 1.5 to 3 hours, respectively. The ratio of $AUC_{0\text{-}6}$ in the plasma to $AUC_{0\text{-}6}$ in the dialysate was 0.535.
CONCLUSION: A single dose of 300mg/L IP clindamycin in CAPD patients can achieve therapeutic concentration in the peritoneal cavity. However, it is hard to say 300mg/L IP clindamycin in CAPD patients is good enough to treat systemic infection. Further study is needed to confirm whether or not a therapeutic concentration of clindamycin in the peritoneal cavity is truly effective in treating systemic infection or not.

309E. A comparison of venlafaxine XR and paroxetine or placebo in the short-term treatment of panic disorder. *Mark Pollack, MD*[1], Richard Mangano, MD[2], Richard Entsuah, PhD[2], Evan Tzanis, BS[2]; (1)Massachusetts General Hospital, Boston, MA; (2)Wyeth Pharmaceuticals, Collegeville, PA.

OBJECTIVE: To compare the short-term efficacy and tolerability of venlafaxine extended release (XR) with paroxetine and placebo in outpatients with panic disorder (PD).
METHODS: Outpatients aged ≥18 years with primary diagnosis of DSM-IV PD (± agoraphobia) for ≥3 months were randomly assigned to receive, using titration, venlafaxine XR (75 mg/day, n=156 or 225 mg/day, n=160), paroxetine 40 mg/day (n=151), or placebo (n=157) for 12 weeks. The primary efficacy measure was the percentage of patients free of full-symptom panic attacks (≥4 symptoms) at endpoint, analyzed by logistic regression with baseline severity as covariate. Additional secondary efficacy variables included PAAS full- and limited-symptom panic attacks, PDSS mean and response rate (≥40% score reduction from baseline), Phobia Scale (PS) fear and anxiety factors, HAM-A and CGI®CS means, median change in anticipatory anxiety, percentage of CGI-I responders (patients with score of 1 or 2), and remission rate (no panic attacks and CGI-S score = 1 or 2).
RESULTS: At endpoint, all active treatment groups showed a significantly ($P<0.01$) greater percentage of patients free of full-symptom (but not limited-symptom) panic attacks than placebo and were superior ($P<0.05$) on all other reported secondary measures. The venlafaxine XR 225 mg group had a significantly higher percentage of panic-free patients ($P<0.05$) and greater PDSS score improvement ($P<0.05$) than paroxetine. Both drugs were generally well tolerated.
CONCLUSION: Venlafaxine XR (75 mg/day and 225 mg/day) and paroxetine 40 mg/day are well tolerated and effective in the short-term treatment of PD.
Presented at the Annual Meeting of the College of Psychiatric and Neurologic Pharmacists, San Diego, CA, March 10-13, 2005.

310E. A 6-month, randomized controlled study of venlafaxine XR in the treatment of posttraumatic stress disorder. *Jonathan Davidson, MD*[1], David Baldwin, DM, FRCPsych[2], Dan J. Stein, MD[3], Enrique Kuper, BCETS, FAAETS[4], Isma Benattia, MD[5], Saeed Ahmed, MD[5], Bing Yan, MD[5], Ron Pedersen, MS[5], Jeff Musgnung, MT[5]; (1)Duke University Medical Center, Durham, NC; (2)University of Southampton, Southampton, United Kingdom; (3)University of Stellenbosch, Cape Town, South Africa; (4)Centro de Stress Traumatico, Buenos Aires, Argentina; (5)Wyeth Research, Collegeville, PA.

OBJECTIVE: To compare the efficacy of venlafaxine XR and placebo for treating moderate to severe PTSD.
METHODS: In this international, double-blind trial, 329 (ITT population) adult patients with a primary diagnosis of DSM-IV PTSD, PTSD symptoms for ≥6 months, and 17-item Clinician-Administered PTSD scale (CAPS-SX_{17}) score ≥60 were randomly assigned to treatment with flexible-dose venlafaxine XR (37.5 mg to 300 mg/d, starting with 37.5 mg; n=161) or placebo (n=168) for 24 weeks. The primary efficacy measure was baseline-to-endpoint change in CAPS-SX_{17} score; secondary assessments included remission (CAPS-SX_{17} ≤20), time to remission, PTSD symptom-free days, and changes in PTSD and depression symptoms, stress vulnerability, resilience, quality of life (QOL), functioning, and global illness severity. Parametric and nonparametric tests were performed, as appropriate.
RESULTS: The mean maximum dose of venlafaxine XR was 221 mg/day. Mean changes in CAPS-SX_{17} total scores were -51.7 for venlafaxine XR and -43.9 for placebo ($P=0.006$). Remission rates were 50.9% for venlafaxine XR and 37.5% for placebo ($P=0.013$). Median time to remission was 87.0 days for the venlafaxine group and 130.0 days for placebo ($P=0.0165$). The venlafaxine XR group also showed significantly greater improvement at endpoint than placebo for symptom-free days ($P=0.007$), and significantly greater improvement ($P<0.05$) in PTSD and depression symptoms, stress vulnerability, resilience, global severity, QOL, and functioning. Withdrawal rates were slightly lower for venlafaxine XR than placebo, with no significant difference in dropouts attributable to adverse events.
CONCLUSION: Venlafaxine XR was effective and well tolerated in the short-term and continuation treatment of PTSD.
Presented at the Annual Meeting of the College of Psychiatric and Neurologic Pharmacists, San Diego, CA, March 10-13, 2005.

311. A new formula and a table for adjusting phenytoin dosage regimen. *Gamal Hussein, Pharm.D.*; Loma Linda University School of Pharmacy, Loma Linda, California, CA.

Proper estimation of phenytoin dosage that achieves therapeutic plasma levels improves antiepilepsy therapy and patient outcomes. While calculation procedures and graphic methods are available to aid clinicians with dosage adjustment, they are not commonly utilized in clinical practice due to their complexity and other limitations. A new formula and a simple table were derived to estimate the percentage of dosage change that is required to achieve a desired phenytoin plasma concentration in adult patient population. To predict the new dose, the only requirements are the current dose and a single steady state plasma level. % Change in dose={Desired conc.x(current conc. + 6)}/{Current conc. x (desired conc.+ 6)} The formula was validated utilizing 46 sets of phenytoin doses and plasma levels from a previously published study. A comparison of the predicted dose and the actual dose was performed. In 87% of the cases, the predicted dose was within 6% of the actual dose. The estimated mean prediction error was -0.46%. Over-prediction occurred in 4.4% with a maximum over-prediction in dosage of 11%. Under-prediction occurred in 8.7% with a maximum under-prediction in dosage of 15%. This new method and the table with their limitations and modification for use in different patient populations will be presented.

312. Ethanol does not enhance cocaine's cardiovascular effects. *S. Casey Laizure, Pharm.D.*, Robert B. Parker, Pharm.D.; University of Tennessee Dept of Pharmacy, Memphis, TN.

PURPOSE: Controversy continues over the cocaine-ethanol interaction. Though it's well known that ethanol increases the cardiovascular effects of cocaine by inhibiting cocaine clearance, it has also been postulated that ethanol enhances cocaine's cardiovascular effects independent of the pharmacokinetic interaction. This study investigated the cardiovascular pharmacodynamics of the cocaine-ethanol interaction to determine if additive or synergistic activity occurred.
METHODS: Dogs(n=6) were administered 3mg/kg of IV cocaine alone and in combination with 1g/kg of IV ethanol on separate study days. Blood pressure, heart rate, and ECG were monitored continuously and blood samples collected periodically after drug administration. The concentration-time data were analyzed using noncompartmental methods and concentration-effect data fitted to a simple Emax model using WinNonlin. Parameters were compared between the two treatment phases by a paired *t*-test.
RESULTS: The administration of ethanol before cocaine resulted in a decrease in cocaine clearance. There were no differences in any of the other pharmacokinetic or pharmacodynamic parameter values between the cocaine alone and cocaine+ethanol phases. Cocaethylene wasn't detected after coadministration of cocaine and ethanol.

	Cocaine	Cocaine+Ethanol
Pharmacokinetics		
k(min^{-1})	0.016 ± 0.0040	0.0119 ± 0.0041
V(L/kg)	2.5 ± 0.61	3.1 ± 0.97
Cl(L/min)	1.24 ± 0.123	0.79 ± 0.283*
C_{max}(ng/ml)	2838 ± 497	2804 ± 1016
Pharmacodynamics		
Maximum Effect over Baseline		
Heart Rate	49 ± 31%	53 ± 28%
Systolic BP	46 ± 13%	49 ± 28%
Diastolic BP	88 ± 44%	79 ± 37
QRS	18 ± 10%	24 ± 10%

Simple E_{max}	Eo	EC-50	E_{max}	Eo	EC-50	E_{max}
Heart Rate (beats/min)	93 ± 16	4482 ± 5330	188 ± 62	96 ± 15	1477 ± 1239	164 ± 47
Systolic BP (mmHg)	152 ± 22	276 ± 161	224 ± 19	148 ± 23	565 ± 404	233 ± 35
Diastolic BP (mmHg)	94 ± 15	619 ± 164	166 ± 13	94 ± 10	403 ± 183	153 ± 9
QRS (msec)	76 ± 7	11797 ± 6014	128 ± 32	61 ± 8	599 ± 7549	94 ± 17

*p<0.05

CONCLUSIONS: Ethanol administration reduced cocaine clearance; however, ethanol did not enhance the effects of cocaine in this model. Our data suggests that the increased cardiovascular effects that occur with the coadministration of cocaine and ethanol are due to the decrease in cocaine clearance.

313. Evaluation of clinician opinions regarding the usefulness of vancomycin levels. *Julie A. Hixson-Wallace, Pharm.D., BCPS*, Maria L. Sikking, Pharm.D. student; Mercer University Southern School of Pharmacy, Atlanta, GA.

PURPOSE: To establish opinions of clinicians regarding usefulness of vancomycin serum levels.
METHODS: A cover letter and one-page survey were sent to 900 clinicians around the country. Three categories of clinicians were included: infectious disease physicians (IDMDs), general practice physicians (GPMDs), and pharmacists (RPhs) involved in pharmacokinetic monitoring. Questions regarded how often levels are measured, desired peak and trough, perceptions of cost, perceptions of liability, average length of therapy, comfort with trough ranges, and demographics of patients served.
RESULTS: The overall response rate was 27%: 29.3% for IDMDs, 1.6% for GPMDs, and 46.3% for RPhs. Most clinicians draw levels "almost always" or "sometimes," with more IDMDs drawing levels "always" than RPhs, (p<0.0001). A majority of clinicians draw trough levels only, with more RPhs drawing trough levels only vs. IDMDs and more IDMDs drawing both peaks and troughs vs. RPhs (p=0.0330). Most clinicians are "very comfortable" or "comfortable" with troughs between 11-15 mg/ml. Comfort levels were similar between IDMDs and RPhs (p=NS). Clinicians are "uncomfortable" with troughs in the range of 16-20 mg/ml. However, RPhs were more comfortable with the higher range than the IDMDs (p=0.0154). The monitoring of levels was perceived as necessary with certain patient populations: renally impaired, concomitant nephrotoxic therapy, continuing therapy, geriatrics, and concomitant ototoxic therapy.
CONCLUSIONS: Clinicians are comfortable with troughs up to 15 mg/ml. Also, the reasons clinicians chose that negatively and positively affect their decision to draw levels are inconsistent. We postulate two reasons for this discrepancy: there is still much confusion over the necessity of drawing levels and their importance in patient care or clinicians have varying patient populations or disease states in which they find it necessary to draw levels while they do not find it necessary for other patients.

314E. Comparing the remission rates of low therapeutic doses of venlafaxine or selective serotonin reuptake inhibitors in depressed patients. *Bing Yan, MD*[1], Jay Graepel, PhD[1], Diane Sloan, PharmD[2]; (1)Wyeth Research, Collegeville, PA; (2)Medesta Publications, Cardinal Health, Wayne, NJ.

PURPOSE: This analysis was designed to compare short-term remission rates between venlafaxine and 2 selective serotonin reuptake inhibitors (SSRIs) in depressed patients receiving fixed low therapeutic doses of either treatment.
METHODS: To date, more than 30 randomized, double-blind, active-controlled trials have compared venlafaxine and selected SSRIs in the treatment of depression, and 5 of these studies included patients receiving fixed low therapeutic doses of both treatments. Individual patient data were pooled to evaluate efficacy and tolerability in 952 depressed patients treated with venlafaxine/venlafaxine extended release (XR) 75 mg (n=482) or 20 mg of fluoxetine (3 studies; n=240) or paroxetine (2 studies; n=230). Remission ($HAM\text{-}D_{17}$ score ≤7) rates were compared at week 8 or the last observed endpoint, using the last-observation-carried-forward method.
RESULTS: In the overall data set, 50% of patients achieved remission with venlafaxine/venlafaxine XR 75mg. In the 3 fluoxetine studies, remission rates were 48% for venlafaxine vs 37% for fluoxetine (P=0.014); in the 2 paroxetine studies, remission rates were 52% for venlafaxine vs 45% for paroxetine (P=0.116). Overall discontinuation due to adverse events was similar: 15% venlafaxine/venlafaxine XR, 13% fluoxetine, and 14% paroxetine.
CONCLUSION: Previous meta-analyses of depression studies have suggested advantages for venlafaxine relative to fluoxetine and perhaps others SSRIs across a wide range of dosages. The present report demonstrates that venlafaxine treatment is associated with high remission rates even at low therapeutic doses. The difference in remission rates between venlafaxine and fluoxetine was significant, while the difference between venlafaxine and paroxetine was not.
Presented at the Annual Meeting of the World Federation of Biological Society, Vienna, Austria, June 28–July 3, 2005.

315E. Meta-analysis of all known randomized clinical trials comparing venlafaxine and selective serotonin reuptake inhibitors. *Michael Thase, MD*[1], Richard Entsuah, PhD[2], Saeed Ahmed, MD[2], Diane Sloan, PharmD[3], Charles B. Nemeroff, MD, PhD[4]; (1)University of Pittsburgh Medical Center, Pittsburgh, PA; (2)Wyeth Research, Collegeville, PA; (3)Medesta Publications, Cardinal Health, Wayne, NJ; (4)Emory University School of Medicine, Atlanta, GA.

PURPOSE: Previous meta-analyses comparing venlafaxine and selective serotonin reuptake inhibitors (SSRIs) generally have not included studies by sponsors other than Wyeth. We now report a meta-analysis of all known studies from all funding sources.
METHODS: Forty-eight randomized controlled trials (RCTs) comparing venlafaxine to citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, or sertraline in the treatment of depression were identified and available for inclusion. Odds ratios (OR) for remission ($HAM\text{-}D_{17}$ score ≤7 at week 8 or endpoint [whenever possible] or the closest available equivalent) were computed. Funnel plot analysis was used to assess selection bias.
RESULTS: The OR for remission in the previous meta-analysis of 33 Wyeth-sponsored RCTs was 1.30 (95% CI 1.17-1.44). The updated meta-analysis, with the inclusion of the original 33 studies and all additional studies, yielded similar results, with an OR of 1.256 (95% CI 1.165-1.367). Neither visual inspection of the funnel plots nor specific statistical tests revealed any evidence of study selection bias.

CONCLUSION: Taken as a whole, these findings confirm and extend prior meta-analyses suggesting that venlafaxine therapy is more effective than SSRIs when grouped together, and specifically fluoxetine and paroxetine when compared individually. The inclusion of all available studies, regardless of sponsor, did not change the outcome. Of note, it remains unclear if the observed advantage for venlafaxine extends beyond 8 weeks of therapy and if it is consistent across all individual SSRIs.
Presented at the Annual Meeting of the Society of Biological Psychology, Atlanta, GA, May 19-21, 2005.

316E. Bioequivalency of pioglitazone and metformin combination tablets vs coadministration tablet. *Aziz Karim, PhD*, Charlie Cao, PhD, Alfonso Perez, MD; Takeda Global Research and Development Center, Lincolnshire, IL.

Two open-label, randomized, crossover studies were conducted to determine the bioequivalency of pioglitazone (PIO) and metformin (MET) after single-dose administration of fixed-dose combination tablets: PIO 15 mg/MET 500 mg or PIO 15 mg/MET 850 mg. For each fixed dose strength, 66 healthy male and female subjects (mean age=32.0 and 31.3 years, respectively; ≥110 lbs; body mass index <30 kg/m^2) were randomly assigned to 1 of 6 treatment sequences (2 test formulations; 1 coadministered tablets as reference). Three 1-day dosing periods were separated by 7-day washout periods during which blood samples were collected up to 72 hours postdose. Micronized formulation results are presented.

	90% CI of LS Mean Test: Reference		
	$AUC_{0\text{-}tlqc}$	$AUC_{0\text{-}\infty}$	C_{max}
PIO 15 mg/	(91.0, 104.9)	(97.6, 107.6)	(86.2, 104.7)
MET 500 mg	(97.9, 107.5)	(98.1, 107.6)	(94.8, 103.4)
PIO 15 mg/	(90.0, 100.1)	(90.6, 99.3)	(89.9, 104.7)
MET 850 mg	(98.3, 106.8)	(98.2, 107.5)	(96.9, 106.9)

For either dose, the 90% CIs of all LS mean ratios for both doses were within 80%-125% required to establish bioequivalency. Also, Tmax and λz were not statistically different, and $T_{1/2}$ and CL/F showed no notable differences between combination dose and respective individual PIO or MET tablets. Safety profiles were similar based on the occurrence of adverse events and clinical laboratory, vital sign, ECG, and physical examination findings. In conclusion, peak and total exposures (C_{max} and AUCs) of PIO and MET observed after single-dose administration of both doses of combination tablets (PIO 15 mg/MET 500 mg and PIO 15 mg/MET 850 mg) were bioequivalent to those observed after administration of the separate commercial tablets. Each dose of combination tablet was safe and well tolerated.
Presented at the Annual Meeting of the American College of Clinical Pharmacology, Rockville, MD, September 11-13, 2005.

317E. Food effects of pharmacokinetics of pioglitazone and metformin administered as a combination tablet. *Aziz Karim, PhD*, Charlie Cao, PhD, Alfonso Perez, MD; Takeda Global Research and Development Center, Lincolnshire, IL.

An open-label, randomized, crossover study was conducted to compare the peak and total exposures of pioglitazone (PIO) and metformin (MET) after single-dose administration of a fixed-dose combination tablet (PIO 15 mg/MET 850 mg) when given under fasting vs fed conditions. A total of 28 healthy subjects (mean age, 32.7 years; ≥110 lbs; body mass index <30 kg/m^2) were randomly allocated to 1 of 2 treatment sequences. The micronized particle formulation was tested in 2 periods and another was tested in 2 other periods. All dosing periods were separated by 7-day washout periods during which blood samples were collected up to 72 hours postdose. Results are presented for the micronized particle formulation, which was found most suitable for development in other trials.

	90% CI of LS Mean Ratio (with:w/o food)		
	$AUC_{0\text{-}tlqc}$	$AUC_{0\text{-}\infty}$	C_{max}
PIO	(102.1, 124.7)	(100.6, 122.4)	(92.8, 117.7)
MET	(81.2, 93.0)	(80.9, 93.8)	(65.4, 79.1)

A total of 15 male and 12 female subjects completed; 1 withdrew due to a protocol deviation. For PIO, all 90% CIs of the LS mean ratios were within 80%-125%, as were ratios for the MET AUC(0-tlqc) and $AUC_{0\text{-}\infty}$. Peak exposure of MET showed a food effect; decreases were 13%, 13%, and 28% for AUC(0-tlqc), $AUC_{0\text{-}\infty}$, and C_{max}, respectively. Drug dosing with food resulted in T_{max} prolongations from 1.6 to 3.5 hours (PIO) and from 2.4 to 3.2 hours (MET). In conclusion, these results indicate a lack of food effect on total and peak PIO exposure and on total MET exposure. The magnitude and direction of the food effects in this fixed-dose combination study were similar to those reported for coadministered PIO and MET tablets.
Presented at the Annual Meeting of the American College of Clinical Pharmacology, Rockville, MD, September 11-13, 2005.

318. Evaluation of a Simplified Method to adjust Vancomycin Trough Concentrations. *Larry A. Bauer, Pharm.D.*; University of Washington, Seattle, WA.

PURPOSE: Compare a simplified method of adjusting vancomycin trough concentrations with a Bayesian computer method in patients with stable renal function. Patients receiving vancomycin for various infections were studied (n=126, age=22–77y, weight=54–117kg, gender=77M/49F, estimated CrCl=17–137ml/min). Patients were initially administered 1 gm using a dosage interval deemed appropriate for renal function by the prescriber. Steady-state concentrations (within 30" of the next dose) were prospectively measured for dosage adjustment. Dosage intervals were individualized to achieve new trough concentrations (Cnew) of 5-15 µg/ml: Cnew=(Iold/Inew)Cold, where Cold was the initial concentration, and Iold and Inew are the old and new dosage intervals, respectively. For comparison, Cnew was also computed using a Bayesian computer program. The initial measured concentration was 11.9 ± 4.6 µg/ml, and the adjusted measured concentration was 9.3 ± 2.8 µg/ml (mean±SD). The predicted concentrations for the adjusted levels were 9.3 ± 3.0µg/ml for the Bayesian method and 9.8 ± 2.2 µg/ml for the simplified method. Statistical analysis for predictive methods (means, 95% CI) was used. The mean prediction error (ME), mean squared prediction error (MSE) and root mean squared prediction error (RMSE) were: Bayesian: ME=-0.035 µg/ml (-0.15–0.076), MSE=0.40 (0.32–0.48), RMSE=0.63µg/ml (0.57–0.70); simplified: ME=0.48µg/ml (0.089–0.88), MSE=5.3 (4.4–6.2), RMSE=2.3 µg/ml (2.1–2.5). Relative to the 2 methods, the delta MSE was 4.9 (4.0–5.8), and the delta ME equaled 0.52 (0.11–0.92). The simplified method was easy to use at the patient's bedside and did a reasonable job of predicting adjusted trough concentrations. The Bayesian method is established and considered to be one of the "gold standards" for therapeutic drug monitoring. However, it requires access to a computer and considerable time to conduct. The Bayesian method is more precise (delta MSE values) and less biased (delta ME values) compared to the simplified method ($p<0.05$). Given the current trends in vancomycin concentration monitoring, clinicians may find the average error associated with the simplified method (RMSE=2.3 µg/ml) acceptable for routine use.

319. Amifostine and WR1065 pharmacokinetics (PK) in children with medulloblastoma. *Susannah E. Motl, Pharm.D.*, Burgess B. Freeman, III, Pharm.D., Maryam Fouladi, M.D., Lisa C. Iacono, Pharm.D., Amar Gajjar, M.D., Feng Bai, Ph.D., Clinton F. Stewart, Pharm.D.; St. Jude Children's Research Hospital, Memphis, TN.

PURPOSE: Standard therapy for pediatric medulloblastoma includes adjuvant cisplatin-based chemotherapy. Roughly 50% of children experience cisplatin-related ototoxicity, requiring cisplatin dosage reductions. In an attempt to reduce ototoxicity, amifostine was included in a institutional cisplatin-based pediatric medulloblastoma regimen. The objective of this study was to determine the disposition of amifostine and WR1065, the active thiol metabolite, in children with medulloblastoma.
METHODS: Amifostine 600 mg/m^2 was administered as two 1-minute boluses prior to and midway through a 6-hour cisplatin infusion. Blood samples were taken prior to and at serial time points after each amifostine dose. Plasma amifostine and WR1065 concentrations were determined using a validated HPLC method with electrochemical detection. A four-compartmental model was simultaneously fit to the amifostine and WR1065 data, and PK parameters including volumes of distribution (Vd), elimination (Ke) and inter-compartmental rate constants were estimated using ADAPT II, with clearances (CL) and terminal half-lives ($T_{1/2}$) calculated using standard equations.
RESULTS: Adequate concentration-time data were available from 24 patients with 38 PK studies [18 male, 6 female; median age (range) 7.8 yrs (3.4–20.5)]. Median (range) plasma CLs for amifostine and WR1065 were 1.6 L/min/m^2 (0.5–4.3) and 2.3 L/min/m^2 (0.4–4.1), respectively. Amifostine displayed rapid elimination with median (range) $T_{1/2}$, of 11 min (2–287), whereas the median (range) $T_{1/2}$ for WR1065 was 52 min (10–320).
CONCLUSIONS: Our plasma amifostine and WR1065 PK results appear similar to those previously reported for adults and a limited pediatric population. Analyses of the relationship between amifostine and WR1065 PK and ototoxicity are ongoing. Our results may have broad implications for the otoprotection of children with medulloblastoma, and other solid tumors whose therapy may include cisplatin. Results of these analyses may also provide insight into the optimal dosing of amifostine in children receiving cisplatin.

320E. The bioequivalence of telithromycin administered orally as crushed tablets versus tablets swallowed whole. *SJ Kovacs, PharmD*[1], CL Lippert, PhD[2], C. Qui, PhD[1], B. Lavin, MPH, FACP[1]; (1)sanofi-aventis, Bridgewater, NJ; (2)Quintiles Inc., Kansas City, MO.

PURPOSE: This study was perfomed to establish whether administration of telithromycin as crushed tablets was bioequivalent to the administration of whole tablets.
METHODS: This was an open-label, single-dose, randomized, 2-period, crossover study with a 6-day washout between periods ó Treatment A: telithromycin 800 mg (2 x 400-mg Ketek® tablets, sanofi-aventis), swallowed whole with 240 mL water; Treatment B: telithromycin 800 mg (2 x 400-mg

tablets), crushed and mixed in 240 mL of nutritional supplement drink (Ensure®, Abbott Laboratories) followed by 120 mL water. Blood samples were collected predose and 0.5, 1, 1.5, 2, 3, 4, 6, 8, 10, 12, 16, and 24 hours post-dose. Plasma was assayed for telithromycin concentration by a validated liquid chromatography/mass spectrometry method. Exposure measures were computed by noncompartmental methods using WinNonLin® Professional (Pharsight Corporation). Peak plasma concentration (C_{max}) and area under the 24-hour concentration–time curve ($AUC_{0–24}$) were determined from observed data. Average bioequivalence criteria were applied.
RESULTS: Thirty-two of 34 randomized subjects received telithromycin by both methods of administration and completed the study. The 90% confidence intervals for the geometric mean ratios of $AUC_{0–24}$ (0.966, 1.139) and C_{max} (0.854, 1.051) were within the 0.80–1.25 range. Median time to C_{max} was 3.00 hours for both treatments. Both methods of administration were well tolerated.
CONCLUSIONS: Crushing telithromycin tablets and administering them with a nutritional supplement drink is bioequivalent to the administration of whole tablets. Breaking or crushing telithromycin tablets could be a viable alternate method of administration for patients unable to swallow whole tablets.
Presented at the Annual Meeting of the American Society for Clinical Pharmacology, Orlando, FL, March 2-5, 2005.

321. Zolpidem modified-release 12.5 mg improves measures of sleep continuity in a model of sleep disturbance (traffic noise) compared with standard zolpidem 10 mg. *Neil Stanley, PhD*[1], Ian Hindmarch, PhD[1], Eric Legangeux, MD[2], Stephen Emegbo, MSc[1]; (1)HPRU Medical Research Centre, University of Surrey, Guildford, United Kingdom; (2)Sanofi-Aventis Research, Malvern, PA.

PURPOSE: To evaluate the pharmacodynamic profile of 8 galenic formulations of zolpidem MR combining different doses of immediate- and extended- release zolpidem in comparison with standard zolpidem 10 mg in a traffic noise model of insomnia.
METHODS: A Phase I randomized, double-blind, placebo- and reference-controlled, 10-way crossover study conducted in 36 healthy volunteers (age 18 to 40 y, 20 male) comparing single nocturnal doses of 8 zolpidem MR formulations (A-H, up to 15 mg) or standard zolpidem 10 mg to placebo. Study periods were separated by ≥7 day wash-out. A traffic noise model induced sleep continuity difficulties. Polysomnography (PSG) criteria and sleep architecture were recorded for 8 h postdose. Psychometric testing was conducted 8 and 9 h postdose (immediately and 1 h after awakening).
RESULTS: Hourly PSG analysis showed Formulation E (12.5 mg) significantly reduced the mean number of awakenings up to 5 h postdose when compared with placebo and standard zolpidem. Psychomotor test performance was not significantly different from placebo or standard zolpidem 8 and 9 h postdose. The proportion of time spent in sleep stages 1-4 or in REM sleep was similar following placebo, standard zolpidem, or zolpidem MR.
CONCLUSIONS: In a pharmacodynamic model, zolpidem MR 12.5 mg (Formulation E) improved measures of sleep continuity during the middle of the night (3-5 h postdose) compared to both standard zolpidem 10 mg and placebo without compromising next-day psychomotor performance or sleep architecture. All zolpidem MR formulations and standard zolpidem were well tolerated with no safety issues observed.

322. Pharmacokinetic profile of a zolpidem modified-release formulation in comparison with standard zolpidem. *Estelle Weinling, PhD*[1], Stuart McDougall, PhD[2], Frederic Andre, PhD[1], Catherine Dubruc, PhD[1], Gabrio Bianchetti, PhD[1], Emmanuel Krupka, MD.[3]; (1)Sanofi-Synthelabo Research, Chilly-Mazarin, France; (2)Sanofi-Synthelabo, UK Research Division, Northumberland, United Kingdom; (3)Larime, France.

PURPOSE: To evaluate relative bioavailability and plasma pharmacokinetic profile of single oral doses of zolpidem modified-release (MR) formulations (10 mg and 12.5 mg) compared to standard zolpidem 10 mg.
METHODS: A Phase I randomized, open-label, crossover study was conducted. Healthy, Caucasian, male volunteers (n=24, age 18-45 y) received single oral doses of zolpidem MR 10 mg and 12.5 mg, or standard zolpidem 10 mg. Blood samples (n=18) were collected up to 16 h postdose. Treatment periods were separated by a 7-day washout. The following pharmacokinetic parameters were determined by noncompartmental analysis : maximum plasma concentration (C_{max}), time to maximum concentration (t_{max}), elimination half life ($t_{1/2}z$), terminal elimination rate constant (l), area under the curve (AUC), mean residence time (MRT), and half-value duration (HVD). Comparisons between treatments were performed by ANOVA with a level of significance of P<.05.
RESULTS: Initial absorption was rapid with no significant difference for tmax between zolpidem MR and standard zolpidem. With zolpidem MR 12.5 mg, C_{max} values were moderately lower (ratio of 0.82) compared with standard zolpidem. Following zolpidem MR 12.5 mg, plasma concentrations were maintained above those observed with standard zolpidem for a longer period of time, and particularly from 3–6 hrs postdose. This was confirmed by an increase of the HVD from 2.3 hrs for standard zolpidem to 4.6 hrs for zolpidem MR 12.5 mg. The mean terminal half-life was similar for all 3 groups tested.
CONCLUSION: Zolpidem MR 12.5 mg provided the appropriate pharmacokinetic characteristics to extend plasma concentration into the middle of the night (3-6 hrs postdose), while retaining the same rapid onset of action (tmax) and mean terminal half-life.

323E. In silico evaluation of gatifloxacin (G) pharmacodynamics (PD) vs. Salmonella typhi (ST) in adults. *Olanrewaju O. Okusanya, Pharm.D.*, Alan Forrest, Pharm.D, Brent M. Booker, Pharm.D, Patrick F. Smith, Pharm.D; University at Buffalo, Buffalo, NY.

PURPOSE: Our aim was to use a PD model, derived from an in vitro infection model (IVM), linked with simulated human PK, to predict the impact of different dosage regimens of G, on time course of CFU for ST.
METHODS: 2 clinical ST isolates (MIC 0.5 & 4mg/L) were investigated. IVM experiments, with serial sampling over 24 h, at a range of G exposures, were fit by a PD mixture model (capacity limited replication, 1st order bacteria death (kd), & G effect as a Hill-type model enhancing kd. Strains were described as having 2-3 subpopulations (SP): a predominant 'sensitive' SP, ED50(concentration at 1/2 maximal effect) of 15 & 28xMIC & 'resistant' SP, ED50 of 154 & 153/364 x MIC for each strain, respectively. This PD model & G PK model & parameters, from normal volunteers, were used to predict PD responses to 3 dosing regimens: 400mg IV q24h without (QD) or with (fQD) a frontload (1st dose of 800mg) & 800mg IV q24h (dQD). All modeling & simulations were performed using ADAPT II.
RESULTS: For MIC=4, compared to growth control (GC), the AUCb for the all the regimens was reduced by 55–60% with a majority of the AUCb being the resistant SP. For the MIC=0.5, the QD reduced the AUCb of the GC by ~2.3 log, & other regimens resulted in a further 1.3 log decline from QD. There was no difference over 48h between the other 2 regimens.
CONCLUSIONS: Based on these simulations, the usual G QD regimen will be effective at MICs < 0.5. The effect of higher doses of G is more marked, when given at higher bacteria titers (front loading) and similar to doubling the dose. G, however, may not provide adequate activity at MIC > 4 even when the dose is doubled.
Presented at the 45th Interscience Conference on Antimicrobial Agents and Chemotherapy, New Orleans, LA, September 21-24, 2005.

324. Pharmacokinetics and safety of alvimopan, a novel, oral, peripherally acting mu-opioid receptor (PAM-OR) antagonist, and in patients with renal Impairment. *Joseph Foss, MD*[1], Thomas C. Marbury, MD[2], Armen Melikian, PharmD[3], Virginia Schmith, PhD[4], Wei Du, PhD[1], Bruce Wallin, MD[1]; (1)Adolor Corporation, Exton, PA; (2)Orlando Clinical Research Center, Orlando, FL; (3)Drug Development Resources, LLC, Mountain Lakes, NJ; (4)GlaxoSmithKline, Philadelphia, PA.

PURPOSE: Alvimopan (6 mg and 12 mg) is currently investigational for the management of postoperative ileus after laparotomy. This study evaluated the pharmacokinetics and safety of alvimopan in patients with renal impairment.
METHODS: Patients with mild (creatinine clearance rate [CLcr] of 51-80 mL/min; n=6), moderate (CLcr of 31-50 mL/min; n=6), or severe (CLcr of ≤30 mL/min; n=6) renal impairment and age-weight matched normal controls (CLcr of >80 mL/min; n=6) received a single oral dose of alvimopan 12 mg in this phase I, single-center, open-label study. Blood and urine samples were collected before dosing and for 5 days after dosing. Standard noncompartmental methods were used to calculate pharmacokinetic parameters (± standard deviations) of alvimopan and its amide hydrolysis product (primary metabolite; ADL 08-0011). Safety was assessed by continuous adverse event (AE) monitoring.
RESULTS: Pharmacokinetics of alvimopan in patients with renal impairment were similar to those in normal controls. Alvimopan C_{max} (ng/mL) and total exposure (AUC(0-∞) in hr·ng/mL) were highest in the mild renal impairment group (C_{max}=15.7 ± 9.4; AUC(0-∞)=69.1 ± 40.1), intermediate in the severe renal impairment group (C_{max}=11.8 ± 5.4; AUC(0-∞)=62.2 ± 38.3), and lowest in the moderate renal impairment (C_{max}=10.8 ± 4.9; AUC(0-∞)=49.9 ± 22.5) and control groups (C_{max}=11.3 ± 4.5; AUC(0-∞)=46.1 ± 19.1). The level of renal function generally correlated inversely with ADL 08-0011 C_{max} and AUC(0-∞), with levels being highest in the severe renal impairment group (C_{max}=10.3 ± 12.2; AUC(0-∞)=508.3 ± 1280.8), intermediate in the moderate renal impairment group (C_{max}=7.4 ± 10.0; AUC(0-∞)=281.3 ± 323.2), and lowest in the mild renal impairment (C_{max}=4.3 ± 3.0; AUC(0-∞)=154.3 ± 84.6) and control groups (C_{max}=2.5 ± 3.7; AUC(0-∞)=161.7 ± 242.9). There was low incidence of AEs in all groups. Hematology, biochemical, and urinalysis data showed minimal changes from baseline levels.
CONCLUSIONS: A single dose of alvimopan 12 mg was generally well tolerated in patients with mild to severe renal impairment. In general, there was no relationship between renal function and plasma alvimopan pharmacokinetics.

325. Pharmacokinetics of alvimopan, a novel, oral, peripherally acting mu-opioid receptor (PAM-OR) antagonist, and its primary metabolite in the elderly. *Joseph Foss, MD*[1], Thomas C. Marbury, MD[2], Armen Melikian, PharmD[3], Virginia Schmith, PhD[4], Wei Du, PhD[1], Bruce Wallin, MD[1]; (1)Adolor Corporation, Exton, PA; (2)Orlando Clinical Research Center, Orlando, FL; (3)Drug Development Resources, LLC, Mountain Lakes, NJ; (4)GlaxoSmithKline, Philadelphia, PA.

OBJECTIVE: To evaluate the pharmacokinetics (PK) of alvimopan (ADL 8-2698) and its primary metabolite (ADL 08-0011) in elderly volunteers.
PURPOSE: Elderly volunteers (age ≥ 65 years) received a single oral dose of alvimopan 12 mg in this phase I, single-center, open-label, PK study. Adverse events (AEs) and PK parameters (maximum observed plasma drug concentration [C_{max}], time to C_{max} [T_{max}], area under the plasma drug concentration time curve [$AUC_{0-\infty}$], half-life [$t_{1/2}$], clinically relevant $t_{1/2}$, oral clearance, and volume of distribution) were evaluated for 96 hours after dosing.
METHODS: Mean age of volunteers (N = 18) was 73 years and 89% were Caucasian. For alvimopan, mean C_{max} was 9.57 ng/mL and the median Tmax, was 1.5 hours. Alvimopan levels then decreased in a monophasic or biphasic pattern, with a $t_{1/2}$ of 5.1 hours (clinically relevant $t_{1/2}$ of 2.7 hours), resulting in a mean exposure ($AUC_{0-\infty}$) of 38.1 hr‾ng/mL. For ADL 08-0011, mean C_{max} was 4.56 ng/mL, which occurred 1 to 48 hours after dosing (median Tmax, 36 hours). ADL 8-2698 levels then decreased to minimal levels by 96 hours resulting in a mean exposure ($AUC_{0-\infty}$) of 201.0 hr‾ng/mL. The PK parameters for ADL 08-0011 were more variable compared with alvimopan. Few AEs were reported, and most were mild in intensity. The most common AE was abdominal pain.
CONCLUSIONS: The PK profile of a single dose of alvimopan 12 mg in elderly volunteers was consistent with that previously reported for a population of younger volunteers (mean age, 30 years; alvimopan C_{max} = 12.1 ng/mL, $AUC_{0-\infty}$ = 46.4 hr‾ng/mL; Foss et al, The American Society for Clinical Pharmacology and Therapeutics Annual Meeting, March 2-5, 2005). Alvimopan 12 mg is well tolerated in elderly people, and no dose adjustments are needed.

326. Efficacy of alvimopan, a peripherally activing mu-opioid receptor (PAM-OR) antagonist, and timing of preoperative dosing: pharmacodynamic and pharmacokinetic consideration in patients undergoing open laparotomy. *Yehuda Kariv, M.D.*[1], Eugene Viscusi, MD[2], Bruce Wolff, MD[3], Conor Delaney, MD, PhD[4], Anthony Senagore, MD, MS, MBA[5], Wei Du, PhD[6], Lee Techner, DPM[6], Bruce Wallin, MD[6]; (1)Cleveland Clinic Foundation, Cleveland, OH; (2)Jefferson Medical College, Thomas Jefferson University, Philadelphia, PA; (3)Mayo Clinic, Rochester, MN; (4)Case Western Reserve University, Cleveland, OH; (5)Medical College of Ohio, Toledo, OH; (6)Adolor Corporation, Exton, PA.

PURPOSE: To determine the timing range for alvimopan preoperative dosing based on achieving and maintaining effective (free) concentrations of alvimopan at the receptor site during the period of maximal opioid exposure (perioperatively). Free plasma concentration after alvimopan (single dose) will achieve/exceed Ki for receptor antagonism for 6-10 hours of the dosing interval in 50% of patients.
METHODS: Analysis was completed using the pooled modified intent-to-treat population from 3 phase III, randomized, placebo-controlled trials of alvimopan 6 mg (n=502) and 12 mg (n=508) versus placebo (n=501). Time of induction of anesthesia was used as a surrogate for start of surgery. Summary statistics were performed on elapsed time and number of patients with preoperative dosing ≤2 or >2 hours (88% of patients dosed between 0.5-5.0 hours). Covariate analysis was conducted to evaluate whether timing of the preoperative dose influenced time to recovery of gastrointestinal (GI) function. A Cox proportional hazard model with treatment effect and a covariate of time from preoperative dose to time of induction was fitted to the data.
RESULTS: Mean elapsed time from preoperative dose to start of induction was 2.9 ± ;1.4 (placebo), 3.0 ± ;1.53 (alvimopan 6 mg), and 2.9 ± ;1.34 hours (alvimopan 12 mg). Overall, 22.6% and 73.5% of patients received alvimopan ≤2 and >2 hours before surgery, respectively. Analysis of the treatment effect revealed a significant difference between alvimopan 6 mg versus placebo (hazard ratio [HR]=1.25; P=0.001) and alvimopan 12 mg versus placebo (HR=1.29; P<0.001) in time to recovery of GI function. Covariate analysis demonstrated that timing of the preoperative dose did not significantly influence time to recovery of GI function (HR=1.03; P=0.185).
CONCLUSIONS: Patients dosed ≤2 hours before surgery had similar GI recovery compared with patients dosed >2 hours before surgery. Dosing 0.5-5.0 hours before the scheduled start of surgery should provide adequate mean levels of alvimopan.

327E. Evaluation of the efficacy and safety of eszopiclone over six months of treatment in patients with insomnia. Andrew Krystal, M.D., M.S.[1], James K. Walsh, Ph.D.[2], Thomas Roth, Ph.D.[3], Robert Rubens, M.D.[4], Phebe Wilson, M.S.[4], *John Niewoehner, Pharm.D.*[4], Thomas C. Wessel, M.D.[4]; (1)Duke University Medical Center, Durham, NC; (2)Sleep Medicine and Research Center, St. Luke's Hospital, Chesterfield, MO; (3)Henry Ford Hospital Sleep Disorders Center, Detroit, MI; (4)Sepracor Inc., Marlborough, MA.

PURPOSE: Eszopiclone is a non-benzodiazepine insomnia treatment. Results of a second randomized, double-blind 6-month study are presented.
METHODS: Adults (21-64) with DSM-IV primary insomnia sleeping <6.5 hours and/or sleep latency (SL)>30 minutes received nightly placebo (n=280) or eszopiclone 3mg (n=550) for 6-months followed by a two-week placebo run-out. Patient-reported endpoints included sleep and daytime function (alertness, daytime sleepiness, ability to function/concentrate, physical well-being).
RESULTS: At all monthly assessments, eszopiclone significantly improved SL, wake time after sleep onset (WASO), total sleep time (TST), and sleep quality versus placebo (p<0.0001). Eszopiclone patients had average changes from baseline of -39.8, -19.6, and 80.9 minutes for latency, WASO, and TST, respectively. The Insomnia Severity Index indicated that more eszopiclone patients had no clinically meaningful insomnia at Month 6 (50% versus 19%, p<0.0001). Eszopiclone significantly improved all monthly daytime parameters vs placebo (p<0.05). Pharmacologic tolerance was not observed, nor was rebound insomnia or withdrawal effects. Eszopiclone was well tolerated; the most common adverse event was unpleasant taste.
CONCLUSIONS: Results were consistent with previous 6-month data and indicate that, in this study, nightly use produced consistent and sustained improvements across all sleep and daytime parameters, and was well tolerated with no pharmacologic tolerance, withdrawal or rebound insomnia observed.
Presented at the 57th Annual Meeting of the Institute on Psychiatric Services, San Diego, CA, October 5-9, 2005.

328. Retrobulbar block: the role of Vitrase® (hyaluronidase ovine) as an adjuvant to reduce the time required between injection of anesthetic and surgical incision. *James A. Gow, M.D.*[1], James F. Weller, M.D.[2], Ulysses M. Tandoc, MD[2], Robert J. Cionni, MD[2], Rachel M. Sacks, BS[1], Lisa R. Grillone, PhD[1], Tim R. McNamara, PharmD.[1]; (1)ISTA Pharmaceuticals, Inc., Irvine, CA; (2)Cincinnati Eye Institute, Cincinnati, OH.

PURPOSE: Vitrase (6200 USP, lyophilized) is a non-thimerosal containing, highly purified, ovine hyaluronidase and FDA approved. This study was designed to quantify the ability of hyaluronidase ovine to shorten the time between first application of anesthetic, surgical incision, and post-operative recovery time.
METHODS: Forty adult subjects scheduled for cataract extraction were enrolled. Hyaluronidase ovine was reconstituted to 150 units/mL with sodium chloride for injection. The solution was combined with 5.0 mL of 2% lidocaine (total 6 mL). anesthetic/hyaluronidase ovine solution (2.5–5.0 mL) was administered by retrobulbar injection. If necessary, a second injection from the same anesthetic/hyaluronidase ovine solution was administered. Time of first injection of block and time of surgical incision were recorded. Akinesia was measured 2-23.5h post-operatively in 6 directions of gaze on a 4 point scale from no movement (1) to full movement (4).
RESULTS: 24/40 (60%) subjects were male; mean age was 66 years (34 to 85). Mean initial dose of hyaluronidase ovine for all subjects was 93.1 Units. Mean dose of hyaluronidase ovine for subjects requiring a second injection of anesthetic/Hyaluronidase ovine alone or with topical anesthetic (n=6) was 47.9 Units. Mean total dose of hyaluronidase ovine for all subjects (n=40) was 100.3 Units. Mean time from initial injection of anesthetic/Hyaluronidase ovine dose to surgical incision was 12 ± 3.87 minutes. 31 eyes (77.5%) recovered with Akinesia scores of 21-24 assessed between 2-23.5 hours after initial injection of anesthetic/Hyaluronidase ovine. 1 (2.5%) subject reported a complication (corneal abrasion from speculum). No deaths or SAEs were reported.
CONCLUSIONS: Hyaluronidase ovine, administered with injected anesthetics prior to ophthalmic surgery, may reduce the time required between injection of anesthetic and surgical incision. Recovery was rapid with no untoward events. Hyaluronidase ovine is a safe and efficacious adjuvant to increase absorption and dispersion of anesthetics used for ophthalmic surgery.

329. Extemporaneous compounding of medications used in pediatric nephrology: is stability adequate? *Renee F. Robinson, PharmD*; The Ohio State University College of Medicine, Children's Hospital, Department of Pediatrics, Division of Nephrology, Columbus, OH.

PURPOSE/BACKGROUND: Most new drugs being marketed in the United States are not labeled for and are not commercially available in an appropriate dosage form for pediatric use. Extemporaneous formulations play an important role in the administration of medications to infants and children; however, variability in both compounding procedures and recipes may result in inconsistencies of drug administered to infants and children.
METHODS: To determine current clinical practices and the potential impact of medication administration on infants and children we mailed 102

extemporaneous medication surveys to pediatric pharmacies in the United States and Canada. References used and the medications currently compounded in the scope of pediatric nephrology were addressed. Institutions were asked to provide recipes not published, expirations of the formulation and criteria to determine expiration of the compounded medication.
RESULTS: Of the inpatient and outpatient pharmacies surveyed (n=102), 19.6% responded despite the monetary incentive. Most institutions used published texts (Handbook on Injectable Drugs (Trissel), Pediatric Drug Formulations (Nahata et al), Pediatric Dosage Handbook (Taketomo et al), and Extemporaneously Formulations (Jew et al) for their main references. Few institutions used primary literature in their decision and only 35% of institutions used internet references. Of the medications explored, 80% of institutions compound enalapril, and 40% compound lisinopril while benazepril, fosinopril, quinapril and ramipril remain untested. Only 20% of institutions compound losartan. Candesartan, irbesartan, and valsartan remain in tablet form only. Of the calcium channel blockers 65% of institutions reported compounding diltiazem, 50% verapamil, 50% amlodipine, 50% nifedipine, and none reported using felodipine. Lastly of the beta-blockers, 75% of institutions reported compounding atenolol, 55% metoprolol, and 35% labetalol.
CONCLUSION: Increased funding is necessary to develop stable formulations, conduct studies, publish results and increase awareness for practitioners of the primary literature to ensure that infants and children and receive what practitioners prescribe.

330. A predictive vancomycin dose calculator for patients with end stage liver disease. *Jiwon W. Kim, Pharm.D.*, Kevin B. Livengood, Pharm.D., Paula V. Phongsamran, Pharm.D.; USC School of Pharmacy and USC University Hospital, Los Angeles, CA.

PURPOSE: To examine the change in vancomycin pharmacokinetics in patients with end stage liver disease (ESLD) and to create a predictive vancomycin dose calculator utilizing observed pharmacokinetic parameters in this patient population.
METHODS: A retrospective chart review of 33 patients with ESLD who received IV vancomycin therapy was conducted to collect demographic and clinical information. Observed vancomycin pharmacokinetic parameters were compared to estimated values calculated from the population-based kinetics. A nested ordinary least squares (OLS) regression approach was used to create a predictive dose calculator, in which estimated and observed Kel and clearance (Cl) were used to predict vancomycin dose and frequency.
RESULTS: Estimated vancomycin pharmacokinetic parameters were significantly different from the actual values. The dose calculator created was a function of patient gender, serum creatinine (SCr), and volume of distribution (Vd): dose = 856–180 * gender–640 * SCr + 14 * Vd. The dose frequency calculator created was a function of gender and SCr: frequency = 11 + 5 * gender + 18 * SCr. The means and associated confidence intervals for the difference between actual and predicted Kel, Cl, dose, and frequency were 0.0002 (-.0047–.005) hr-1, -1.098 (-5.26–3.07) ml/min, 17.39 (-69.21–103.99) mg/day, and -0.564 (-3.37–2.25) hr, respectively. The means and associated confidence intervals for the difference between actual and a priori estimated Kel, Cl, dose, and frequency were -0.039 [-.05–(-.028)] hr^{-1}, -39.36 [-52.47–(-26.24)] ml/min, -817.79 [-1090.37–(-545.21)] mg/day, and 11.80 (8.64–14.97) hr, respectively. The comparisons for the four differences were all significant at the level of $p<0.000001$.
CONCLUSION: A vancomycin dose calculator created from the observed pharmacokinetic parameters of patients with ESLD may be utilized to predict a more appropriate initial dosing regimen compared to population-based kinetics in this patient population.

331E. Pharmacodynamic modeling of telithromycin and azithromycin vs. genotypically characterized (mefA and ermB) macrolide resistant strains of Streptococcus pneumoniae **simulating free serum and free epithelial lining fluid concentrations.** *Ayman M. Noreddin, MSc., Ph.D.*[1], Daryl Hoban, PhD[2], George G. Zhanel, Pharm.D., Ph.D.[3]; (1)College of Pharmacy, University of Minnesota, Duluth, MN; (2)International Health Management Associates, Inc., Schaumburg, IL; (3)University of Manitoba, Winnipeg, MB, Canada.

PURPOSE: The purpose of this study was to compare the pharmacodynamics (PD) of Teli and azithromycin (Azi) versus macrolide-resistant SPN simulating free serum (S) and free epithelial lining fluid (ELF) concentrations in an in vitro model.
METHODS: Five PCR-positive mefA, one PCR-positive ermB and a control PCR-negative mefA, ermB strain of SPN were studied. A one compartment in vitro pharmacodynamic model was used with starting inocula 1x106 CFU/ml. Teli was added to the model simulating a dosage of 800mg PO OD and Azi was added simulating a dosage of 500mg/250mg PO OD (S: free drug Cpmax 0.2µg/ml, $t_{1/2}$ 68 hr, free AUC ~2; ELF: free drug C_{max} 1µg/ml, $t_{1/2}$ 68 hr, free AUC ~10). Samples were obtained over 24 hours to assess viable growth and selection of resistance.
RESULTS: Both S and ELF Teli concentrations eradicated (lowered inoculum below level of detection) all PCR-positive mefA, ermB and wild type SPN from the model within 6 hours. No difference in the rate or extent of killing (ò 3 log10 reduction) occurred between the test and control strains or between S and ELF concentrations. Azi S and ELF concentrations eradicated macrolide-susceptible SPN but did not eradicate macrolide-resistant SPN regardless of resistance phenotype.
CONCLUSIONS: Both Teli and Azi eradicated macrolide-susceptible SPN. Teli but not Azi, completely eradicated both mefA and ermB SPN from the model with no regrowth over 24 hour. Teli offers promise for the management of respiratory infections caused by macrolide-resistant SPN.
Published in Pharmacotherapy 2005;25(3):474.

332E. Monte Carlo simulation of bactericidal activity versus P. aeruginosa of levofloxacin 500 mg, 750 mg, and 1000 mg once daily compared to gatifloxacin 400 mg once daily administered to critically ill patients. *Ayman M. Noreddin, MSc., Ph.D.*[1], Daryl Hoban, PhD[2], George G. Zhanel, Pharm.D., Ph.D.[2], A. Reese, M. Ostroski, T. Marras, C. Chan; (1)College of Pharmacy, Univeristy of Minnesota, Duluth, MN; (2)Univeristy of Manitoba, Winnipeg, MB, Canada.

PURPOSE: This study aimed to assess the probability of Levofloxacin (Levo) compared to Gatifloxacin (Gati) achieving favorable pharmacodynamic (PD) targets for bacterial eradication and prevention of resistance development in *S. pneumoniae* in both elderly (≥ 65 years) and younger (< 65 years) patients with CAP.
METHODS: As part of an ongoing study comparing the clinical outcome of Levo vs. cefuroxime + erythromycin in hospitalized patients with CAP, demographics including age, weight, gender, race and renal function were gathered and analyzed from 263 elderly (≥ 65 years) and 48 younger patients (< 65 years). Previously described and validated population pharmacokinetic (PK) models of Levo and Gati in patients with CAP were utilized. Free-drug $AUC_{0\text{-}24}$ were simulated in Plasma (P) using Levo dosing at 500 mg, 750 mg and 1000 mg OD as well as Gati 200 mg and 400 mg OD. Use of Monte Carlo Simulation allowed for the full variability of encountered drug clearance to be accounted. *S. pneumoniae* susceptibility data were obtained from the Canadian Respiratory Organism Susceptibility Study (CROSS) study (an annual, national, ongoing surveillance study which has collected 8014 isolates from 1997-2004).
RESULTS: Probability of target attainment (free $AUC_{0\text{-}24}$/MIC of 30) of Levo and Gati, respectively, is shown in the following tables.

Target Free-Drug $AUC_{0\text{-}24}/MIC_{all}$		30
All Patients	500 mg	92.3%
750 mg	97.8%	
1000 mg	98.3%	
Elderly Patients	500 mg	95.5%
750 mg	98.5%	
1000 mg	99.2%	
All Patients	400 mg	96.6%
200 mg	87.7%	
Elderly Patients	400 mg	97.7%
200 mg	91.4%	

CONCLUSIONS: For all patients and for elderly hospitalized patients with CAP, Levo 750 mg and Gati 400 mg showed high probability for target attainment of free $AUC_{0\text{-}24}$/MIC of 30.
Published in Pharmacotherapy 2005;25(3):473-4.

333. Theoretical considerations for predicting the effect of gastric bypass surgical procedures on the absorption of commonly used medications. *Travis L. Gatesman, PharmD*, Richard H. Parrish II, Ph.D.; Shenandoah University, Winchester, VA.

BACKGROUND: The effects of three major gastric bypass surgeries, Roux-en-Y (RGB), biliopancreatic diversion (BPD), and biliopancreatic diversion with duodenal switch (BPDD), on medication absorption are unknown. These surgical methods involve elimination of most of the small intestine, where many medications are absorbed. The percent ionization and absorption of any medication can be predicted by knowing duodenum and jejunum pH and a medication's pKa.
OBJECTIVES: To determine percent ionization for the top 50 medications at various pHs; to determine the percent of medication not absorbed as a result of these surgeries; and to predict dose changes necessary to maintain a therapeutic effect.
METHODS: The pKa values of the top 50 medications of 2001 were collected. Using the Henderson-Hasselbach equation, a percent ionization was calculated at a range of intestinal pHs, then charted to determine the amount of medication absorbed at each pH. The percentage of medication not absorbed was calculated by the amount of digestive tract bypassed in each surgery.
RESULTS: Sources of pKa included manufacturer information (42%), package insert (13%), and Merck Index (10%); 35% of medications did not have pKa

information available. BPD and RGB had the greatest decreases in absorption (0.18% and 0.11% per medication, respectively).
CONCLUSION: Only 23% of the pKas were accessed from written resources; this information needs to be more readily accessible to determine absorption of all medications. BPDD showed the smallest reduction in absorption of procedures. Fluoxetine, olanzapine, and zolpidem had the greatest predicted reduction in absorption.

Pharmacy Administration

334. Hospital pharmacists' professional satisfaction influenced by sense of calling and knowledge applicability. *Chanuttha Ploylearmsang, M.P.H.*[1], Petcharat Pongchareonsuk, Ph.D.[2], Thawatchai Vorapongsathorn, Ph.D.[3], Rungpetch Sakulbumrungsil, Ph.D.[4]; (1)Faculty of Pharmacy, Mahasarakham University, Mahasarakham, Thailand; (2)Faculty of Pharmacy, Mahidol University, Bangkok, Thailand; (3)Faculty of Public Health, Mahidol University, Bangkok, Thailand; (4)Faculty of Pharmaceutical Science, Chulalongkorn University, Bangkok, Thailand.

PURPOSE: The study objective was to examine influences of sense of calling and knowledge applicability on professional satisfaction among hospital practitioners.
METHODS: Hospital pharmacists in the public and private sectors were surveyed using a cross-sectional mail survey. A self-administered questionnaire was developed with four parts; respondent demographics, attitudes on profession (belief in public service, sense of calling, and belief in continuing competence), level of knowledge applicability and professional satisfaction. Overall, 620 samples from stratified sampling throughout the country were selected. Influences of sense of calling and knowledge applicability on professional satisfaction among hospital pharmacists were analyzed using multiple regression.
RESULTS: A total of 434 (70.0%) usable questionnaires were returned for analyses, consisting of 347 (80.0%) responses from public hospital and 87 (20.0%) from private hospital pharmacists. Significant factors influencing professional satisfaction were sense of calling (b=2.03, p<0.001), knowledge applicability (b=0.28, p<0.001), executive position (b=5.90, p<0.01), and duration of work (b=-0.22, p<0.05). These variables accounted for 33.5% of the variance in professional satisfaction (Adjusted R^2=0.33). Sense of calling showed the highest influence on professional satisfaction (Adjusted R^2=0.21).
CONCLUSIONS: Professional satisfaction was related to the quality and efficiency of pharmacy services. It is considered that to increase professional satisfaction among practising pharmacists the following are needed: diminishing bureaucracy from a vertical-lined position, supporting the dedication and personal commitment to his/her work and increasing the opportunity of applying pharmacy knowledge in his/her practice.

335. Field-based medical science liaison job satisfaction: three-year results. *Erin L. Albert, RPh, MBA*[1], Cathleen M. Sass, MBA, Pharm.D.[2]; (1)Sepracor, Indianpolis, IN; (2)Sepracor, Cincinnati, OH.

PURPOSE: The field based Medical Science Liaison (MSL) is well established within the pharmaceutical/biotechnology industries. We report on an ongoing annual survey regarding job satisfaction associated with this role.
METHODS: A 33-question survey was developed on job satisfaction in 2005. It was posted on a web-based survey host site (www.surveymonkey.com) for 2.5 months and received 136 responses. Previous years' surveys, 2003 and 2004, received 106 and 137 responses, respectively.
RESULTS: The majority of MSLs continue to have a pharmacy degree, but the number of PhDs is increasing within the role. MSLs are generally satisfied with their careers. However, job satisfaction is declining. Male respondents continued to receive higher salaries than their female MSL counterparts, but the disparity between average salaries is decreasing. Other results are reported within this analysis for the first time. These include a comparison between the responses of pharmacists vs. other professionals within the MSL role.
CONCLUSIONS: Intellectual challenge continues to be an important factor when considering job satisfaction. The importance of salary and benefits has increased over the course of 3 years. Managers must continue to identify which factors the individual values and address those issues to increase job satisfaction and retention.

Psychiatry

336E. Duloxetine vs. placebo in the treatment of elderly patients with MDD. Joel Raskin, MD[1], Curtis Wiltse, PhD[2], Jeff Dinkel, na[2], Alan Siegel, MD[3], Javaid Sheikh, MD[4], *Wahiba Estergard, PharmD*[5], Jimmy Xu, PhD[2], Benjamin Rotz, RPh[2], Richard Mohs, PhD[2]; (1)Eli Lilly Canada, Scarborough, ON, Canada; (2)Eli Lilly and Company, Indianapolis, IN; (3)Yale University School of Medicine, New Haven, CT; (4)Stanford University School of Medicine, Stanford, CA; (5)Eli Lilly and Company, Phoenix, AZ.

HYPOTHESES: Primary: Duloxetine improves cognition in elderly MDD patients. Secondary: Duloxetine is effective and safe in the treatment of depressive symptoms in elderly MDD patients.
METHODS: Patients at least 65 years old were randomized (2:1) to duloxetine 60 mg once daily (n=207) or placebo (n=104) for 8 weeks. The primary outcome measure was a prespecified composite cognitive score based on 4 tests that measured verbal learning and memory, selective attention, and executive functioning. Secondary measures included the Geriatric Depression Scale (GDS), the Hamilton Depression Scale (HAMD17), and standard safety and tolerability assessments.
RESULTS: Patients had a median age of 72 (65-89). Duloxetine demonstrated significantly greater improvement in the composite cognitive score vs. placebo (least squares mean change from baseline to endpoint of 1.95 [SE=.30] vs. 0.76 [SE=.40], p=.013). Duloxetine showed significantly (p<.001) greater reductions in both HAMD17 (-6.49 vs. -3.72) and GDS total scores (-4.07 vs. -1.34) compared with placebo. HAMD17 response (37.3% vs. 18.6%, p<.001) and remission (27.4% vs. 14.7%, p=.014) rates at endpoint were significantly higher in patients on duloxetine than those on placebo. Among the pain measures, duloxetine demonstrated greater improvement vs. placebo on VAS for back pain and time in pain while awake. Discontinuation rates due to adverse events were similar for duloxetine and placebo (9.7% vs 8.7%). Significantly more placebo than duloxetine patients discontinued due to lack of efficacy (9.6% vs 2.9%). Common treatment-emergent adverse events included dry mouth, nausea, constipation, dizziness, diarrhea, fatigue, and somnolence. Rates of measured orthostatic hypotension did not differ significantly between duloxetine and placebo (15.6% vs. 20.5%). Rates of discontinuation-emergent adverse events were similar for duloxetine and placebo (14.2% vs 10.0%).
CONCLUSIONS: Duloxetine improved cognition and depression, and was safe and well-tolerated, in elderly MDD patients.
Presented at the 8th Annual International Meeting of the College of Psychiatric and Neurologic Pharmacists, San Diego, CA, March 10-13, 2005.

337E. Olanzapine-fluoxetine combination versus lamotrigine for bipolar depression. Eileen Brown, PhD[1], Doug Williamson, MD, MRCPsych[1], Ahmed Deldar, PhD[1], Paul E. Keck Jr., MD[2], *Wahiba Estergard, PharmD*[1], David Adams, PhD[1]; (1)Eli Lilly and Company, Indianapolis, IN; (2)University of Cincinnati College of Medicine and Cincinnati Veterans Affairs Medical Center, Cincinnati, OH.

PURPOSE: Determine the efficacy of olanzapine-fluoxetine combination compared with lamotrigine for treatment of bipolar I depression.
METHODS: The acute phase of a randomized, double-blind study compared olanzapine-fluoxetine combination (6/25, 6/50, 12/25, or 12/50 mg/day, n=205) with lamotrigine (200 mg/day; n=205) in bipolar I depression over 7 weeks. Efficacy measures included Clinical Global Impression Severity (CGI-S) (primary outcome measure), Montgomery-Asberg Depression Rating Scales (MADRS) and Young-Mania Rating Scale (YMRS). Analytical techniques included mixed-models repeated measures analysis on change from baseline and Fisher's exact test for categorical comparisons.
RESULTS: Patients treated with olanzapine-fluoxetine combination had greater improvement than lamotrigine-treated patients across the 7-week treatment period on CGI-Severity (p=.002), MADRS total score (p=.002) and YMRS (p=.001). Time to response (50% decrease in MADRS) was significantly (p=.010) shorter for olanzapine-fluoxetine-treated patients. Serious adverse events occurred more frequently in lamotrigine-treated patients (OFC 1.0%, LMG 5.4%; p=.012). Adverse events were more frequent with olanzapine-fluoxetine-treated patients (≥10% patients and p<.05) were somnolence, increased appetite, dry mouth, sedation, weight gain and tremor. Weight (p<.001), cholesterol (p<.001) and triglycerides (p=.001) were significantly elevated with olanzapine-fluoxetine treatment compared to lamotrigine.
CONCLUSIONS: Patients had greater bipolar improvement on olanzapine-fluoxetine combination than lamotrigine.
Presented at the Annual Meeting of the American Psychiatric Association, Atlanta, GA, May 21-26, 2005.

338E. Discontinuation from schizophrenia treatment is driven by poor symptom response: a post-hoc analysis of four atypical antipsychotics combined. Hong Liu-Seifert, Ph.D., Bruce J. Kinon, MD, *Wahiba Estergard, PharmD*, David Adams, PhD; Eli Lilly and Company, Indianapolis, IN.

PURPOSE: Antipsychotic treatment discontinuation can interrupt therapeutic progress and lead to illness exacerbation. Treatment discontinuation results from controlled clinical trials were utilized to explore reasons for this phenomenon.
METHODS: This was a post-hoc, pooled analysis of four randomized, double-blind clinical trials that had duration of 24-28 weeks, enrolling 1627 patients with schizophrenia or a related disorder. Analyses were conducted combining all atypical antipsychotic treatment groups in the studies

RESULTS: A majority of patients (53%) discontinued early from their antipsychotic treatment. Poor psychiatric response/symptom worsening was the most frequent reason for treatment discontinuation, which was substantially more common than discontinuation due to medication intolerability. This phenomenon was corroborated by discontinued patients showing inadequate symptom improvement, compared to completers based on the Positive and Negative Syndrome Scale (PANSS) total scores. Discontinuation due to poor response was overwhelmingly linked to patient perception as compared to physician conclusion alone (80% vs. 20%). Discontinuation due to patient perception of poor response appeared to occur particularly early in the treatment course. Patients who discontinued due to medication intolerability showed a rate of response comparable to that of patients who completed the study.
CONCLUSIONS: Treatment discontinuation may lead to illness exacerbation and undermine therapeutic progress. In these studies, poor response to treatment and worsening of underlying psychiatric symptoms, and to a lesser extent, intolerability of medication were the primary contributors to treatment discontinuation. Our findings suggest that adherence may be enhanced by effective symptom control as objectively measured as well as subjectively perceived. Such strategies may improve patient engagement in long-term therapy and increase likelihood of achieving treatment goals.
Presented at the Annual Meeting of the Society of Biological Psychiatry, Atlanta, GA, May 19-21, 2005.

339E. Efficacy of extended-release carbamazepine in bipolar disorder: results of two pooled clinical trials. Richard H. Weisler, MD[1], Robert Hirschfeld, MD[2], Andrew J. Cutler, MD[3], Thomas Gazda, MD[4], Terrance Ketter, MD[5], Paul Keck, MD[6], Alan Swann, MD[7], Amir Kalali, MD[8], *Rishit R. Patel, PharmD*[9]; (1)Duke University Medical School and University of North Carolina College of Medicine, Durham, NC; (2)University of Texas Medical Branch at Galveston, Galveston, TX; (3)University of South Florida, Tampa, FL; (4)St. Luke's Medical Center, Scottsdale, AZ; (5)Stanford University School of Medicine, Stanford, CA; (6)University of Cincinnati College of Medicine, Cincinnati, OH; (7)University of Texas Medical School at Houston, Houston, TX; (8)Quintiles CNS Therapeutics, San Diego, CA; (9)Shire US Inc., Wayne, PA.

PURPOSE: To evaluate the efficacy of extended-release carbamazepine capsules (ERC-CBZ; Shire) in a combined study population of patients with Bipolar I Disorder.
METHODS: Data analysis was performed using pooled data from 2 nearly identically designed 3-week, double-blind, placebo-controlled, phase 3 trials of ERC-CBZ monotherapy. Four hundred forty-three patients, aged 18 to 76 years with a DSM-IV diagnosis of bipolar disorder (manic or mixed), were randomized to double-blind treatment with either ERC-CBZ or placebo. Efficacy was assessed by Young Mania Rating Scale (YMRS), Clinical Global Impression–Severity (CGI-S), Clinical Global Impression–Improvement (CGI-I), and Hamilton Depression Rating Scale (HDRS).
RESULTS: Two hundred forty of 443 patients (54.2%) completed the study. Treatment with ERC-CBZ was associated with significant improvements in mean YMRS total scores, using last observation carried forward (LOCF) analyses, at all time points (P<.0001). At end point, significant reductions in YMRS total scores were observed in both manic (P<.0001) and mixed (P<.01) patients. Furthermore, significant improvements were shown in CGI-I and CGI-S scores. Total score improvements in HDRS were observed in ERC-CBZ–treated mixed patients (P<.05) at end point.
CONCLUSION: Results confirm previous findings that ERC-CBZ is effective in the treatment of bipolar I disorder. Moreover, subgroup analyses of efficacy in manic and mixed patients proved that ERC-CBZ is successful in treating manic and depressive symptoms.
Presented at the U.S. Psychiatric and Mental Health Congress, San Diego, CA, November 18-21, 2004.

340E. Efficacy of switching to carbamazepine extended-release capsules in bipolar disorder. Richard H. Weisler, MD[1], Robert Hirschfeld, MD[2], Andrew J. Cutler, MD[3], Thomas Gazda, MD[4], Terence A. Ketter, MD[5], Paul E. Keck Jr., MD[6], *Brian Scheckner, Pharm.D.*[7]; (1)Duke University Medical School and University of North Carolina College of Medicine, Durham and Chapel Hill, NC; (2)University of Texas Medical Branch at Galveston, Galveston, TX; (3)University of South Florida, Tampa, FL; (4)St. Luke's Medical Center, Scottsdale, AZ; (5)Stanford University School of Medicine, Stanford, CA; (6)University of Cincinnati College of Medicine and Cincinnati Veterans Affairs Medical Center, Cincinnati, OH; (7)Shire US Inc., Wayne, PA.

PURPOSE: Evaluate the efficacy of extended-release carbamazepine capsules (ERC-CBZ) in the treatment of patients switched from lithium, olanzapine, and valproate for the treatment of their bipolar disorder.
METHODS: This analysis is of pooled data from 2 randomized, placebo-controlled phase III trials of ERC-CBZ monotherapy in the treatment of bipolar disorder. Efficacy was assessed with the Young Mania Rating Scale (YMRS), the Clinical Global Impression–Severity (CGI-S) scale, the CGI-Improvement (CGI-I) scale, and the Hamilton Depression Rating Scale (HDRS).
RESULTS: When compared to placebo, there were statistically different reductions in YMRS change in patients previously on lithium and valproate who were switched to ERC-CBZ. There were also significant reductions in HDRS change and CGI-S change versus placebo (and a trend toward significance for YMRS change) for those patients previously on olanzapine who were switched to ERC-CBZ. Clinical Global Impression-Improvement responder rates indicated trends towards significance for each of the 3 populations of patients (previously on olanzapine, lithium, or valproate) when compared to those patients on placebo, but the changes were not significant.
CONCLUSIONS: These data suggest that ERC-CBZ is an effective therapy for patients (previously on valproate, lithium, and olanzapine) with bipolar disorder as evidenced by improvements in the YMRS, HDRS, and CGI-S rating scales.
Presented at the 158th Annual Meeting of the American Psychiatric Association, Atlanta, GA, May 21-26, 2005.

341E. Safety and tolerability of extended-release carbamazepine in bipolar disorder: results of two pooled clinical trials. Richard H. Weisler, MD[1], Robert Hirschfeld, MD[2], Andrew J. Cutler, MD[3], Thomas Gazda, MD[4], Terrance Ketter, MD[5], Paul Keck, MD[6], Alan Swann, MD[7], Amir Kalali, MD[8], *Rishit R. Patel, PharmD*[9]; (1)Duke University Medical School and University of North Carolina College of Medicine, Durham, NC; (2)University of Texas Medical Branch at Galveston, Galveston, TX; (3)University of South Florida, Tampa, FL; (4)St. Luke's Medical Center, Scottsdale, AZ; (5)Stanford University School of Medicine, Stanford, CA; (6)University of Cincinnati College of Medicine, Cincinnati, OH; (7)University of Texas Medical School at Houston, Houston, TX; (8)Quintiles CNS Therapeutics, San Diego, CA; (9)Shire US Inc., Wayne, PA.

PURPOSE: To evaluate the safety and tolerability of extended-release carbamazepine capsules (ERC-CBZ; Shire) in a combined study population of patients with Bipolar I Disorder.
METHODS: Data analysis was performed using pooled data from 2 identically designed 3-week, double-blind, placebo-controlled, phase 3 trials of ERC-CBZ monotherapy. Four hundred forty-three patients, aged 18 to 76 years with a DSM-IV diagnosis of bipolar disorder (manic or mixed), were randomized to double-blind treatment with either ERC-CBZ or placebo. Safety and tolerability were assessed by measurements of weight, blood glucose, cholesterol, and QTc, as well as adverse event monitoring.
RESULTS: No clinically significant weight gain in patients treated with ERC-CBZ was observed. Moreover, no significant changes were detected in blood glucose and QTc between treatment groups. No blood dyscrasias, or ECG adverse events were observed. Treatment with ERC-CBZ caused a modest increase in total cholesterol of 21.1 mg/dL. Common treatment-emergent adverse events that occurred in ERC-CBZ–treated group included dizziness (38%), somnolence (28%), and nausea (27%); however, these events were transient, and most occurred during the first week of treatment.
CONCLUSION: Extended-release carbamazepine capsules were found to be safe and tolerable in the treatment of patients with bipolar I disorder. Adverse events were mostly transitory and mild to moderate in nature.
Presented at the U.S. Psychiatric and Mental Health Congress, San Diego, CA, November 18-21, 2004.

342E. Extended-release carbamazepine capsules as monotherapy for bipolar disorder: effect on plasma cholesterol levels and body weight. Terence A. Ketter, MD[1], *Brian Scheckner, Pharm.D.*[2]; (1)Stanford University School of Medicine, Stanford, CA; (2)Shire US Inc., Wayne, PA.

PURPOSE: Several agents for the treatment of bipolar disorder have been shown to increase plasma cholesterol (TC) levels and body weight. Here we report the effect of carbamazepine extended-release capsules (CBZ-ERC) on these parameters.
METHODS: Changes in TC and body weight were analyzed from two 3-week, randomized, double-blind, placebo-controlled studies. Treatment with CBZ-ERC was initiated at 200 mg twice daily and titrated to final doses between 200 and 1600 mg/d. Measurements of random TC and body weight were taken at baseline and day 21. In a 6-month extension study, patients who completed one of two 3-week studies were dosed with blinded blister cards during the first 19 days to allow for CBZ-ERC titration in patients previously on placebo. Patients received CBZ-ERC doses of 200 to 1600 mg/d. Body weight measurements were taken at day 1 (representing day 21 of the previous 3-week studies), day 14, and monthly thereafter; random TC was measured at day 1 and month 6.
RESULTS: Statistically significant increases in mean TC were observed only in patients treated with CBZ-ERC in both 3-week trials (301 study: 196 ± 44 mg/dL [baseline] vs 220 ± 49 mg/dL [end point]; 304 study: 178 ± 40 mg/dL [baseline] vs 199 ± 44 mg/dL [end point]; both *P*<.0001). In the 6-month extension study, no significant changes in mean TC were demonstrated in

patients who were previously treated with CBZ-ERC. However, patients who were previously given placebo showed a statistically significant increase in mean TC (197 ± 42 vs 218 ± 32; *P*<.001). A low incidence of clinically significant weight change (≥7% from baseline) was observed in all studies.
CONCLUSIONS: Monotherapy with CBZ-ERC leads to a significant increase in TC; however, no further increase was observed in long-term therapy. A low incidence of clinically significant weight change was observed in short-term and long-term therapy. Additional studies measuring non-fasting cholesterol values are needed.
Presented at the 45th Annual Meeting of the New Clinical Drug Evaluation Unit, Boca Raton, FL, June 6-9, 2005.

343E. The efficacy of extended-release carbamazepine therapy in older patients with bipolar disorder. Terence A. Ketter, MD[1], *Steven D. Valliere, PharmD, MS*[2]; (1)Stanford University School of Medicine, Stanford, CA; (2)Shire US Inc., Wayne, PA.

PURPOSE: Bipolar disorder among older adults is an increasing public health problem. Two recent randomized, double-blind, placebo-controlled trials conducted using nearly identical protocols demonstrated that monotherapy with carbamazepine extended-release capsules (CBZ-ERC) is effective for the treatment of acute manic and mixed episodes in patients with Bipolar I Disorder. Here we pool the data from these 2 trials to determine the efficacy of CBZ-ERC in older patients with bipolar disorder.
METHODS: This post hoc analysis was performed on pooled data from 2 randomized, placebo-controlled, phase 3 trials of CBZ-ERC monotherapy in the treatment of Bipolar I Disorder. Efficacy was assessed using the Young Mania Rating Scale (YMRS).
RESULTS: We examined the differences in YMRS scores between patients ages 50 and older treated with placebo (n = 29; mean age 55.7 ± 5.4) or with CBZ-ERC (n = 34; mean age 55.2 ± 4.7), and patients younger than 50 treated with CBZ-ERC (n = 180; mean age 34.5 ± 8.3). There were no statistically significant differences between patients treated with placebo, CBZ-ERC patients age 50 and above, and CBZ-ERC patients under 50 in YMRS baseline scores (26.9, 27.4, 27.7, respectively), YMRS end point scores (20.3, 16.9, 15.1, respectively; LOCF), and YMRS change (6.6, 10.6, 12.6, respectively; LOCF). Although there was no significant difference in the percentage of responders between CBZ-ERC patients at least 50 and patients under 50, the percentage of responders was significantly higher in CBZ-ERC patients ≥ 50 than in the placebo group (55.9% vs 24.1%; *P* = .02). Linear regression analysis indicated no correlation between YMRS change and age in either the CBZ-ERC or placebo group.
CONCLUSIONS: Though further research is necessary, these data suggest that CBZ-ERC is effective in treating patients over 50 years of age as measured by YMRS response.
Presented at the 6th International Conference on Bipolar Disorders, Pittsburgh, PA, June 16-18, 2005.

344E. Trending analysis of the StART study. Stephen V. Faraone, PhD[1], David A. Mays, PharmD, MBA, BCPS[2], *Paul Hodgkins, PhD, RAC*[2]; (1)Department of Psychiatry, Syracuse, NY; (2)Shire Pharmaceuticals Inc., Wayne, PA.

PURPOSE: The objective of this study was to analyze the StART data to determine the potential long-term effects of MAS XR and atomoxetine treatment in children with ADHD.
METHODS: A trending analysis was completed in children aged 6–12 years with ADHD (combined or hyperactive/impulsive subtype) to analyze the duration of time needed for atomoxetine outcomes to equal the MAS XR outcomes that were observed at the end of the 3-week StART study. To compute the data for the trending analysis, it was first necessary to analyze the available study data using a nonlinear model. A nonlinear model was essential because a linear model (eg, simple regression) would allow for impossible forecasts, such as negative scores on outcome measures. The model also assumes that, over a period of time, each treatment will eventually produce the best possible outcome.
RESULTS: Atomoxetine did not demonstrate efficacy equivalent to that of MAS XR for clinically significant outcomes (eg, SKAMP normalization), but did match the efficacy of MAS XR for softer outcomes (eg, demonstrating any improvement). Because there are many ways to view these trending analysis data, several types of results were analyzed and are presented. On the CGI, the proportion improved gives the "soft" outcome. Soft outcomes are useful for demonstrating the fairness of our model, allowing the eventual equivalence of atomoxetine and MAS XR.
CONCLUSIONS: The results of this trending analysis suggest that the efficacy of MAS XR at week 3 of the StART study remains superior to that of atomoxetine throughout an 11-week projection. Even with an 11-week projection, atomoxetine did not match the efficacy of MAS XR at week 3. This method assumes that the model used to fit the actual data is a good predictor of the results observed in a trial extended to 11 weeks.
Presented at the Annual Meeting of the American Academy of Child and Adolescent Psychiatry, Toronto, ON, Canada, October 18-23, 2005.

345E. Mixed amphetamine salts and atomoxetine efficacy in school-aged children with ADHD. Scott H. Kollins, PhD[1], Sharon B. Wigal, PhD[2], James J. McGough, MD[3], David A. Mays, PharmD, MBA, BCPS[4], *Chris Paap, PharmD*[5]; (1)Duke University Medical School, Durham, NC; (2)Child Development Center, University of California Irvine, Irvine, CA; (3)David Geffen School of Medicine at UCLA, Los Angeles, CA; (4)Shire Pharmaceuticals Inc., Wayne, PA; (5)Shire, National Medical Science Liaison Manager/Medical Information, Newport, KY.

OBJECTIVE: To compare the efficacy and time course of effect of MAS XR and atomoxetine in school-aged girls and boys with ADHD.
METHODS: A post hoc analysis from a randomized, double-blind, multicenter, parallel-group, forced-dose–titration, laboratory school study of school-aged girls and boys 6–12 years of age with ADHD was undertaken to assess the efficacy of MAS XR vs atomoxetine. The primary efficacy variable was behavior, measured using the deportment subscale of the SKAMP teacher rating scale. Secondary efficacy variables included attention, measured using the attention subscale of the SKAMP, and academic performance, measured by math test scores.
RESULTS: Fifty seven girls and 146 boys were randomized to receive either MAS XR or Atomoxetine. No significant differences were observed in baseline and demographic characteristics between girls and boys for the treatment groups. SKAMP deportment scores for girls revealed a greater improvement in behavior in the MAS XR group at endpoint. ANCOVA revealed the mean change in SKAMP deportment scores from baseline to endpoint was significantly greater for the MAS XR group (P<.0001). Mean SKAMP deportment scores for boys were also similar for both treatment groups at baseline but greater improvement in behavior in the MAS XR group was noted. ANCOVA revealed that the mean change in SKAMP deportment scores from baseline to endpoint was significantly greater for the MAS XR group (P<.0001). The results for both sexes on the SKAMP attention subscale scores followed the same pattern. In addition, significant improvements in academic productivity were observed in both the MAS XR and atomoxetine groups.
CONCLUSIONS: The results from this analog classroom study show that MAS XR resulted in greater improvements in attention and behavior in school-aged children diagnosed with ADHD. Improvement in these symptoms was significantly greater for both all subjects receiving MAS XR compared with those receiving atomoxetine.
Presented at the Annual Meeting of the American Academy of Child and Adolescent Psychiatry, Toronto, ON, Canada, October 18-23, 2005.

346E. Naturalistic study of mixed amphetamine salts XR for adult ADHD. David W. Goodman, MD[1], Margaret Weiss, MD, PhD[2], Lawrence D. Ginsberg, MD[3], Paul Hodgkins, PhD, RAC[4], David A. Mays, PharmD, MBA, BCPS[5], *Hilary Mandler, PharmD*[6]; (1)Johns Hopkins, Lutherville, MD; (2)Women's and Children's, Vancouver, BC; (3)Red Oak Psychiatry Associates, Houston, TX; (4)Shire Pharmaceutical Inc., Wayne, PA; (5)Shire Pharmaceuticals Inc., Wayne, PA; (6)Shire Pharmaceuticals, Wayne, PA.

PURPOSE: The primary objective of this study was to evaluate the safety and tolerability of MAS XR in adults with ADHD in North American community practice settings.
METHODS: This multicenter, prospective, open-label study enrolled eligible American and Canadian subjects for up to 10 weeks of treatment with MAS XR 10–60 mg once daily. A 7-day washout period was required for previously treated patients. Treatment with MAS XR was initiated at 20 mg/d 1 day following the baseline visit. The first 2 weeks of treatment were a dose-evaluation period during which investigators had the option to adjust the dose in 10- to 20-mg increments at weekly intervals to attain optimum effectiveness and tolerability. Patients received 8 additional weeks of MAS XR treatment after the optimum dose was determined. The endpoint for the effectiveness variables was defined as the last available valid postbaseline measure.
RESULTS: Treatment with MAS XR was tolerable. The most commonly reported AEs were mild to moderate in severity and included headache, dry mouth, insomnia, and weight decrease. Interim analysis of the first 200 participants showed that, when treated with an optimal dose of MAS XR for up to 10 weeks, patients with no previous ADHD pharmacologic treatment experienced a 63% improvement in ADHD-RS total scores, those previously treated with a nonstimulant medication experienced a 53% improvement, and those previously treated with a stimulant medication experienced a 65% improvement. The interim analysis of the intent-to-treat population (n=203) showed that the mean change in ADHD-RS scores from baseline to endpoint were significantly improved for patients who were previously untreated (P<0.0001), previously treated with stimulant medication (P<0.0001), and previously treated with nonstimulant medication (P=0.0005).
CONCLUSIONS: This study demonstrated the safety, tolerability, and efficacy of MAS XR treatment in adults with ADHD in a community practice setting through QoL improvements.

Presented at the Annual Meeting of the American Academy of Child and Adolescent Psychiatry, Toronto, ON, Canada, October 18-23, 2005.

347E. Safety of extended-release carbamazepine in bipolar disorder: implications of polypharmacy. Lawrence D. Ginsberg, MD[1], *Larry Segars, PharmD, BCPS*[2]; (1)Red Oak Psychiatry Associates, Houston, TX; (2)Shire US Inc., Wayne, PA.

PURPOSE: The intent of this retrospective review of the charts of 300 patients was to analyze the safety of carbamazepine extended-release capsules (CBZ-ERC) (Shire, Wayne, PA) when given in combination with other psychotropic agents for the treatment of bipolar disorder.
METHODS: Data were obtained from the charts of 300 patients aged 18 to 70 years who met DSM-IV criteria for bipolar disorder. Polypharmacy with CBZ-ERC combined with other psychotropic agents was investigated. Safety was analyzed by comparing the adverse event profiles of patients on CBZ-ERC monotherapy with the profiles of patients on polypharmacy (therapeutic agents were analyzed separately).
RESULTS: When compared to those patients on CBZ-ERC monotherapy, patients taking CBZ-ERC together with other psychiatric agents (antipsychotics, antiepileptics, selective serotonin reuptake inhibitors, other antidepressants, anxiolytics, lithium, and attention-deficit/hyperactivity disorder medications) were no more likely to report gastrointestinal, nervous system, or dermatological adverse events.
CONCLUSIONS: These real-world data suggest that CBZ-ERC is safe in the treatment of patients with bipolar disorder, both as monotherapy and as polytherapy combined with other psychiatric agents.
Presented at the 6th International Conference on Bipolar Disorder, Pittsburgh, PA, June 16-18, 2005.

348E. The effectiveness of changing to carbamazepine extended-release capsules in bipolar disorder. Lawrence D. Ginsberg, MD[1], *Larry Segars, PharmD, BCPS*[2]; (1)Red Oak Psychiatry Associates, Houston, TX; (2)Shire US Inc., Wayne, PA.

PURPOSE: Evaluate the efficacy of carbamazepine extended-release capsules (CBZ-ERC) in the treatment of patients switched from other therapeutic agents for the treatment of their bipolar disorder.
METHODS: Data were obtained from the charts of 187 patients aged 5-70 years who met DSM-IV criteria for bipolar disorder. Clinical response to CBZ-ERC therapy was defined as a score of 3 or lower on the Clinical Global Impression–Improvement (CGI-I) scale. Relapse was defined as a change in CGI-I to 4 or greater in those subjects who had previously achieved clinical response.
RESULTS: Data from patients switched to CBZ-ERC from lamotrigine, valproic acid, olanzapine, oxcarbazepine, lithium, and other formulations of CBZ (immediate-release and extended-release tablets) were analyzed. All groups of patients had mean Clinical Global Impression–Severity (CGI-S) scores above 4.5 at initiation of CBZ-ERC treatment. Scores on the CGI-I indicated that all groups of patients improved after the switch to CBZ-ERC; mean scores for all groups were 2.3 or lower. Interestingly, those patients previously on oxcarbazepine (mean CGI-S score, 5.1) improved dramatically in this analysis (mean CGI-I score, 2.1 at best visit).
CONCLUSIONS: CBZ-ERC are efficacious in the treatment of patients with bipolar disorder switched from other therapies, and may represent an important treatment option in this population.
Presented at the 158th Annual Meeting of the American Psychiatric Association, Atlanta, GA, May 21-26, 2005.

349E. Comparative efficacy of amphetamine and atomoxetine by symptom severity. James J. McGough, MD[1], Sharon B. Wigal, PhD[2], Joseph Biederman, MD[3], Thomas J. Spencer, MD[3], David A. Mays, PharmD, MBA, BCPS[4], *Hilary Mandler, PharmD*[4]; (1)David Geffen School of Medicine, Los Angeles, CA; (2)Child Development Center, University of California Irvine, Irvine, CA; (3)Harvard University and Massachusetts General Hospital, Boston, MA; (4)Shire Pharmaceuticals Inc., Wayne, PA.

OBJECTIVE: To evaluate the effect of MAS XR and atomoxetine on behavior in children with ADHD who had marked or severe impairment at baseline in an analog classroom environment. Other objectives included an evaluation of the effect of MAS XR and atomoxetine on attention in children with ADHD depending on symptom severity.
METHODS: This was a post hoc, analysis of subjects with "markedly" or "severely mentally ill" symptom scores on the CGI-S at baseline, who participated in the StART trial. The primary efficacy measure was the SKAMP Teacher Rating deportment subscale score. Secondary efficacy measures included: SKAMP Teacher Rating attention subscale score; PERMP–10-minute written math test; Conners' 10-Item Global Index Scale, Parent Version (CGIS-P); andCGI-S and CGI-Improvement (CGI-I).
RESULTS: A total of 215 children were randomized to receive double-blind treatment with MAS XR or atomoxetine in the full StART study. Of these subjects, 71 were determined to be markedly or severely ill at baseline. In the MAS XR treatment group, 82% were improved at endpoint and demonstrated ò 30% improvement from baseline on SKAMP deportment (P<0.0001) subscale scores compared with 34% treated with Atomoxetine. SKAMP deportment subscales for subjects not improved at baseline were reduced by -C0.44 overall for MAS XR subjects and -C0.18 for atomoxetine subjects at endpoint. MAS XR and atomoxetine subjects with improvement at endpoint had a statistically significantly increased number of math problems attempted and solved correctly at each weekly study visit and overall compared to baseline (P<0.0001).
CONCLUSIONS: Among the subjects with baseline CGI-S scores of marked or severe impairment in StART who were improved at endpoint, a larger proportion demonstrated improvement during treatment with MAS XR (82%) than with atomoxetine (34%). MAS XR was more efficacious than atomoxetine overall in both improved and not improved subjects in number of problems attempted and answered correctly.
Presented at the Annual Meeting of the American Psychiatric Association, Atlanta, GA, May 21-26, 2005.

350. The selegiline transdermal system: cardiovascular safety from a randomized, double-blind, placebo-controlled trial. *Dan L. Zimbroff, MD*[1], Alan D. Feiger, MD[2]; (1)Pacific Clinical Research Medical Group, Upland, CA; (2)Feiger Health Research Center, Wheat Ridge, CO.

PURPOSE: Monoamine oxidase inhibitors (MAOIs) are effective antidepressants; however, due to cardiovascular risks, the older, orally administered MAOIs require a tyramine restricted diet. Selegiline, an MAOI, has been developed as a transdermal patch, which was evaluated without the need for dietary tyramine restrictions. This study assessed the safety and efficacy of the selegiline transdermal system (STS) in patients with major depressive disorder (MDD); the results herein compare the cardiovascular effects of STS versus placebo in MDD patients.
METHODS: This was a randomized, double-blind, placebo-controlled, multicenter, parallel-group study in adult patients with MDD (single episode or recurrent). After a screening period (up to 28 days), patients were assigned to STS (20 mg/20 cm^2) treatment or matching placebo without dietary restrictions for 8 weeks, with physician-permitted dose escalation up to 40 mg/40 cm^2. Blood pressure, heart rate, 12-lead electrocardiograms and adverse events (AEs) were recorded.
RESULTS: A total of 265 patients (132 STS [52 male and 80 female] and 133 placebo [63 male and 70 female]) were randomized into the study, which 206 patients (100 STS and 106 placebo) completed. There were no clinically meaningful differences in cardiovascular assessments between STS and placebo. No serious cardiovascular AEs were reported. Fifteen STS (11.4%) patients and seven (5.3%) placebo patients reported cardiovascular AEs, including vasodilatation (five STS [3.8%], one placebo [0.8%]), postural hypotension (four STS [3.0%], one placebo [0.8%]), hypotension (one STS [0.8%]), tachycardia (three STS [2.3%]), hypertension (one STS [0.8%], three placebo [2.3%]), palpitation (one STS [0.8%], two placebo [1.5%]) and migraine (one STS [0.8%]). No clinically significant QTc prolongation events were reported.
CONCLUSION: Despite the absence of dietary restrictions, STS did not cause any significant cardiovascular AEs in this 8-week study compared with placebo, suggesting that the cardiovascular risk associated with MAOIs is low when selegiline is administered transdermally.

351. The selegiline transdermal system: preliminary evidence for minimal sexual dysfunction. *Alan D. Feiger, MD*[1], Dan L. Zimbroff, MD[2]; (1)Feiger Health Research Center, Wheat Ridge, CO; (2)Pacific Clinical Research Medical Group, Upland, CA.

PURPOSE: A relatively high incidence of sexual dysfunction is associated with currently available antidepressants, such as selective serotonin reuptake inhibitors and serotonin/norepinephrine reuptake inhibitors. Selegiline, a monoamine inhibitor, has been developed as a transdermal patch delivering sustained and central nervous system targeted antidepressant levels of selegiline, which was evaluated without the need for dietary restrictions. This study assessed the safety and efficacy of the selegiline transdermal system (STS) in patients with major depressive disorder (MDD); the results herein compare the incidence of sexual side effects in MDD patients administered STS versus placebo.
METHODS: This was a randomized, double-blind, placebo-controlled, multicenter, parallel-group study in adult patients with MDD (single episode or recurrent). After a screening period (up to 28 days), patients were randomly assigned to STS (20 mg/20 cm^2) treatment or a matching placebo patch without dietary restrictions for 8 weeks, with dose escalation up to 40 mg/40 cm^2 permitted at the discretion of the physician. Adverse events (AEs) were reported throughout the study.
RESULTS: A total of 265 patients (132 STS [52 male and 80 female] and 133 placebo [63 male and 70 female]) were randomized into the study, of which 206 patients (100 STS and 106 placebo) completed the study. Treatment

emergent AEs relating to sexual function included impotence (one placebo patient [0.8%]), decreased libido (one STS patient [0.8%]), increased libido (one placebo patient [0.8%]) and abnormal sexual function (verbatim term: decreased ability to achieve orgasm) (one STS patient [0.8%]). No statistically significant difference between the two treatment groups was reported. No patients withdrew from therapy due to sexual side effects.
CONCLUSION: A low incidence of sexual dysfunction was reported by patients administered STS. The relatively high incidence of sexual dysfunction associated with currently available antidepressants can lead to non-adherence. Thus STS may offer an alternative for these patients.

352. Metabolic outcomes of psychiatric inpatients on atypical antipsychotics and hypoglycemics: a 6-month pilot study. *Benjamin Chavez, Pharm.D.*[1], Jose A. Rey, Pharm.D.[2]; (1)Rutgers, State University of New Jersey/ Nova Southeastern University, Piscataway, NJ; (2)Nova Southeastern University, Ft Lauderdale, FL.

BACKGROUND: There is a known association between atypical antipsychotics and risk for diabetes. There is evidence showing an association between both the development of diabetes and the worsening of hyperglycemia. However, the exact mechanism by which this occurs is not known. If one hypoglycemic class shows better glycemic control in diabetic patients receiving atypical antipsychotics, the mechanism by which the atypicals affect glycemic control could be theorized.
OBJECTIVES: 1) Determine if one class of hypoglycemic provides better glycemic control for psychiatric patients receiving atypical antipsychotics, 2) Examine if any of the atypical antipsychotics are related to poorer metabolic control than others
METHODS: The records of all the patients at a state psychiatric hospital (n=288) were reviewed to identify patients on hypoglycemic agents and atypical antipsychotics. Inclusion criterion was that they were being monitored for glycemic control. The data collection included weights, body mass indexes, fasting blood glucoses, hemoglobin A1Cs, lipid panels, Axis I diagnoses, Axis III diagnoses, age, sex, ethnicity, and current medications. Data was collected and assessed over a 6 month period. Hypoglycemic control was assessed with fasting blood glucoses and hemoglobin A1C. Metabolic control was assessed with weight changes, body mass indexes, and lipid panels.
RESULTS: A total of 46 patients on atypical antipsychotics were assessed, and 30 of these 46 were also on a hypoglycemic agent. The hypoglycemic agents were divided into sulfonylureas, biguanides, thiazelinediones, and insulin. There were no statistically significant differences in glycemic control between the hypoglycemic agents. However, a numerical trend in improvement was seen with the insulin sensitizers, biguanides and thiazelinediones. All the atypical antipsychotics groups had an increase in weight gain, but none were statistically significant due to the small number of patients per group. There was no statistically significant difference between atypicals and lipid control.

353. Medication evaluation of risperidone, long acting injection in a severely ill, chronic, in-patient schizophrenic population. *Jose A. Rey, Pharm.D.*; Nova Southeastern University, Ft Lauderdale, FL.

PURPOSE: Several options have been developed to improve medication adherence, a significant issue among the schizophrenic population. With the combined benefit of improved efficacy against negative symptoms, improved side effect profile, and guaranteed compliance, risperidone, long acting injection (R-LAI) provides practitioners with an exciting, new alternative. The objective of this study is to evaluate R-LAI among a severely ill, chronic, in-patient schizophrenic population.
METHODS: A retrospective chart review was conducted at a state psychiatric hospital between December 2003 and May 2005 to evaluate clinical outcomes with R-LAI therapy (25mg, 37,5mg, and 50mg). Primary efficacy measures included the PANSS assessment and subscales, which were conducted at baseline, 6-months after R-LAI initiation, and at the time of discharge from the hospital. Secondary measurements included discharge rates, evaluation of combination psychotropic therapy, and laboratory measurements.
RESULTS: Sixty-five patients were included in the analysis (mean age 41.1; 61.5%% male; 44.6% white). The number of patients receiving R-LAI 25mg, 37.5mg, and 50mg at baseline were 54, 9, 2, respectively; and, at 6 months, 3, 23, 9 respectively. After an average of 3.70 months, 18.5% (n=12) had discontinued R-LAI; after an average of 3.21 months and a mean dose of 33.33mg, 27.7% (n=18) were discharged on R-LAI. Interestingly, the mean number of total psychotropics and antipsychotic agents per patient remained consistent throughout therapy. Changes in metabolic parameters were not statistically significant (n=49). Statistically significant improvements in the Positive, General Psychopathology, and Total PANSS scores were found (n=28): Positive (30.6 to 23.9, p<0.001); General Psychopathology (58.6 to 47.3, p<0.01); Total PANSS (115.2 to 94.1, p<0.01), respectively. There was no statistically significant difference in the Negative Scale (26.0 to 22.9, p=0.13).
CONCLUSION: Our initial evidence supports the efficacy of R-LAI among this difficult-to-treat, in-patient population.

354. The first year of safety experience with post-marketing use of olanzapine's intramuscular formulation. Sebastian Sorsaburu, MD, Kenneth Hornbuckle, DVM, PhD, Debbie Blake, BS, Debbie Falk, BS, Mary Anne Dellva, MS, Janice Carlson, PhD, Robert W. Baker, MD, Patrizia Cavazzoni, MD, *John P. Houston, MD*; Eli Lilly and Company, Indianapolis, IN.

PURPOSE: Agitation is common in patients with psychiatric disorders, often requiring the use of intramuscular (IM) medications for its management. Agitation is difficult to treat because of the unpredictable consequences of this state on organ systems. Psychotropic polypharmacy may increase the risk of a fatal outcome.
METHODS: Lilly maintains a safety database containing worldwide postmarketing AEs (including literature and spontaneous reports). This report addresses postmarketing AEs reported in patients treated with olanzapine IM treatment through December 31, 2004.
RESULTS: During the first year post-launch, the estimated worldwide patient exposure to olanzapine IM was 278,600; 91 cases were reported in patients treated with olanzapine IM (mean age=46.5 years, range 11-98 years; 56% male, 43% female, 1% unknown). The psychiatric conditions included schizophrenia (20%), bipolar disorder (13%), unspecified psychosis (8%), dementia (6%), and substance abuse (3%). Reported concomitant benzodiazepine use was 42%, and concomitant use of one or more antipsychotics other than olanzapine was 39%. The primary AEs in the cases were categorized as cardiovascular (28%; e.g. hypotension), central nervous system (23%; e.g. sedation), psychiatric (15%; e.g. agitation), respiratory (6%; e.g. pulmonary embolism), or other (29%; e.g. increased blood creatine phosphokinase). Fifteen fatalities were reported. The majority of patients had schizophrenia (n=10) and had multiple concomitant medications (benzodiazepines = 73%, other antipsychotics = 87%). The primary events reported in these cases were cardiovascular (47%), respiratory (20%), central nervous system (20%), or other (13%). Thirteen of the fatal cases had medically important comorbidities or other contributing or confounding factors.
CONCLUSIONS: Most of the fatal cases presented with serious concurrent medical conditions and polypharmacy. Given the known challenges associated with the management of agitation and consistent with accepted optimal medical practice, careful monitoring of patients with severe acute agitation treated with IM antipsychotics is advisable, especially when multiple medications are used.

355E. Adjunctive eszopiclone and fluoxetine in major depressive disorder and insomnia: effects on sleep and depression. W. Vaughn McCall, MD, MS[1], Mauricio Fava, MD[2], Daniel J. Buysse, MD[3], Robert Rubens, MD[4], Thomas C. Wessel, MD[4], Judy Caron, PhD[4], David Amato, PhD[4], *Andrea J. Anderson, PharmD*[4], Thomas Roth, PhD[3]; (1)Wake Forest University Department of Psychiatry and Behavioral Medicine, Clinical Science Building, Winston-Salem, NC; (2)Massachusetts General Hospital, Boston, MA; (3)University of Pittsburgh School of Medicine, Western Psychiatric Institute and Clinic, Pittsburgh, PA; (4)Sepracor Inc., Marlborough, MA; (5)Henry Ford Hospital Sleep Disorders Center, Detroit, MI.

PURPOSE: Insomnia can co-exist with depression. This study evaluated the efficacy of eszopiclone in patients with major-depressive-disorder (MDD) and co-morbid insomnia during concurrent fluoxetine treatment.
METHODS: Patients who met DSM-IV criteria for MDD and insomnia received 10 weeks of fluoxetine QAM and were randomized to nightly eszopiclone 3mg (n=270) or placebo (n=275) for 8 weeks; additional inclusion criteria were sleep latency (SL) ≥30 minutes, wake-time-after-sleep-onset (WASO) ≥45 min, and total sleep time (TST) ≤390 min. Subjective sleep and daytime function were assessed weekly. Depression was assessed with the HAM-D17 (every 4 weeks) and the Clinical-Global-Impression Improvement (CGI-I) and Severity scales (CGI-S) each visit. Depression response=50% or greater decrease from baseline HAM-D17; remission=HAM-D17≤7.
RESULTS: Compared with fluoxetine-placebo, fluoxetine-eszopiclone co-administration resulted in significantly decreased SL and WASO, and greater TST at each treatment visit (p<0.03); higher ratings across the treatment period in sleep quality and depth (p<0.005); and higher ratings of daytime alertness, ability to concentrate, and well-being (p≤0.02). The Insomnia-Severity-Index indicated that more eszopiclone patients had no clinically meaningful insomnia at Week 8 (55% versus 37%, p=0.0004). Eszopiclone co-administration resulted in significantly decreased HAM-D17 scores at Week 4 (p=0.01) with progressive improvement at Week 8 (p=0.002). These differences remained significant after removing the insomnia items at Week 8 (p=0.04). At Week 8, significantly more eszopiclone patients were responders (59% vs 48%, p=0.009) and remitters (42% vs 33%, p=0.03). CGI-I and CGI-S scores were significantly improved with eszopiclone co-administration (p<0.05). Treatment was well-tolerated, with similar adverse event and dropout rates. Unpleasant taste was more common with eszopiclone.

CONCLUSIONS: In this study, eszopiclone/fluoxetine co-administration was well tolerated and associated with significantly improved sleep and daytime function. Significant improvements in several of the antidepressant measurements were observed in the eszopiclone/fluoxetine arm as compared to the placebo/fluoxetine arm in patients with MDD and insomnia.
Presented at the 45th Annual Meeting of the New Clinical Drug Evaluation Unit, Boca Raton, FL, June 6-9, 2005.

356E. Depression screening in primary care. *Patricia L. Canales, Pharm.D.*; University of Texas-Pan American and the University of Texas at Austin, Edinburg, TX.

PURPOSE: This study aimed to identify the rate of depression in an indigent Hispanic primary care population, identify patient factors that correlate to the occurrence of depression, and compare depression primary care services before and after the initiation of depression self-screening. The main hypothesis was that depression screening will be associated with an increase in depression diagnoses, new orders for antidepressants, and/or counseling referrals.
METHODS: Medical charts and medication records were reviewed retrospectively for the 6 months prior to the initiation of depression screening services and the 6 months following the initiation of depression screening services. All patients 18 years or older presenting to the clinic site for general medical care underwent screening with the Quick Inventory for Depressive Symptoms-Self-Rated (QIDS-SR). Depression primary care services under evaluation included documentation by the provider indicating awareness of screening results, documentation of further assessment, counseling referrals made, initiation of antidepressant medication, drug selection and dosing, and duration of treatment.
RESULTS: Preliminary findings show that 31% of patients (N=134) who underwent screening scored a 12 or greater, consistent with moderate depressive symptoms. One-third of this 31% scored a 21 or greater, consistent with severe symptoms. Of those who scored a 12 or greater, only one was started on antidepressant therapy. Acknowledgement of the screening score by the provider was noted in progress notes of only two patients.
CONCLUSIONS: While data analysis is pending, it is evident that depression screening has improved depression detection but has not influenced depression management by primary care providers.
Published in Pharmacotherapy 2005;25(3):139.

357. Do different antipsychotic agents used to treat schizophrenia have varying effects on the risk of coronary heart disease? *Craig I. Coleman, PharmD*, C. Michael White, PharmD; University of Connecticut/Hartford Hospital, Hartford, CT.

PURPOSE: Antipsychotic agents are chronic therapies with differing effects on total cholesterol. Although the relationship between total cholesterol and coronary heart disease (CHD) mortality risk is well described, the risk of CHD mortality due to changes in total cholesterol arising from different antipsychotics has not been appreciated. The aim of this study was to model the predicted impact of different antipsychotic agents on patients' risk of CHD mortality using Monte Carlo simulation.
METHODS: This study uses a Monte Carlo simulation of 6-year CHD mortality based on total cholesterol effects for people using the different antipsychotic agents. In this model the cholesterol data from study 054 for ziprasidone, risperidone, olanzapine, haloperidol, thioridazine and quetiapine were incorporated into multiple 1,000 patient Monte Carlo simulations. These simulations were used to determine each populations 6-year risk of CHD mortality using the equation derived from the Multiple Risk Factor Intervention Trial [6-Year CHD Death Risk = 0.577 e 0.0113 (total cholesterol); R2=0.98]. The percentage risk of having CHD death within 6-years with 95% confidence intervals is reported.
RESULTS: The order of CHD mortality risk from highest to lowest was thioridazine (5.27%; CI 5.02–5.52) = olanzapine (5.15%; CI 5.11–5.19) > quetiapine (4.92%; CI 4.87–4.97) = risperidone (4.92%; CI 4.89–4.95) > ziprasidone (4.02%; CI 3.89–4.15) > haloperidol (3.51%; CI 3.34–3.67).
CONCLUSIONS: Based on our model, the choice of antipsychotic agent may be associated with marked differences in CHD mortality risk over 6-years versus other agents.

536. Evaluation of antipsychotic utilization and ethnicity in the pharmacotherapy of chronic and persistent neuropsychiatric illness. *Kara Shirley, Pharm.D., BCPS, BCPP*, Department of Pharmacy Practice, Albany College of Pharmacy, Albany, NY.

PURPOSE: Recent investigations have reported atypical antipsychotics to be underutilized in African American schizophrenics. Our investigation examines the extent and type of variation in antipsychotic prescription patterns for patients with schizophrenia, schizoaffective and other psychotic disorders, as they relate to ethnicity and antipsychotic utilization patterns.
METHODS: Our IRB approved retrospective chart review examined inpatients discharged from the Capital District Psychiatric Center 2001 through 2004. Ethnicity was described as observed race from chart records. Antipsychotic utilization data were collected for each patient discharged. Primary measures of clinical antipsychotic efficacy included: length of stay and rate of subsequent readmission, and change in Global Assessment of Functioning Scale (GAF) and Abnormal Involuntary Movement Scale scores. Exclusion criteria included patients who were under 18 years of age, received more than four medications for their primary Axis I diagnosis or who were psychotic due to a General Medical Condition. Antipsychotic prescription patterns were compared using both univariate and multivariate analyses with Tukey's statistic conducted for multiple comparisons. Results were considered statistically significant when p values were less than 0.05.
RESULTS: This investigation did not find any statistically significant ethnic disparities in antipsychotic utilization rates. Routine utilization of the GAF as our sole measure of efficacy limited our ability to associate severity of illness and atypical antipsychotic utilization. Additional limitations include the naturalistic nature of this investigation as well as our relatively small sample size n=280. Although observations of prior antipsychotic utilization were included, no direct measures of prior adherence were available. Other possible explanations for variable utilization rates include differing perceptions of appropriate pharmacotherapy, outpatient access to services, expectations about pharmacotherapy and sociocultural issues.

Pulmonary

358E. Switching from ipratropium to tiotropium improves short-term clinical outcomes in patients with chronic obstructive pulmonary disease. *Craig S. Conoscenti, MD*[1], Steven Kesten, MD[1], Walter Vincken, MD[2], Jan A. van Noord, MD[3], Piet Cornelissen, PhD[4]; (1)Boehringer Ingelheim, Ridgefield, CT; (2)Academic Hospital University of Brussels, Brussels, Belgium; (3)Atrium Medical Centre, Heerlen, Netherlands; (4)Boehringer Ingelheim bv, Alkmaar, Netherlands.

PURPOSE: Tiotropium 18mcg daily has proven superior to ipratropium bromide 36mcg qid for multiple outcomes in trials of up to one year. However, it is assumed that short-term fluctuations in clinical status do not occur when patients are switched from ipratropium to tiotropium. This post-hoc analysis investigated potential changes in clinical status when treatment was switched from ipratropium to tiotropium in COPD patients.
METHODS: From previously-reported, one-year clinical trials (tiotropium vs. ipratropium), we conducted a post-hoc analysis in patients receiving ipratropium prior to randomization who either continued with blinded ipratropium or were switched to blinded tiotropium. We compared outcomes over the first 4 weeks on variables indicating clinical improvement or deterioration. Variables included %patients with mean weekly change in AM PEFR of ≥5% or ≥10%, or in albuterol use of ≥1 puff/day, and mean weekly %patients who had a COPD exacerbation. Outcomes were defined by relative risk (RR) (%tiotropium/%ipratropium).
RESULTS: Of the entire cohort (n=535), 332 patients were receiving ipratropium prior to randomization. Cohort mean age=65 years; %men=85%. Mean baseline FEV_1=1.14L (%predicted=41%). RR for increases or decreases in AM PEFR and albuterol use were:

	AM PEFR				Albuterol (puffs/day)	
	Increase ≥5%	Decrease ≥5%	Increase ≥10%	Decrease ≥10%	Increase ≥1	Decrease ≥1
Week 1	1.60	0.63	1.52	0.42	1.00	1.17
Week 2	1.90	0.50	1.76	0.61	0.72	1.31
Week 3	1.78	0.46	1.95	0.26	0.63	1.41
Week 4	1.77	0.38	1.64	0.40	0.83	1.38

In the first week, 4 exacerbations occurred in the tiotropium group compared with 0 in the ipratropium group. Cumulative RR of a COPD exacerbation over Weeks 2, 3 and 4 were 1.16, 0.93, and 1.00.

CONCLUSION: Patients switched to tiotropium from ipratropium were more likely to have improvements in these short-term clinical outcomes than if they had remained on ipratropium. Funding: Boehringer Ingelheim
Published in Chest 2004;126(4):837S-8S.

Rheumatology

359E. Febuxostat vs allopurinol controlled trial in subjects with hyperuricemia and gout (FACT): a multicenter, phase 3, randomized, controlled, double-blind clinical study. *Michael A. Becker, MD*[1], H. Ralph Schumacher Jr., MD[2], Robert L. Wortmann, MD[3], Patricia A. MacDonald, NP[4], William A. Palo, MS[4], Denise Eustace, BS[4], Nancy Joseph-Ridge, MD[4]; (1)University of Chicago, Pritzker School of Medicine, Chicago, IL; (2)University of Pennsylvania School of Medicine, Veterans Affairs Medical Center, Philadelphia, PA; (3)University of Oklahoma, Dept of Internal

Medicine, Tulsa, OK; (4)TAP Pharmaceutical Products, Inc, Lake Forest, IL.

PURPOSE: Safety and urate-lowering efficacy of febuxostat, a novel non-purine selective inhibitor of xanthine oxidase, and allopurinol were compared in a 52-week study.
METHODS: Subjects (760) with gout and serum urate levels (sUA) ≤8.0 mg/dL were randomized to once daily febuxostat 80 mg or 120 mg, or allopurinol 300 mg. Primary endpoint was the proportion of subjects in each treatment group with last 3 monthly sUA <6.0 mg/dL.
RESULTS: Most subjects were male (96%), Caucasian (77%), ≤45 years (70%), and had gout a mean of 12 years. Comorbid conditions included hypertension (44%), hyperlipidemia (34%), cardiovascular disease (CVD) (10%), obesity (62%), and alcohol use (66%). Only 44% of subjects had a recent history of urate-lowering therapy. Proportions of subjects achieving the primary endpoint were 53% (febuxostat 80mg), 62% (febuxostat 120mg), and 21% (allopurinol 300mg) ($p<0.05$ for each febuxostat group versus allopurinol). Proportion of subjects with sUA <6.0 mg/dL at Week 52 was significantly greater in each febuxostat group (81%: 80 mg; 82%: 120mg) compared to allopurinol (39%) ($p<0.05$). Most adverse events (AEs) were mild to moderate in severity. Incidence of treatment-related AEs, including liver function abnormalities, diarrhea, headache, joint-related signs/symptoms, and musculoskeletal/connective tissue symptoms, was similar across treatment groups. Four non-treatment-related deaths occurred; 47 subjects across all treatment groups reported other serious AEs, most related to cardiac disorders in those with underlying CVD and/or risk factors.
CONCLUSION: Significantly greater proportions of subjects receiving febuxostat 80 mg or 120 mg achieved sUA <6.0 mg/dL compared with subjects receiving allopurinol 300 mg. Febuxostat was safe and well tolerated at 80 mg and 120 mg daily.
Published in Arthritis Rheum 2004;50:4103-4.

Substance Abuse/Toxicology

360. Illicit use of specific prescription stimulants: prevalence, motives, and routes of administration. *Christian J. Teter, Pharm.D., BCPP*[1], Sean E. McCabe, M.S.W., Ph.D.[2], James A. Cranford, Ph.D.[2], Carol J. Boyd, MSN, Ph.D., RN, FAAN[2]; (1)Northeastern University & McLean Hospital, Boston, MA; (2)University of Michigan, Ann Arbor, MI.

PURPOSE: The primary goal of this study was to build upon our previous work (Teter et al. Journal of American College Health 2005; 53:253-262) in order to (1) identify specific prescription stimulants often used illicitly by college students, and (2) characterize motives for illicit use of prescription stimulants and routes of administration associated with this form of drug use by college students.
METHODS: In 2005, a random sample of college students (n = 4,580) self-administered a Web-based survey. The survey contained a variety of items pertaining to the illicit use of prescription stimulants. An extensive list of prescription stimulants was provided using a check-all-that-apply format. This allowed students to indicate the specific prescription stimulants they had illicitly used during the past year.
RESULTS: The lifetime and past-year prevalence of illicit use of stimulant medication was 8.5% and 6.0%, respectively. Approximately three of every four (76%) illicit prescription stimulant users reported using amphetamine/dextroamphetamine (e.g., Adderall) in the past year and approximately one in four (25%) reported using methylphenidate (e.g., Ritalin, Concerta, Metadate, Methylin). The motives for illicit use most commonly reported were to help with concentration (65%) and to help study (60%). Other common motives included to increase alertness (48%), get high (31%) and experimentation (30%). Nearly every illicit user (95%) reported oral administration although 38% reported snorting prescription stimulants.
CONCLUSIONS: College students continue to illicitly use prescription stimulants for a variety of reasons and many are using them via the intranasal route. This study is the first to provide empirical evidence that illicit use of amphetamine/dextroamphetamine (e.g., Adderall) is more prevalent than illicit use of methylphenidate formulations. These results have important implications for research as well as education and prevention efforts aimed at reducing illicit use of prescription stimulants.

Transplant/Immunology

361. Limited sampling strategies for mycophenolic acid area under the concentration-time curve in lung transplant recipients. *Lillian S. L. Ting, BSc.(Chem), MSc.(Pharm)student*[1], Nilufar Partovi, BSc(Pharm), PharmD[2], Robert D. Levy, MD, FRCPC[3], K. Wayne Riggs, BSc(Pharm), PhD[1], Mary H. H. Ensom, BS(Pharm), PharmD, FCCP[4]; (1)University of British Columbia, Vancouver, BC, Canada; (2)University of British Columbia and Vancouver General Hospital, Vancouver, BC, Canada; (3)University of British Columbia, St. Paul's Hospital and BC Transplant Society, Vancouver, BC, Canada; (4)University of British Columbia and Children's & Women's Health Centre of British Columbia, Vancouver, BC, Canada.

PURPOSE: To define optimal limited sampling strategies (LSSs) for mycophenolic acid (MPA) monitoring and to test their predictive performance in lung transplant recipients.
METHODS: Following written informed consent and upon administration of a steady-state morning mycophenolate mofetil dose, blood samples were collected at 0,0.3,0.6,1,1.5,2,4,6,8,10, and 12 hours from 19 lung transplant recipients. Total plasma MPA concentrations were measured by a validated high-performance liquid chromatography method with ultraviolet detection and pharmacokinetic parameters analyzed by non-compartmental modeling (WinNonlin 4.1). Patients were randomly divided into the index group (n=10) and validation group (n=9). LSSs for estimating area under the concentration-time curve (AUC) were determined using the index group data by multiple regression analysis with forward stepwise elimination (Statistica® 5.1). Potential LSSs were restricted to 3 or fewer time points within the first 2 hours post-dose. The validation group data were used to test the predictive performance [coefficient of determination (r^2), bias and precision] of LSSs developed from the index group. All concentrations and AUC values were log-transformed to normalize the data.
RESULTS: The correlation between AUC and single concentrations was generally poor (r^2 range 0.18 to 0.73). The best LSSs for 2- and 3-concentrations (and their predictive performance) were:

Equation 1: LogAUC=0.241LogC0+0.406LogC2+1.140; bias=-5.82 precision=5.97%; r^2=0.828

Equation 2: LogAUC=0.153LogC0+0.327LogC0.6+0.354LogC2+1.000; bias=-3.70%; precision=5.81%; r^2=0.873

CONCLUSIONS: To our knowledge, these are the first precise and accurate limited sampling strategies for predicting MPA AUC developed specifically for lung transplant recipients. These optimal and most clinically feasible LSSs are based collectively on the number of blood samples required, r^2, bias and precision. Our study template provides a guide for other centers to develop accurate and precise LSSs specific to their own patient population.

362. Genetic variation in UDP-glucuronosyltransferases and metabolism of mycophenolic acid in lung transplant recipients: a preliminary study. *Lillian S. L. Ting, BSc.(Chem), MSc.(Pharm)student*[1], Olivier Bernard, BSc.(Pharm), MSc.[2], Chantal Guillemette, PhD[2], Mary H. H. Ensom, BS(Pharm), PharmD, FCCP[3]; (1)University of British Columbia, Vancouver, BC, Canada; (2)CHUL Research Center, Laval University, Quebec City, QC; (3)University of British Columbia and Children's & Women's Health Centre of British Columbia, Vancouver, BC, Canada.

PURPOSE: Due to wide inter-patient variability observed in the pharmacokinetics of mycophenolic acid (MPA) and MPA glucuronide (MPAG) in lung transplant recipients, the purpose of this study was to assess associations between polymorphisms in UDP-glucuronosyltransferase (UGT) genes with the MPAG/MPA metabolic ratio.
METHODS: Following written informed consent, blood samples were obtained at 0,0.3,0.6,1,1.5,2,4,6,8,10 and 12 hours after mycophenolate mofetil administration to 15 patients. Concentrations of MPA and MPAG were determined by a validated high-performance liquid chromatography method with ultraviolet detection. Metabolic ratios (MPAG/MPA) were log-transformed. Genetic polymorphisms in the UGT1A1, UGT1A8 and UGT1A9 genes were identified by direct sequencing of polymerase chain reactions and compared to a reference sequence. Both heterogeneous and homogeneous polymorphisms were pooled as one group. One-way analysis of variance was used to correlate polymorphisms with PK metabolic ratios.
RESULTS: Three, seven and two known polymorphisms were investigated for the UGT1A1, UGT1A9 and 1A8 genes, respectively. Trends ($0.1<p<0.2$) were observed with higher MPAG/MPA ratios for the UGT1A8 $A^{173}G$ variant and with lower MPAG/MPA ratios for the UGT1A8 variant $C^{277}Y$. Due to the small sample size, no associations with MPAG/MPA ratios were observed for UGT1A1 and UGT1A9 promoter and coding region polymorphisms.
CONCLUSIONS: This pilot study shows a trend toward correlation between UGT1A8 genetic polymorphisms and metabolic ratios of MPA. These observations prompt a larger study to identify UGT genes that could influence MPA metabolism in order to individualize immunosuppressive therapy in this patient population.

363E. Early corticosteroid elimination with extended thymoglobulin therapy provides lower acute rejection compared to steroid treated controls in simultaneous kidney pancreas transplantation. *Tiffany E. Kaiser, Pharm.D.*, Rita R Alloway, PharmD, Gautham Mogilishetty, MD, Prabir Roy-Chaudhury, MD, Adele H Rike, PharmD, E Steve Woodle, MD, Michael J Hanaway, MD; University of Cincinnati, Cincinnati, OH.

PURPOSE: Initial experiences with early corticosteroid elimination (ECE) in simultaneous kidney pancreas transplant (SKPT) using induction and 3 drug

maintenance immunosuppression (IS) has resulted in good graft survival and low rejection rates. We demonstrate our results in ECE SKPT utilizing Thymoglobulin induction (TI) and 2 drug maintenance IS.
METHODS: 41 consecutive SKPT at a single center (1999–2004) were retrospectively analyzed for graft and patient survival, rejection and medication related toxicities at one year post-transplant (txp). Both groups received TI and maintenance IS of FK and MMF. The control group (n=20) was maintained on chronic corticosteroids (CS) and ECE group (n=21) had CS discontinued on post txp day 5. Statistics included Chi square analysis and Students' *t*-test.
RESULTS: No differences in recipient age at txp, gender or race between groups. Mean followup for control and ECE was 1166 and 288 days respectively. Mean FK levels or daily MMF doses at 3, 6 or 12 months post txp did not differ between groups; ECE group received significantly higher (p=0.0002) median total Thymoglobulin dose (7.4 mg/kg for ECE vs 4 mg/kg control). Biopsy proven acute renal allograft rejection was 30% (6/20) in control, compared to 5% (1/21) in ECE group. Incidence of biopsy proven calcineurin inhibitor toxicity (CIN) was 20% (4/20) in controls, compared to none in ECE group (p=0.01). Patients in ECE group had less blood pressure (BP) medications at 1 year post-txp (compared to pre-txp) than control group, as well as more persistent anemia, and multiple episodes of leukopenia. No PTLD, EBV, CMV or BK virus infection were reported in either group.
CONCLUSIONS: ECE in SKPT recipients has a lower rejection rate than patients maintained on chronic CS. This regimen did not result in infectious complications associated with over-IS and was not associated with an increased risk of CNI toxicity.
Presented at the American Transplant Congress, Seattle, WA, May 20-26, 2005.

364. Steroid withdrawal improves one-year outcomes in pancreas transplantation. *Ghazal Vessal, PharmD*[1], Anne Wiland, PharmD[2], David Klassen, MD[3], Benjamin Philosophe, MD[3], Thomas C. Dowling, Pharm.D., Ph.D.[1], Matthew Weir, MD[3]; (1)University of Maryland, Baltimore, MD; (2)Pharmacy services, University of Maryland Medical System, Baltimore, MD; (3)University of Maryland, School of Medicine, Baltimore, MD.

PURPOSE: To examine the feasibility of a steroid withdrawal protocol in pancreas transplantation.
METHODS: This retrospective study evaluated 28 pancreas transplant recipients who underwent steroid withdrawal (Feb 2002-Dec 2003, WG) and 34 patients transplanted using maintenance steroids (Jan 2001-Sept 2002, MG). Immunosuppression consisted of thymoglobulin induction followed by tacrolimus and mycophenolate mofetil in both groups. Steroids were withdrawn at 21 days post transplant in the WG, and continued in the MG. Rejection rate and survival (patient and graft) were compared between the two groups during a 12 month follow-up period.
RESULTS: There were 11 PTA (pancreas transplant alone), 6 PAK (pancreas after kidney), 5 SPLK (simultaneous pancreas and living kidney), and 6 SPK (simultaneous pancreas and kidney) transplant recipients in the withdrawal group (WG) and 8 PTA, 11 PAK, 13 SPLK and 2 SPK recipients in the maintenance group (MG).Demographic characteristics of recipients and donor variables were similar among both groups. Mean trough levels of tacrolimus were 11.8 ± 2.5, 11.6 ± 5, 7.8 ± 4, and 9.1 ± 6.6 ng/ml in the WG, and 14.6 ± 3.6, 13.9 ± 5, 11.7 ± 5, and 10.6 ± 4.7 ng/ml in the MG at 1, 3, 6, and 12 months post transplant respectively. The one-year rejection rate was 32% and 38% in the WG and MG respectively (P=.41).The one-year graft and patient survival rates were 96.5% and 100% in the WG, and 79.5% and 88% in the MG respectively (P=.05 and .083). Cytomegalovirus (CMV) infection occurred in 18% and 27% of patients in the WD and MG respectively (P= .28). However, the frequency of all other infections was significantly lower in the WG (57%) vs the MG (82.8%) (P=.03).
CONCLUSION: Corticosteroid withdrawal did not increase the rejection rate in pancreas transplant recipients. Maintenance corticosteroid was associated with higher rates of infection and graft loss.

365. Prevalence of hypercholesterolemia and predictors of total cholesterol levels in predominantly African-American renal allograft recipients. *Jennifer L. Clemente, PharmD*[1], Abdolreza Haririan, MD[1], Dale H Sillix, MD[1], Jose M El-Amm, MD[1], Katherina Morawski, RN[1], Miguel S West, MD[1], Scott A Gruber, MD, PhD[1], James Garnick, PharmD, BCPS[2]; (1)Harper University Hospital, Detroit, MI; (2)Banner Good Samaritan Health, Phoenix, AZ.

PURPOSE: Hypercholesterolemia (HC), an important risk factor for atherosclerosis, is common in renal allograft recipients (RAR). The primary objectives of this study were examining the prevalence of HC, determining the fraction of patients with optimal total cholesterol (TC) levels (<200 mg/dl), and identifying predictors of TC in a predominantly African-American (AA) cohort of RAR.
METHODS: Data on donor source, recipient characteristics, TC, liver enzymes and CPK, immunosuppressive regimen, and lipid therapy with its adverse effects were collected from 110 adult RAR (90% AA) transplanted from Apr. 2001 to Sep. 2004 at our institution. HC was defined as TC>200 mg/dl or being on drug therapy. Regression models and chi-square were used to assess the association of potential risk factors with HC and TC.
RESULTS: The percentages of patients with HC at 3, 6, and 12 months were 55% (N=110), 57% (N=93), and 66% (N=71), respectively. Of these, 44(73%) at 3, 37(70%) at 6, and 42(89%) at 12 months were on lipid-lowering agents (32%, 35%, & 31% with suboptimal TC, respectively). Among the variables examined, sirolimus (SRL) and prednisone therapy were independent predictors of TC at 3 and 6 months (coefficient=58.1 & 54.8, P<0.001 & 0.001, for SRL, and coefficient=3.0 & 3.5, P=0.002 & 0.045, for prednisone, respectively). Male sex (coefficient=35.9, P=0.002) was the only variable associated with TC at 12 months. Among patients taking statins, 17 experienced myopathy or elevated liver enzymes or CPK, and only 6 maintained optimal TC levels after change in therapy.
CONCLUSION: This study suggests that HC is prevalent in AA RAR. A significant fraction of patients are not at target levels, and adverse drug effects are not uncommon and can result in treatment failure. SRL and prednisone are independent predictors of TC. Patients receiving these agents should be monitored more closely for HC and treated aggressively.

366. Predictors of cardiovascular risk and events in renal transplant recipients receiving early corticosteroid withdrawal versus chronic corticosteroids. *Adele H. Rike, Pharm.D.*, Gautham Mogilishetty, MD, Rita R. Alloway, Pharm.D., Paul Succop, PhD, Prabir Roy-Chaudhury, MD, PhD, Tiffany E. Kaiser, Pharm.D., Kimi Ueda, Pharm.D., E Steve Woodle, MD; University of Cincinnati, Cincinnati, OH.

PURPOSE: Cardiovascular (CV) disease is the leading cause of death with a functioning graft in renal transplant recipients. Framingham risk score (FRS) has been shown to underestimate CV risk in renal transplant recipients. Incorporation of non-traditional risk factors, such as metabolic syndrome (MS), may more accurately assess CV risk in this population. A primary consideration for minimizing corticosteroids is CV risk reduction. Purpose of this study was to determine risk for coronary heart disease and incidence of MS in patients receiving early corticosteroid withdrawal (ECSWD) and patients on chronic corticosteroids (CCS), comparing risk to occurrence of post-transplant CV events (CVE).
METHODS: 258 ECSWD and 149 CCS patients retrospectively evaluated. FRS was calculated at baseline, 6, 12 and 24 months posttransplant. FRS based on age, gender, smoking, diabetes, HDL, total cholesterol, and blood pressure. MS was defined by NCEP ATP III and WHO guidelines. CVE included sudden death, MI, angina, unstable angina, or CVA/TIA. Repeat measure logistic regression used to determine differences in FRS and MS between groups and correlation of therapy with CVE.
RESULTS: 54 patients experienced 72 total CVE. Mean follow-up was 755 312 days and mean time to CVE was 14.8 8.3 months. Demographics similar between groups. FRS increased significantly with time in both groups (p=0.0001). FRS was not significantly different between groups at any time point. New onset MS was significantly greater in patients receiving CCS (p=0.015). MS correlated with increase in CVE (p=0.032). CVE were significantly increased in CCS group compared to ECSWD (p=0.024).
CONCLUSION: FRS was similar between groups. ECSWD regimens decrease CV risk and CVE compared to CCS. New onset MS is significantly higher with CCS. Presence of MS increases CV risk and correlates with more CVE. Incorporation of other risk factors into FRS may more accurately predict CV risk in renal transplant recipients.

367. Timing of renin-angiotensin system blockade in renal transplantation. *Lisa M. Taylor, Pharm.D.*, Kelly M Smith, Pharm.D., Daniel A. Lewis, Pharm.D., Thomas H Waid, M.D., Timothy M Clifford, Pharm.D.; University of Kentucky Chandler Medical Center, Lexington, KY.

PURPOSE: Chronic allograft nephropathy (CAN) is a leading cause of late renal allograft loss. The use of angiotensin converting enzyme inhibitors (ACE-Is) and angiotensin receptor blockers (ARBs) in renal transplantation is controversial. Our objective was to determine the effect of early (< 1 month; Group 1) versus late (1- 6 months; Group 2) initiation of ACE-I/ARB following transplantation on long-term graft function, graft and patient survival.
METHODS: Retrospective chart review of patients receiving renal transplant prior to November 2003, ACE-I/ARB initiation within six months post-transplant, and 12 months follow-up. Patients less than 18 years of age, incarcerated, or pregnant were excluded. Patient demographics, transplant information, and serum creatinine (SrCr) were collected at baseline, 1, 3, 6, and 12 months. The primary endpoint was SrCr at 12 months with secondary endpoints of SrCr at 3 and 6 months, allograft and patient survival.
RESULTS: The time of initiation of ACE-I/ARB post-transplantation was 9.2 ± 4.9 days (range 3 to 17) and 90.2 ± 40.3 days (range 40 to 166) in group 1 and group 2, respectively (P = <0.001). At six months, SrCr was higher in group 1 (1.62 ± 0.39 vs. 1.3 ± 0.4 mg/dL; P = 0.045), but similar at 12

months. Patient and allograft survival rates were 100% in both groups.
CONCLUSIONS: The time of initiation of an ACE-I or ARB following transplantation does not affect long-term graft function. These agents can be used in renal transplant patients immediately post-transplantation. However, larger studies are warranted to assess their role in CAN prevention.

368. Pharmacokinetic predictors of treatment efficacy and adverse effects following mycophenolate therapy in lung transplant recipients. Stephanie Tsang, BSc.(Pharm), student[1], *Lillian S. L. Ting, BSc.(Chem), MSc.(Pharm)student*[1], Nilufar Partovi, BSc(Pharm), PharmD[2], Robert D. Levy, MD, FRCPC[3], Mary H. H. Ensom, BS(Pharm), PharmD, FCCP[4]; (1)University of British Columbia, Vancouver, BC, Canada; (2)University of British Columbia and Vancouver General Hospital, Vancouver, BC, Canada; (3)University of British Columbia, St. Paul's Hospital and BC Transplant Society, Vancouver, BC, Canada; (4)University of British Columbia and Children's & Women's Health Centre of British Columbia, Vancouver, BC, Canada.

PURPOSE: To identify pharmacokinetic parameters that may be used to predict treatment efficacy and adverse effects following mycophenolate mofetil (MMF) therapy in lung transplant recipients.
METHODS: Following informed consent, pharmacokinetic parameters of mycophenolic acid (MPA) and its glucuronidated metabolites (MPAG and AcMPAG) were determined (via high performance liquid chromatography with ultraviolet detection) from 21 lung transplant recipients on steady-state MMF therapy by serial blood sampling. Pharmacokinetic parameters [MPA area-under-the-curve0-12h(AUC); free MPA AUC(fAUC); MPA maximum and minimum concentrations; MPAG AUC; AcMPAG AUC; MPAG/MPA and AcMPAG/MPA metabolic ratios] were calculated (WinNonlin 4.1), and patients' medical charts reviewed for incidences of rejection and adverse effects. Only incidences occurring while patients were on the same immunosuppressant regimen (prednisone and tacrolimus or cyclosporine) as the pharmacokinetics assessment day were considered for analyses (Fisher's-exact test).
RESULTS: Patients were: 11 males/10 females, mean(± ;SD) 4.6 ± 4.2years post-transplant, 48.1 ± 14.2years old and weighed 71.0 ± 17.5kg. Significant results ($p \leq 0.05$): • MPA AUC (>40 vs. <40 µg*h/mL) and infections (yes vs. no) • AcMPAG/MPA metabolic ratio (>0.80 vs. <0.80) and anemia (yes vs. no) • AcMPAG AUC (>50 vs. <50 µg*h/mL) and gastrointestinal toxicities (yes vs. no) Trends ($0.05 < p \leq 0.2$): • MPA fAUC (>5 vs. <5 µg*h/mL), AcMPAG AUC (>50 vs. <50 µg*h/mL), AcMPAG/MPA metabolic ratio (>3 vs. <3) and infections (yes vs. no) • AcMPAG AUC (>27 vs. <27 µg*h/mL) and anemia (yes vs. no) • AcMPAG/MPA metabolic ratio (>4 vs. <4) and gastrointestinal toxicities (yes vs. no) • MPA AUC (<32 vs. >32 µg*h/mL) and rejection (yes vs. no)
CONCLUSIONS: Although AcMPAG induces toxicity in vitro, this is the first study examining this metabolite in lung transplant recipients. MPA AUC, MPA fAUC, AcMPAG AUC, and AcMPAG/MPA metabolic ratio were the best predictors of clinical endpoints for lung transplant recipients on MMF therapy, and may be used in the future to individualize treatment response.

369. Role of daclizumab as a calcineurin inhibitor-sparing agent following heart transplantation. *Jennifer M. Namba, Pharm.D.*, Kenneth W. Kenyon, Pharm.D., BCPS, Daniel P. Fishbein, M.D.; University of Washington Medical Center, Seattle, WA.

PURPOSE: Renal dysfunction is a frequent complication of heart transplantation and may be worsened or precipitated by initiation of calcineurin inhibitors (CI). This study sought to evaluate the efficacy of daclizumab (Zenapax®), an interleukin-2 receptor antagonist, as a short-term substitute for calcineurin inhibitors in heart transplant patients with renal insufficiency.
METHODS: A retrospective chart review was performed on patients receiving a heart transplant between July 2000 and December 2003. Data were collected for all patients (n=82) for one year following transplantation. Serum creatinine (SCr), rate of rejection and incidence of infection were assessed for patients receiving daclizumab (n=39) and compared against a control group receiving standard care with CI (n=43).
RESULTS: Post-operative initiation of CI therapy was delayed in the daclizumab group (8.65 ± 8.26 days) versus the control group (2.80 ± 1.79 days). In the daclizumab group, SCr remained stable upon CI initiation and values at 1 year were similar to the control group. Rejection rates were comparable between groups. The number of infections per patient was greater in the daclizumab group than the control group (1.18 ± 1.19 vs. 0.70 ± 0.86; p=0.04). Infections were most likely to occur within the first 30 days of transplantation (p=0.0006) and resulted primarily from bacterial etiologies (p=0.02)
CONCLUSIONS: In the setting of renal insufficiency, daclizumab appears to be an effective alternative to early initiation of CI that does not increase the risk of rejection. The correlation between daclizumab administration and infection is concerning and merits further investigation.

370. Should patients with hepatitis C virus be treated with interferon products prior to liver transplant? *Renee M. Devine, Pharm.D.*, Thomas G. Heffron, M.D., Andrei C. Stieber, M.D., Kathleen M. Connor, PA-C, Greg A. Smallwood, Pharm. D.; Emory Healthcare, Atlanta, GA.

PURPOSE: To assess the outcomes of patients transplanted for Hepatitis C with previous exposure to alfa interferon (IFN)/pegylated interferon (PIFN) or in combination with ribavirin (RBV). Our hypothesis is that patients who have been exposed to IFN pre-transplant may experience worse outcomes after transplant.
METHODS: Single-center, retrospective review of patients transplanted for HCV from December 1998 to November of 2004. Patients must have received a primary graft for a diagnosis of HCV and demonstrate survival greater than 3 months. Primary endpoint is the effect of IFN exposure on post transplant outcomes including evidence of histologic (biopsy proven) recurrence, time to recurrence, and response to additional IFN/PIFN. Disease free and patient survival will also be assessed.
RESULTS: Patients transplanted for HCV (n=131) were divided into a pre-treatment (n=45) or a non-treatment (n=82) group. No demographic differences were noted between groups. Of the patients treated 67% (n=30) completed a full course of therapy with only a 10% response rate. Following transplant histologic recurrence for the pre-treated (n=41) vs. non-treated (n=60) group was [(91 vs. 73%);p=0.012] with a mean time of (181.3 ± 236.8 vs. 303.4 ± 327.7;p=0.031) days. IFN/RBV or PIFN/RBV therapy has been initiated for recurrent HCV in both the pre-treated (n=18) and non-treated (n=37) groups (44% vs. 62%;p=0.078) with no significant difference in response rates (50% vs. 51%;p=NS). The pre-treatment group had significantly lower disease free survival [(20% vs. 48%); p=0.0005] as well as overall survival at both 1 and 2 years [(79.7% vs. 90.5%);(65.7% vs. 81.7%); p=0.05] using the Kaplan-Meier log rank method.
CONCLUSIONS: Based on our single-center findings the question of whether patients should receive IFN therapy prior to transplant remains unanswered. It would seem that patients who receive IFN therapy prior to transplant have poorer outcomes than those who did not.

371. Living donors for liver transplantation: considerations for medication dosing. *Lisa M. McDevitt, Pharm.D., BCPS*[1], Roman Schumann, M.D.[2], Iwona Bonney, Ph.D.[2], Jeffrey T. Cooper, M.D.[2]; (1)Massachusetts College of Pharmacy and Health Sciences, Boston, MA; (2)Tufts-New England Medical Center, Boston, MA.

PURPOSE: Right hepatic lobe donation for liver transplantation results in temporary hematologic and biochemical alterations in the donor. We present a case demonstrating significant alterations of carbamazepine dosing and serum concentrations after right lobe donation as well as the results of a retrospective review of our live liver donors. Our objective was to examine hepatic function and albumin concentrations up to one month after right lobe donation.
METHODS: Following IRB approval, demographic and perioperative data for 34 donors were reviewed. Albumin, PT, and T bili were collected at baseline and on post-operative days 1, 7, and 28. Child-Pugh scores were calculated at each interval to assess hepatic function.
RESULTS: Donors (21M, 13F) were between 26 and 56 years old (43.3 ± 9.1) with a BMI (kg/m2) of 27.7 ± 4.2. Mean percent of liver resected was 58.8 ± 8.5. All patients had Child-Pugh scores of 5 at baseline. The median (range; n) Child-Pugh scores were 8 (7-11; n=26), 7 (6-9; n=26), and 6 (5-9; n=23) on post-operative days 1, 7, and 28, respectively. Pre-operative albumin was 4.1 ± 0.3 gm/dl (n=30), decreasing by 44% to a 1st week albumin nadir of 2.29 ± 0.32 gm/dl (n=30). The 3rd week albumin nadir was 2.71 ± 0.62 gm/dl (n=18).
CONCLUSION: Live liver donors experience impaired hepatic function that may extend up to one month after donation. This mandates careful attention to medication dosing in this population particularly for medications that are hepatically metabolized or highly protein bound.

372. A retrospective analysis to evaluate the efficacy of valganciclovir versus ganciclovir for the prevention of cytomegalovirus disease in kidney and kidney-pancreas transplant recipients. *Helen L. Triemer, PharmD*, Chris M Heath, PharmD, Greg A Smallwood, PharmD; Emory Healthcare, Atlanta, GA.

PURPOSE: Valganciclovir (VGCV) 900mg QD is the approved dose for cytomegalovirus (CMV) prophylaxis for kidney (K) and kidney-pancreas (KP) transplant recipients. VGCV 450mg QD has been shown to provide similar drug exposure as ganciclovir 1000mg TID, our previous CMV prophylactic regimen. We utilized VGCV 450mg QD for patient convenience and decreased cost prior to the approval of the 900mg dose. Our purpose was to evaluate the efficacy of VGCV 450mg QD compared to GCV 1000mg TID in the prevention of CMV disease (CMV-D) 12-months post transplant.
METHODS: This retrospective study was conducted in patients receiving K or KP transplant from 6/2001–5/2004. Patients were excluded if the baseline

CMV serostatus of the donor (D) and recipient (R) was negative. All patients received the same immunosuppression regimen. Antiviral therapy was administered for 3-months post transplantation.
RESULTS:

	VGCV (06/01–10/02)	GCV (11/02–05/04)
Total patients	160	143
Demographics		
Age: mean	47.4	47.6
Male/Female	96 (60%)/64 (40%)	72 (50%)/71 (50%)
K/KP	135(84%)/25(16%)	112 (78%)/31(22%)
Deceased Donor TX	129 (81%)	118 (83%)
Antibody Induction (AI)	65 (40.6%)	56 (39.2%)
High risk (D+/R-)	26 (16%)	21 (15%)
Mod risk (D+/R+,D-/R+)	134 (84%)	122 (85%)
Results		
12 month CMV-D	10 (6.3%)	14 (9.8%)
High risk group	7/26 (27%)	7/21 (33%)
Moderate risk group	3/134 (2.2%)	7/122 (5.7%)
CMV-D who received AI	5/65 (7.7%)	8/56 (14.3%)
Rejection prior to CMV-D	0/10	2/14

CONCLUSIONS: No difference was found in the 12-month incidence of CMV-D. CMV-D rates were acceptable with VGCV 450mg QD. Acute rejections and antibody induction therapy did not increase CMV-D incidence. A high incidence of CMV-D was noted in the D+/R- group which may warrant a change in CMV prophylactic strategies in this group.

373. T cell responses to influenza vaccine viruses by lung transplant patients. *Mary S. Hayney, PharmD*, Nicholas A. Wiegert, BS; University of Wisconsin, Madison, WI.

PURPOSE: Lung transplant patients are at high risk of morbidity and mortality from influenza infection because of altered lung physiology and immunosuppression. Annual influenza immunization is recommended because protection is short-lived and the vaccine composition changes. Antibody responses to newly introduced influenza vaccine viruses have been shown to be lower in lung transplant patients. We hypothesized that differential responses to influenza viruses by lung transplant and healthy individuals will be measured.
METHODS: Twelve lung transplant patients and 12 healthy individuals were immunized with the 2004-05 influenza vaccine. Peripheral blood mononuclear cells (PBMC) were isolated with the trans-vivo delayed-type hypersensitivity (DTH) assay from blood samples obtained following immunization. PBMC alone, with influenza vaccine antigens in combination and individually were injected into the footpads of immunodeficient mice. The resulting swelling is an index of human T cell sensitization. Twelve subjects in each group yields α=0.05 and power = 95% using t tests to detect the difference of 20 x10^{-4} inches in DTH reactivity.
RESULTS: The vigor of the response to all three influenza antigens from the 2004-05 season in a single injection were similar between the lung transplant and healthy groups (30.8+5.6 vs. 22.1+2.8 x10^{-4} inches; p=0.18). However, the response to the A/New Calendonia (H1N1) virus by transplant patients was much greater than the healthy controls' response. (mean 32.9 ± 4.8 vs. 12.1 ± 3.5 x10^{-4} inches; p<0.005; *t* test) Responses to the other influenza viruses were similar between the groups. The transplant patients have repeatedly been immunized with the A/New Caledonia virus as it has been in the vaccine for the past five seasons.
CONCLUSION: Although lung transplant patients have been shown to mount lower antibody responses to influenza vaccine, the vigor of their T cell responses is similar to those of healthy control individuals. These responses may be important in T cell memory.

374E. Identification of mutations in the CMV genome conferring ganciclovir resistance in liver transplant recipients. *Greg A. Smallwood, Pharm.D.*, Katie Casper, MS, Jennifer Lenheman, PharmD, Thomas Heffron, MD; Emory Healthcare, Atlanta, GA.

BACKGROUND: Resistant human cytomegalovirus (CMV) has been demonstrated in both the HIV populations as well as other solid organ transplant recipients. Resistance to antivirals has been, to date, isolated to the UL54 (polymerase) and UL97 (phosphotransferase) genes.
PURPOSE: To identify mutations in CMV virus infecting liver transplant recipients that are clinically resistant to ganciclovir therapy.
METHODS: Patients were routinely followed by weekly, serial blood draws for CMV by polymerase change reaction (PCR). Genomic DNA was isolated from serum obtained from liver transplant patients seroconverting. At time of seroconversion, patients were started on ganciclovir IV 5mg/Kg Q12H or valganciclovir 900 mg BID. Presence of CMV was confirmed by quantitative PCR (COBAS AMPLICOR CMV assay, Roche). The UL54 (polymerase) and UL97 (phosphotransferase) genes were amplified by PCR using a series of nested primers. The resulting PCR fragments were sequenced and aligned to the wild type CMV strain AD169 (GI 59591) and analyzed for mutations.
RESULTS: Patients clinical resistant (n = 8) to ganciclovir had to be switched to foscarnet prior to viral clearance. Serum was obtained from patients (28 patients, 84 samples) seroconverting. Those mutations, which resulted in changes in amino acids and which were not known polymorphisms, appear to convey ganciclovir resistance. Several unreported, new mutations of the UL 54 gene have been isolated in clinically resistant patients. These mutations include including D870N, G354S and G874R and appear to confer clinical resistance to ganciclovir. Each of these mutations appeared spontaneously with the first PCR seroconversion prior to initiation of treatment without antiviral pressures. Other mutations, including A692S, previously reported as causing foscarnet resistance in fact clinically appear to confer ganciclovir resistance.
CONCLUSIONS: Mutations within the CMV genome are occurring in liver transplantation without previous exposure to ganciclovir and should be addressed clinically by aggressive use of foscarnet.
Presented at the American Transplant Congress of the American Society of Transplant Surgeons and the American Society of Transplantation, Seattle, WA, May 21-25, 2005.

375E. Is sirolimus nephrotoxic in liver transplant recipients? *Greg A. Smallwood, Pharm., D.*, Laurel Davis, RN, Renee Devine, PharmD, Carlos Fasola, MD, Andrei Stieber, MD, Thomas Heffron, MD; Emory Healthcare, Atlanta, GA.

Long term, chronic use of calcineurin inhibitors (tacrolimus and cyclosporine) is known to lead to nephrotoxicity and renal failure. Currently protocols with sirolimus or mycophenolate are used to limit the use of the calcineurins.
OBJECTIVE: The aim of this review is to evaluate long term renal outcomes following institution of a calcineurin limiting protocols.
METHODS: Long-term liver transplant recipients(N= 61) with increased serum creatinines(>1.7 mg/dl) was begun on sirolimus 4mg daily or mycophenolate 1 gram twice daily. Goal of therapy was to wean completely off of the calcineurin inhibitor while maintaining renal function.
RESULTS: The MMF group(n=34) was older[62.4(≠ 8.3) years vs. 52.2(≠ 11.8) years; p=0.001]. The groups were similar in time from transplant [4.5 (≠ 3.1) yr. vs. 3.2 (≠ 2.9)yr.; p= NS]. Continued progression of renal dysfunction was noted in the sirolimus group(n=27) at 1 year, 2year, 3 year and 4 year following conversion [2.7 (≠ 2.0)mg/dl vs. 3.36 (≠ 2.76)mg/dl, vs. 3.24 (≠ 3.1)mg/dl vs. 4.38 mg/dl; p=0.012]. While the MMF maintained renal function between one and 4 years[2.1 (≠ 1.0)mg/dl vs. 2.24 (≠ 1.19)mg/dl, p=0.708]. Larger number of patients in the sirolimus group progressed to transplant or dialysis (n = 8) compared to the MMF group[(n = 2); p=0.014]. Within 3 months of conversion, a number of rejections were noted in each group but similar between sirolimus(n = 8) and MMF(n=2) and similar deaths in each group(6 vs. 5; p=0.594). For opportunistic infections, 2 patients had detectable CMV while on sirolimus and 4 patients had herpes zoster on mycophenolate. Mean follow-up of 1747(≠ 360) days is noted.
CONCLUSIONS: Based on these results, sirolimus may not be the most optimal agent to be used for calcineurin sparing in liver transplantation due to progression of renal dysfunction. Additional, multicenter work should be done to address this observation.
Presented at the American Transplant Congress of the American Society of Transplant Surgeons and the American Society of Transplantation, Seattle, WA, May 21-25, 2005.

376. Safety and efficacy of cinacalcet in solid organ transplant recipients. *Kristine S. Schonder, PharmD*[1], Ron Shapiro, MD[2], Jerry McCauley, MD[2], Mark Carey, MD[2]; (1)University of Pittsburgh School of Pharmacy, Pittsburgh, PA; (2)Thomas E. Starzl Transplantation Institute, Pittsburgh, PA.

PURPOSE: Cinacalcet is a calcimimetic agent approved for the treatment of secondary hyperparathyroidism in patients with chronic kidney disease on dialysis. To date, there have been no studies published on the use of cincalcet in solid organ transplant recipients. This study documents the safety and efficacy of cinacalcet use in kidney and liver transplant recipients.
METHODS: A retrospective analysis was performed on all kidney and liver transplant recipients age 18 years or older who received cinacalcet after FDA approval in March 2004. Medical records were reviewed for: 1) efficacy of cinacalcet in lowering parathyroid hormone (PTH) levels and 2) safety with regards to allograft function and change in immunosuppressive drug levels.
RESULTS: Ten patients met inclusion criteria for the study: 8 kidney transplants and 2 liver transplants with renal failure. Six kidney allografts and both liver allografts were functioning at the time of cinacalcet therapy and throughout the study. Four patients did not have PTH levels after cinacalcet initiation. In the six patients with follow-up levels available, PTH levels decreased in five patients and increased in one patient after cinacalcet was started. Three patients had elevated tacrolimus levels, which did not appear to be related to cinacalcet therapy. None of the patients with functioning kidney or liver allografts experienced alterations in serum creatinine or liver function tests, respectively. One kidney transplant recipient with a functioning

allograft and one liver transplant recipient developed hypocalcemia after cinacalcet therapy initiation, which did not warrant discontinuation of the drug.
CONCLUSION: Based on experience with a limited number of patients, cinacalcet appears to be a safe and effective treatment for hyperparathyroidism in kidney and liver transplantation. Patients should be monitored for hypocalcemia while receiving cinacalcet therapy. Prospective studies are needed to better establish the role of cinacalcet in solid organ transplantation.

377. Immunosuppression in the elderly renal transplant population: is it worth the risk? *Joel C. Reddish, Pharm.D.*, R. Brian Stevens, M.D.; The Nebraska Medical Center, Omaha, NE.

PURPOSE: The elderly are the fastest growing segment of the end stage renal disease (ESRD) population. As a result, more elderly patients are undergoing renal transplantation. It is postulated, that the elderly are particularly vulnerable to the immunosuppressive medications used in renal transplantation. The objective of this study was to examine the effects of immunosuppression on the elderly transplant population as compared to a younger transplant population on a similar immunonosuppressive regimen.
METHODS: In this single-center, retrospective analysis we compared the outcomes of elderly renal transplant patients over one year (n=30) to younger adult renal transplant patients (n=41) using rabbit anti-human thymocyte globulin and a steroid sparing immunosuppression regimen.
RESULTS: Elderly kidney transplant patients were not associated with an increased risk of acute rejection, or patient and graft survival when compared to younger kidney transplant patients at one year post transplant. There was also no difference in serum creatinine, white blood cells, hemoglobin or hematocrit between the two groups at one year. There was a significant difference ($p<0.05$) in blood sugars between the two groups. However, the elderly group had a significantly larger diabetic population prior to transplant (63.3% vs. 28.9%, $p<0.05$).
CONCLUSION: The results suggest that in elderly renal transplant patients, use of a thymoglobulin and steroid sparing protocol can minimize the incidence of over-immunosuppression.

378E. Anemia in kidney transplant recipients on corticosteroid withdrawal immunosuppression regimens. *Kimi R. Ueda, PharmD*, Anil Jain, MD, Rita R. Alloway, PharmD, Paul Succop, PhD, Tiffany E. Kaiser, PharmD, Adele H. Rike, PharmD, Prabir Roy-Chaudhury, MD, PhD; University of Cincinnati, Cincinnati, OH.

PURPOSE: Anemia is associated with cardiovascular morbidity and mortality in chronic kidney disease and continues to be a significant problem post kidney transplantation. Corticosteroid withdrawal (CSWD) immunosuppression regimens have multiple long-term beneficial effects on cardiovascular disease. However, these regimens require the use of alternative immunosuppressive agents, some of which are implicated as risk factors for anemia. The aim of this study was to identify specific variables, with particular attention to immunosuppressant agents, that contribute to the occurrence of anemia in CSWD regimens.
METHODS: Single center, retrospective review of 278 kidney transplant recipients transplanted between January 1, 2000 and September 1, 2004. Patients were classified as having no anemia (Hgb >13mg/dL), mild anemia (Hgb 10-13mg/dL) or severe anemia (Hgb <10mg/dL) at 3, 6 and 12 months post-transplant. Univariate and multivariate analyses were used to identify risk factors. Chi square tested for significance.
RESULTS: Of the 278 kidney transplant recipients, 24% were found to be severely anemic while 64% were found to have mild anemia at some time during the study period. Univariate analysis identified female gender ($p=0.0002$), serum creatinine >2mg/dL ($p=0.02$), chronic allograft nephropathy ($p=0.006$), acute rejection history ($p=0.03$) and calcineurin inhibitor toxicity ($p=0.0005$) as independent risk factors for the occurrence of anemia in CSWD regimens. Multivariate analysis identified female gender as the only significant risk factor when taking into account all other variables ($p=0.02$). The use of thymoglobulin, sirolimus and mycophenolate mofetil (MMF) were not significantly associated with an increased risk.
CONCLUSIONS: This study identified female gender and allograft dysfunction as risk factors for anemia in patients on CSWD regimens. The use of alternate immunosuppressive agents such as thymoglobulin, sirolimus and MMF alone or in combination did not increase the risk of anemia in this patient population. CSWD was not a risk factor for the development of anemia.
Presented at the American Transplant Congress of the American Society of Transplant Surgeons and the American Society of Transplantation, Seattle, WA, May 21-25, 2005.

379. Cyclosporine absorption profiling and its limited sampling strategies in lung transplant recipients. Judith Marin, BSc(Pharm), MSc(Pharm)[1], *Lillian S. L. Ting, BSc.(Chem), MSc.(Pharm)student*[1], Nilufar Partovi, BSc(Pharm), PharmD[2], Robert D. Levy, MD, FRCPC[3], Mary H. H. Ensom, BS(Pharm), PharmD, FCCP[4]; (1)University of British Columbia, Vancouver, BC, Canada; (2)University of British Columbia and Vancouver General Hospital, Vancouver, BC, Canada; (3)University of British Columbia, St. Paul's Hospital and BC Transplant Society, Vancouver, BC, Canada; (4)University of British Columbia and Children's & Women's Health Centre of British Columbia, Vancouver, BC, Canada.

PURPOSE: To evaluate the correlation between cyclosporine absorption profiling (AUC0-4hours) and total area-under-the-curve (AUC_{0-12}hours) in lung transplant patients, and to test the predictive performance of associated limited sampling strategies (LSSs).
METHODS: Data from 14 stable lung transplant recipients enrolled in a previous study were used to calculate pharmacokinetic parameters for the current study. Patients were divided into index (n=8) and validation (n=6) groups. Blood samples were collected at 0,1,2,3,4,5,6,8,9,10 and 12 hours after a steady-state morning cyclosporine dose and were analyzed by fluorescence polarization immunoassay using a specific monoclonal antibody kit. AUC_{0-4} hours were analyzed by non-compartmental modeling (WinNonlin 4.1) and compared to AUC_{0-12} hours (from the previous study). LSSs for estimating AUC_{0-4}hours were established using multiple regression analysis with forward stepwise elimination (Statistica®). Predictive performance [coefficient of determination (r2), bias and precision] of the LSSs was measured using the validation group data.
RESULTS: The correlation between AUC_{0-4} hours and AUC_{0-12} hours was excellent (r2=0.976). As was the case for AUC_{0-12}hours, the best LSS equation included 2 concentrations at 1 and 3 hours: AUC (ng.hr/mL) = 1.03C1 + 2.87C3 + 105.5 (bias=-3.09%; precision=4.97%; r^2= 0.996). Also in concordance with previous results, C0 is the best single-point predictor of AUC_{0-4} hours (bias=-15.19%; precision=25.63%; r^2= 0.996) whereas C2 did not demonstrate good predictive value in this subpopulation (bias=-37.58%; precision=37.58%; r^2= 0.621).
CONCLUSION: For lung transplant recipients, an excellent correlation exists between cyclosporine AUC_{0-4} hours and AUC_{0-12} hours. The optimal and most clinically acceptable LSS describing both pharmacokinetic parameters is the one using C1 and C3. These results can be implemented and directly applied to management of lung transplant recipients.

Urology

380. Patient satisfaction with transdermal oxybutynin: preliminary results from the MATRIX study. *Peter Sand, MD*[1], Karen Delhey, MD[2], Naomi V. Dahl, Pharm.D.[3], MATRIX Investigators[3]; (1)Northwestern University, Evanston, IL; (2)Houston, TX; (3)Watson Laboratories, Morristown, NJ.

PURPOSE: Oral antimuscarinics, effective in treating overactive bladder (OAB), are associated with anticholinergic side-effects. Clinical trials of transdermal oxybutynin (OXY-TDS) in OAB have demonstrated safety and efficacy, with a low incidence of anticholinergic effects. The Multicenter Assessment of Transdermal Therapy in Overactive Bladder with Oxybutynin (MATRIX) evaluates patient satisfaction with this system.
METHODS: MATRIX is an ongoing, multicenter, open-label, prospective, randomized trial of adult OAB patients treated with OXY-TDS for 6 months, and evaluated for safety and patient-reported outcomes. Validated instruments (for QoL, work productivity, and depression) are administered at baseline, 3, and 6 months. Patient satisfaction data are collected monthly, via telephone interview.
RESULTS: Current enrollment is 2770 patients (mean age, 62.3 y; 87% female; 84% Caucasian). The majority (1560) have a history of prior OAB pharmacotherapy (31% with multiple medications; 79% having symptoms for ≥ 2 years). Most frequently used agents: oral extended-release antimuscarinics, tolterodine-ER (54% of patients) and oxybutynin-ER (32%), followed by their IR versions (22-23%), other agents (≤3%). Most common reasons for discontinuation include: lack of efficacy (53%), side-effects (21%), non-compliance (7%). Currently, 1617 patients have used OXY-TDS for ≥1 month. Of these, 69% report being very satisfied or satisfied with patch: specifically, 79% with ease of application, 62% with efficacy, and 81% tolerability. The majority of patients (76%) find OXY-TDS very convenient or convenient, reporting they are either unaware of patch during daily activities (65%), or, if aware, that it never or infrequently affects their activities (71%). When compared to their previous OAB pharmacotherapy, 63% of patients report OXY-TDS offers significant or some benefits, including ease of use (67%), effectiveness (57%), and tolerability (60%).
CONCLUSION: Preliminary data indicate high levels of patient satisfaction with OXY TDS. A majority of patients prefer OXY-TDS to their prior oral OAB treatments. Transdermal therapy may lead to improved compliance.

381. Use of a simple eight-question validated overactive bladder screening tool in Midwestern primary care offices. *Alicia B. Forinash, Pharm.D.*[1],

Mounir Shenouda, M.D.[2], Christopher Conner, Pharm.D., Ph.D.[3], Todd A. Armstrong, Pharm.D.[3]; (1)St. Louis College of Pharmacy; Fairview Heights Medical Group, St. Louis, MO; (2)Fairview Heights Medical Group, Fairview Heights, IL; (3)Pfizer, Inc., St. Louis, MO.

PURPOSE: Although 33 million Americans suffer from overactive bladder (OAB), little has been published about screening patients for this condition. Recently, a simple 8-question OAB screening tool (OAB V8) has been validated. The purpose of this project was to establish a benchmark utilizing the OAB V8 in a large sample of primary care offices across a 4 state region.
METHODS: The OAB V8 screener has patients rate their OAB symptom bother (e.g., frequency) on a scale from 0 (not at all) to 5 (a very great deal). Patients scoring more than 7 are considered to have "probable" OAB. A one-page HIPAA compliant self-administered survey was created using scan form technology and these 8 questions. In addition, patients were asked basic demographic questions including the presence of common OAB risk factors. Patients visiting primary care offices in Iowa, Illinois, Missouri, and Wisconsin from August 2004 through April 2005 were invited to complete this survey. Following data collection, surveys were scanned into an Access database and then imported into SPSS (version 12) for analysis.
RESULTS: We screened 5345 patients for OAB with the OAB V8 screener. The mean age of these volunteers was 50.9 ± 17.4 years (range: 18-89 years) and included 70% females. Participants screened positive for "probable" OAB 41% of the time. Those screening positive were most bothered by "nocturia" and "waking up at night to urinate." Of the 14 common risk factors for OAB, 13 were associated with a positive OAB V8 screen.
CONCLUSIONS: We found a high prevalence of "probable" OAB (i.e., 41%) in a large group of primary care patients in the Midwest. These patients were candidates for further OAB diagnostic workup and possibly pharmacologic intervention. Our results may serve as a benchmark for other OAB V8 screening initiatives.

382. Long-term persistence and compliance with darifenacin treatment for overactive bladder: results of a 2-year open-label extension study. *Simon Hill, MB, BS*[1], Karine Lheritier, PhD[2], Fernando Kawakami, MD[2]; (1)Queen's Park Hospital, Blackburn, United Kingdom; (2)Novartis Pharma AG, Basel, Switzerland.

PURPOSE: Antimuscarinic agents for overactive bladder (OAB) may be poorly tolerated and/or provide insufficient clinical response, leading to poor compliance and persistence. The study reported here assessed persistence and compliance with darifenacin, a muscarinic M_3 selective receptor antagonist, administered in a flexible dosing regimen during a 2-year open-label extension study.
METHODS: Patients with OAB (n=716; 85% female; age 19–89 years) were enrolled in the extension following completion of 12 weeks' randomised, double-blind treatment in placebo-controlled (feeder) studies of darifenacin controlled-release 3.75, 7.5 or 15mg once daily (qd) (Haab et al. 2004; Steers et al. 2005). Darifenacin treatment in the extension was commenced at 7.5mg qd for the first 2 weeks; patients could subsequently up or down-titrate between 7.5mg and 15mg qd. Persistence was calculated from discontinuation rates, while compliance with treatment was assessed based on unused medication counts at clinic visits.
RESULTS: The proportion of patients completing 2 years' open-label darifenacin treatment was 66.3% (n=475). Darifenacin was well tolerated and provided a sustained improvement in OAB symptoms (median 84.4% reduction in incontinence episodes at 2 years; $p<0.001$ vs feeder study baseline). Overall, 8.9% of patients discontinued due to all-causality adverse events and 9.5% due to insufficient clinical response. 87.4% of patients achieved ≥80% compliance with treatment.
CONCLUSIONS: High persistence and compliance rates were observed with darifenacin in this study, which may have resulted in part from the combination of sustained efficacy, good tolerability and the option of flexible dosing (allowing treatment to be tailored according to individual needs).

Women's Health

383. Life after the WHI: evaluation of postmenopausal symptoms and use of alternative therapies after discontinuation of hormone therapy. *Sarah P. Shrader, Pharm.D.*, Kelly R. Ragucci, PharmD; Medical University of South Carolina, Charleston, SC.

BACKGROUND: Many women discontinued the use of hormone therapy (HT) after the results of the Women's Health Initiative (WHI) were published; however, it is unknown how many women continue to experience menopausal symptoms.
PURPOSE: The purpose of this project was to determine the number of women experiencing menopausal symptoms after discontinuation of HT, the number of women subsequently requiring the use of alternative therapies, and the utility of these agents.
METHODS: All postmenopausal women who discontinued HT (Premarin and Prempro) between August 2002 and 2003 were identified through the family medicine electronic medical record (EMR); and 378 were eligible for inclusion. It was determined that with a 10% margin of error and a 95% confidence interval, 78 women needed to be randomly selected to represent the patient population. The EMR of these women was retrospectively reviewed to identify any alternative therapies for menopausal symptoms. Additionally, a telephone survey was administered to assess the patients' perception of the reason for HT discontinuation, recurrence of menopausal symptoms, and utilization and effectiveness of alternative therapies.
RESULTS: Forty-one patients experienced one or more menopausal symptoms after discontinuing HT; and 76% tried at least one alternative medication. Twenty-six women utilized an herbal alternative; soy and black cohosh were the most common at 17% and 6%, respectively. Forty-three women tried an alternative prescription product; the majority tried paroxetine and sertaline at 10% and 12%, respectively. Thirty women reported taking an alternative for osteoporosis, 35% of women utilized calcium supplements. Of the women who utilized an alternative product, 69% of the respondents deemed these agents helpful in alleviating menopausal symptoms.
CONCLUSIONS: The majority of women who have discontinued HT continue to have menopausal symptoms, and these women are willing to try alternative therapies. Additional research is warranted to determine the effectiveness of the alternative menopausal treatment options.

384E. Transplacental passage of vancomycin following single dose administration prior to cesarean section. *Kristin C. Klein, B.S., Pharm.D.*[1], Joann Laiprasert, MD[2], Mark D. Pearlman, MD[2]; (1)University of Michigan Health System and College of Pharmacy, Ann Arbor, MI; (2)University of Michigan Health System, Ann Arbor, MI.

PURPOSE: Intrapartum prophylactic antibiotics are frequently utilized to prevent Group B Streptococcus (GBS) infections in neonates. The Centers for Disease Control and Prevention recommend that vancomycin be utilized for chemoprophylaxis of GBS in women who are allergic to b-lactam antibiotics or who have GBS resistance to erythromcyin or clindamycin. The primary goal of this project was to evaluate maternal serum and cord blood concentrations of vancomycin in pregnant women undergoing cesarean section to determine if adequate drug concentrations were present to prevent GBS infection in neonates.
METHODS: Thirteen women who underwent elective cesarean section were randomly assigned to receive 1 gm of vancomycin either 30 minutes, 1 hour, 4 hours or 6 hours prior to the procedure. Maternal serum, cord blood and amniotic fluid samples were collected for each subject. Vancomycin was infused over 60-90 minutes and concentrations for maternal serum and cord blood were evaluated utilizing a fluorescence polarization immunoassay.
RESULTS: The time from end of vancomycin administration to beginning of procedure ranged from 30-500 minutes. Maternal serum concentrations of vancomycin ranged from 2.6-19.8 µg/mL, while cord blood samples ranged from 2.8-9.4 µg/mL. Cord blood concentrations as a percentage of maternal serum concentrations ranged from 21.4-120%, with cord blood concentrations exceeding serum concentrations at 410 and 500 minutes after end of vancomycin infusion. Seven of the subjects had their vancomycin infusions stopped prematurely due to the development of Red Man's Syndrome, with one patient requiring treatment for moderate hypotension. None of the neonates exhibited adverse events as a result of maternal Red Man's.
CONCLUSIONS: Maternal serum and cord blood concentrations exceeded the commonly accepted minimum inhibitory concentration breakpoint for GBS of 1 µg/mL at all timepoints evaluated. As a result, we believe that vancomycin is a viable alternative for GBS prophylaxis in women allergic to b-lactam antibiotics.
Presented at the Annual Resident Research Day of the University of Michigan, Ann Arbor, MI, May, 25, 2005.

385E. Evaluation of eszopiclone 3 milligrams in the treatment of insomnia associated with menopausal transition. Claudio Soares, MD, PhD[1], Robert Rubens, MD[2], David Amato, Ph.D.[2], Thomas Roth, Ph.D.[3], Judy Caron, Ph.D.[2], *Susan M. Skolly, Pharm.D.*[2], Thomas C. Wessel, M.D.[2]; (1)Women's Health Concerns Clinic, McMaster University, Hamilton, ON, Canada; (2)Sepracor Inc., Marlborough, MA; (3)Henry Ford Hospital Sleep Disorders Center, Detroit, MI.

PURPOSE: Peri-menopausal and menopausal women may develop insomnia. This 4-week study evaluated the efficacy of eszopiclone 3mg for insomnia associated with peri-menopausal transition.
METHODS: Peri-menopausal women (40-60 yrs; n=201), without major psychiatric diagnoses, who met STRAW stages -2, -1, or 1a, reported sleep latency (SL) 30min, and total sleep time (TST) 6hrs/night were randomized to eszopiclone 3mg or placebo nightly. Endpoints included SL, wake time after sleep onset (WASO), TST, awakenings due to hot flashes (HF), daytime HF, physician global evaluations (PGEs), and mood (Montgomery Aspberg

Depression Rating Scale; MADRS).
RESULTS: Eszopiclone produced significantly greater reductions in median SL and WASO each week versus placebo ($p<0.007$) and increases in median TST and sleep quality, $p<0.0002$). Eszopiclone, while not affecting frequency or duration of daytime HF, decreased nocturnal awakenings due to HF ($p<0.05$), and improved total MADRS scores ($p<0.03$) and PGEs ($p<0.0001$). Unpleasant taste was the most frequent adverse event with eszopiclone (17.7% vs 0.5%). Other adverse events were similar across groups.
CONCLUSION: In this study, eszopiclone significantly improved sleep, decreased nocturnal awakenings due to hot flashes, and positively affected mood in peri-menopausal women. PGE of the peri-menopausal transition symptom complex was improved following 4 weeks of treatment.
Presented at the 16th Annual Meeting of the North American Menopause Society, San Francisco, CA, September 28-October 1, 2005.

386. Pharmacokinetics of Labetalol in pregnancy. *Jennifer Hardman, Pharm.D.*[1], Loraine Endres, M.D.[1], Patricia Fischer, RN[1], Thomas Jenkins, M.D.[2], Lori Wollet, RN[2], Sarah Kilpatrick, M.D., Ph.D.[1], Keith Rodvold, Pharm.D.[1], Stacie Geller, Ph.D.[1], Gloria Sarto, M.D., Ph.D.[2], Margaret Miller, Ph.D.[3], James Fischer, Pharm.D.[1]; (1)University of Illinois at Chicago, Chicago, IL; (2)University of Wisconsin, Madison, WI; (3)FDA, Rockville, MD.

PURPOSE: Labetalol is frequently used to treat hypertension in pregnancy. However limited information is available on its pharmacokinetics in these patients. This study examined the population pharmacokinetics of labetalol during and after pregnancy in women with hypertension.
METHODS: Pharmacokinetic (PK) data was prospectively collected in women receiving oral labetalol for hypertension from 4th month of pregnancy through 3 months postpartum. Study entry occurred at any time during this period. A sparse-sample design was used. Three plasma samples were collected on two occasions during the 2nd trimester, 3rd trimester, and 0 to 3 months postpartum. Single samples were obtained at other clinic visits. Drug intake was recorded by electronic monitoring or diary. Population PK modeling was performed with NONMEM by first-order conditional estimation method. Labetalol concentrations were measured by a validated HPLC assay.
RESULTS: Forty-six women, age 18-41 years, contributed 447 plasma concentrations for population analysis. A 2-compartment model with first order absorption and elimination adequately described labetalol PK. Mean (%CV) parameter estimates were: oral clearance (CL/F) 250 (9.8) L/h, apparent volume of distribution of the central compartment (Vc/F) 461 (15.3) L, and apparent steady-state volume of distribution (Vss/F) 2180 (11.9) L. PK parameters showed marked interindividual variability (41%–100%). Body surface area (BSA) and pregnancy were significant ($p<0.001$) covariates for CL/F and Vc/F. CL/F and Vc/F increased proportionally with body surface area and were approximately 30% and 65%, respectively, greater during pregnancy. Increase in CL/F was similar during 2nd and 3rd trimesters. No significant relationships were found with other covariates, including age, race, concurrent diseases or drugs, weight, and hepatic or renal function.
CONCLUSION: Pregnancy and BSA significantly influence labetalol pharmacokinetics in women between 18 and 41 years of age.

CLINICAL PHARMACY FORUM

These abstracts describe the delivery, development, justification, or documentation of innovative clinical pharmacy services; they may be descriptive only and need not contain an evaluative component.

387. Incidence of infusion related reactions with rituximab: effect of pretreatment. *Anthony Gerlach, PharmD, BCPS*; The Ohio State University Medical Center, Columbus, OH.

PURPOSE: Rituximab is a monoclonal antibody that causes infusion related reactions in up to 80% of patients with the first dose and 40% of patients with subsequent doses. The purpose of this study is to prospectively monitor the use of rituximab for safety.
METHODS: Data was prospectively collected for any patients who received rituximab from November 2004 through February 2005. Data collected included demographics, indication, dosing, infusion rate, number of previous doses, use of acetaminophen (APAP) and diphenhydramine pre-treatment and adverse effects. Infusion related reactions were defined as headache, fever, chills, respiratory symptoms (tachypnea and dyspnea), skin reactions, visual disturbances, nausea, hypertension, and hypotension. Statistical analysis was preformed by Fisher's exact test.
RESULTS: Forty-nine patients who received 63 doses with a mean age of 61.3 years were evaluated. The indications for rituximab were: non-Hodgkin's lymphoma 22, chronic lymphocytic leukemia 13, lymphoma 9, myeloma 2, lupus 1, lymphoadenopathy 1 and thrombocytopenia 1. Pre-treatment was documented as given with 47 doses with APAP and diphenhydramine, APAP only with one dose and was not given with 15 doses. Overall, infusion related reactions occurred with 3 doses (4.8%) with all the reactions occurring in those pre-treated with APAP and diphenhydramine and none occurred in those not given pre-treatment ($p= 1$). During the study 15 initial doses were given, 38 doses were given as repeat therapy and 10 doses it is not known if the patient received prior rituximab therapy. Infusion related reactions occurred in two patients receiving a first time dose and none occurred in the prior therapy group ($p=0.07$).
CONCLUSIONS: The overall incidence of infusion related reactions to rituximab was low and use of APAP and diphenhydramine pre-treatment may decrease the development. Further studies are needed.

388. Undetermined international normalized ratio and rising prothrombin time with concurrent use of warfarin and gatifloxacin. *Alan W.Y. Chock, Pharm.D.*, Julie A. Stading, Pharm.D., CDE; Creighton University Medical Center, Omaha, NE.

PURPOSE: To present a case of an undeterminable international normalized ratio (INR) due to an unstoppable rise in prothrombin time (PT) when gatifloxacin was given concurrently with warfarin. Case summary: An 88-year-old white male chronically received warfarin therapy secondary to his mechanical aortic valve replacement. His dose ranged 3.5–4 mg/day within the past year based upon his INRs (therapeutic range: 2.5–3.5). Pertinent past medical history (PMH) included atrial fibrillation, congestive heart failure, chronic obstructive pulmonary disease, gastroesophageal reflux disease, iron deficiency anemia, and weight loss. He has no known allergies to medications, no history of tobacco use, and no consumption of alcohol, grapefruit, or cranberries. Based upon evaluation on May 16, 2005 for progressive cough, back pain and a chest x-ray, the patient was diagnosed with community acquired pneumonia. He was given oral gatifloxacin 400 mg/day for 14 days. On May 20, 2005 his INR could not be determined due to a nonstop increase of his PT. Another blood sample was drawn and resulted in another undeterminable INR. Next, the patient received 10 mg of intravenous vitamin-K and 3 units of fresh frozen plasma. Twelve hours later, the patient's INR was noted to be "therapeutic" and warfarin was decreased to 2 mg/day.
RESULTS: The patient's warfarin dose did not change drastically over the past year. He did not have any recent exacerbation of his PMH. His complete metabolic profile and liver function test were stable or within normal limits. The most recent changes in his medications were 2.5 months prior to the time of presentation.
CONCLUSIONS: Like other fluoroquinolones, gatifloxacin may elevate INRs when given concurrently with warfarin. This is a probable effect based on the Naranjo adverse drug reaction algorithm score of 5. Therefore, close monitoring and adjustment of warfarin may be necessary.

389. Documentation of billing by pharmacists in ambulatory care clinics. Melissa M. Blair, PharmD, BCPS, CDE, Joli D. Fermo, PharmD, BCPS, BC-ADM, CDE, *Kelly Ragucci, PharmD, BCPS, CDE*, Jennifer N. Mazur, PharmD, CDE, Stacy M. Prutting, PharmD, BCPS, CDE, Andrea Wessell, PharmD, BCPS, CDE, Alisa K. Christman, PharmD; Medical University of South Carolina, Charleston, SC.

PURPOSE: The purpose of this study was to quantify the dollar amount billed by ambulatory care clinical pharmacists at 5 university-based clinics. At MUSC, patients are referred to ambulatory care clinical pharmacists for a variety of services. Each time a patient has a face-to-face visit with a clinical pharmacist, a facility ticket is generated and billing occurs based on the services provided and documented during the visit. Regardless of visit level, a flat fee is generated for each facility ticket; however reimbursement for Medicare patients is based on a tiered system.
METHODS: To quantify billing for clinical pharmacy services, visit information was entered into a documentation database, CliniTrend® from January to April 2005. To determine the most accurate estimate of reimbursement, visits were categorized based on level and type of service provided, and patients were classified by insurance coverage. Data were then annualized to estimate yearly billing.
RESULTS: A total of 3,148 clinical pharmacy visits were documented during 4 months of data collection (estimated 9,414 yearly visits). Medicare was the payer for 61.3% of these visits. Management of anticoagulation and multiple disease states were the most common visits, at 57% and 36%, respectively. Most visits (89.6%) were billed at the top levels of service allowed. Clinical pharmacy service billing for the 4 months was $185,529.87, or $556,589.61 over a year's time.
CONCLUSIONS: It is estimated that clinical pharmacists in 5 ambulatory clinics bill for 9,414 visits per year and greater than $550,000. This yields $104,035.44 for each pharmacy position.

390. Implementation of the Laragh treatment method for hypertension in a cardiologist's office. *Randall P. Sharp, Pharm.D., BCPS*[1], Michael H. Mowdy, D.O., FACC[2], Joe A. Witten, D.O.[2], Henry M. Allen, D.O.[3]; (1)Southwestern

Oklahoma State University College of Pharmacy, Weatherford, OK; (2)Cardiovascular Disease Specialists, Oklahoma City, OK; (3)Oklahoma Medical Institute, Oklahoma City, OK.

PURPOSE: According to the 1999-2000 National Health and Nutrition Examination Survey (NHANES) III, only 34% of adults in the United States have controlled hypertension (<140/90 mmHg). The goal of the Laragh treatment method is to use Plasma Renin Activity (PRA) levels to control hypertension using a minimum number of medications. Drug therapy is selected based on the book Laragh's Lessons in Renin System Pathophysiology for Treating Hypertension and its Fatal Cardiovascular Consequences (Elsevier 2002). In this method, patients are classified as having either predominately sodium volume-mediated hypertension (PRA < 0.65 ng/ml/hr) or renin-mediated hypertension (PRA >0.65 ng/ml/hr). Low renin patients are given drugs which decrease body sodium and volume; those with PRA >0.65 ng/ml/hr are treated with drugs that block the activity of the renin-angiotensin system. To obtain blood pressure control with a minimum number of medications in a private cardiologist's office.
METHODS: A baseline ambulatory PRA level was drawn on 48 currently treated patients with uncontrolled hypertension (blood pressure >140/90 mm Hg) who were refractory to previous therapy. Patients were evaluated at least once monthly. Drug therapy was selected and titrated by a clinical pharmacist, in consultation with a cardiologist from September 2004 to May 2005.
RESULTS: Nineteen patients (40%) had volume-mediated hypertension (PRA < 0.65 ng/ml/hr) and twenty nine (60%) had renin-mediated hypertension (PRA > 0.65 ng/ml/hr). Blood pressure was controlled in 37 out of 48 patients (77%). Each patient was on an average of 1.9 anti-hypertensive medications at baseline, compared to an average of 2.1 medications at the end of the eight month period (P=0.253).
CONCLUSIONS: A trend toward better blood pressure control was demonstrated after implementing the pharmacist-directed Laragh method in the clinic, while not significantly increasing the average number of anti-hypertensive medications. The Laragh method provides an effective approach for the treatment of hypertension.

391. Development of patient-centered pharmacotherapy through integration of academic and community pharmacy programs. *Peter M. Brody Jr., Pharm.D.*; State University of New York at Buffalo School of Pharmacy and Pharmaceutical Sciences, Buffalo, NY.

PURPOSE: The goal was to establish innovative clinical services in a community pharmacy setting by combining clinical practice with an academic pharmacy program. This provides patients with a continuity of care through increased pharmacotherapy management and disease state education, while establishing an advanced ambulatory care experiential training site.
METHODS: The faculty member was introduced into the community pharmacy environment to offer various clinical services. Patients were referred to the faculty liaison and Pharm.D. students for free services such as participation in a blood pressure clinic, counseling on complicated drug regimens, and the use of medical devices. They were also given the option to enroll in fee-for-service programs, such as smoking cessation, diabetes education, and the Eckerd PatientCARE™ Network. These patients were followed and tracked on a regular basis documenting weight, heart rate, blood pressure, blood glucose, and medication adherence.
RESULTS: Between January 2004 and May 2005, approximately 2,000 patients were encountered by the faculty member/clinical pharmacist and 28 Pharm.D. students rotating on site. Six patients were enrolled into the Eckerd PatientCARE™ program ($120 per year out of pocket expense) and 53 patients attended the weekly 3-hour blood pressure clinic since it began in March 2005. More than 50 private consultation appointments were held and over 250 blood pressure and heart rate readings were taken.
CONCLUSIONS: The integration of academic and community pharmacy programs between Eckerd and the University at Buffalo School of Pharmacy and Pharmaceutical Sciences has been successful. The WNY Eckerd site is now the hub of an emerging network of community pharmacy patient-care centers. Both programs have grown and continuous development will be necessary. Future plans include the establishment of an ambulatory care residency, development of a web-based data collection tool, program expansion to other pharmacy locations, and third-party reimbursement for cognitive services.

392. Hypertension management in a family medicine residency training program. *Toni L. Ripley, Pharm.D.*, Donald Harrison, Ph.D.; University of Oklahoma College of Pharmacy, Oklahoma City, OK.

PURPOSE: Documentation of hypertension management in patients in a Family Medicine residency training program was done to evaluate success in achieving therapeutic goals defined in the medical literature and to assess the role for clinical pharmacy services.
METHODS: Medical records of 228 patients within the Family Medicine Center from 11/1/02 to 10/31/03 with a diagnosis of hypertension, diabetes, or renal disease were randomly identified. Prescribing patterns and comparison of resident versus faculty practices are reported.
RESULTS: In all patients evaluated, the top five anti-hypertensives were: hydrochlorothiazide, lisinopril, amlodipine, furosemide, and atenolol. In patients with diabetes, the top five anti-hypertensives were: lisinopril, furosemide, hydrochlorothiazide, amlodipine, and combination ACEI/ARB with hydrochlorothiazide. Average number of anti-hypertensives per patient was 2.61. Use of furosemide was not associated with renal dysfunction, heart failure, or left ventricular dysfunction. No differences existed between residents and faculty in the following: number of patients that achieved blood pressure goal, number of anti-hypertensives, type of insurance, or frequency of comorbidities (diabetes, dyslipidemia, current smoker, left ventricular dysfunction, liver dysfunction, renal disease, asthma). Patients without medication insurance were more likely to not be treated with anti-hypertensives compared to those with medication insurance (p=0.024). Patients without medication insurance were most likely prescribed: hydrochlorothiazide, amlodipine, nifedipine, metoprolol, and lisinopril. Type of insurance or lack of insurance was not statistically associated with achieving blood pressure goals or presence of comorbidities.
CONCLUSIONS: Use of furosemide and atenolol are common treatments, but lack adequate data showing cardiovascular event reductions in hypertension. Experienced physician providers in this Family Medicine Center do not appear to manage hypertension better than resident physicians. Faculty physicians do not appear to care for more complicated patients. Lastly, insurance was associated with presence of treatment, but not with achieving blood pressure goals.

393. Racial differences in the prevalence of atrial fibrillation in heart failure: a retrospective review. *Huzefa Master, PharmD*[1], Vicki Groo, PharmD[1], Larisa Cavallari, PharmD[1], Adhir Shroff, MD, MPh[2]; (1)University of Illinois at Chicago College of Pharmacy, Chicago, IL; (2)University of Illinois at Chicago, Chicago, IL.

PURPOSE: The objective of this study was to determine if race is associated with the prevalence of AF in HF. A secondary objective was to identify contributing factors to the racial disparity of AF in HF.
METHODS: A retrospective chart review was conducted. Medical records from all patients followed in the University of Illinois Medical Center Heart Failure Clinic were examined. Patients with a history or current diagnosis of AF were included. Data collected included: patient demographics, comorbidities, laboratory values, echocardiogram results, and medications. Race was self reported in the medical record. Incidence of known risk factors for AF (age, left ventricular function, left atrial size, hypertension, hyperthyroidism, coronary artery disease and diabetes mellitus) were compared by race. The sum of known risk factors was also compared. χ^2 analysis was completed on categorical variables and an ANOVA was completed on continuous variables.
RESULTS: A total of 226 patient charts were reviewed. Forty two patients had a diagnosis/history of AF, with an average age of 62.1 years and 29 were male. A significantly higher percentage of Hispanics had AF (Table 1). The patient groups were similar in regards to comorbidities, echocardiogram results, and medications. No significant differences were found in regards to risk factors for AF and the sum of risk factors (Table 2).
CONCLUSION: The data demonstrates a significant difference in the prevalence of AF between races. This disparity is not explained by a difference in risk factors for AF.

Table 1: AF Prevalence by Race

Race	n (%)*
Caucasian (n = 36)	8 (22.2)
African American (n = 158)	23 (14.6)
Hispanic (n = 32)	11 (34.3)

*p=0.026 Table 2: AF Risk Factors

Race	Average number of AF risk factors#
Caucasian (n=8)	3.0
African American (n=23)	3.5
Hispanic (n=11)	3.5

#p=non-significant

394E. Safety and tolerability of coadministered amlodipine and atorvastatin in patients with concomitant hypertension and dyslipidemia in the Respond study. *Richard A. Preston, MD*[1], J. Wouter Jukema, MD, PhD, FESC, FACC[2], Peter Harvey, MA, MB, BCHIR, MRCGP, DRCOG[3], Franklin Sun, MPhil, MS[4], Lisa Tarasenko, PharmD, MBA[4]; (1)Division of Clinical Pharmacology, Pharmacokinetics and Clinical Research Center, University of Miami School of Medicine, Miami, FL; (2)Dept of Cardiology C5-P, Leiden University Medical Center, Leiden, Netherlands; (3)Crouch Oak Family Practice, Surrey, Addlestone, United Kingdom; (4)Pfizer Inc, New York, NY.

PURPOSE: Amlodipine/atorvastatin combination therapy has been demonstrated to be an effective approach for the management of concomitant hypertension (HTN) and dyslipidemia (DYS). However, a potential barrier to

the use of this treatment might be concerns regarding the occurrence of adverse events (AEs) when coadministering these 2 therapies. We therefore evaluated the safety of coadministered amlodipine plus atorvastatin therapy versus either drug alone or placebo
METHODS: Respond was a randomized, double- blind, multicenter, placebo-controlled, 3x5 factorial study. Patients aged 18–75 years with concomitant HTN/DYS were treated for 8 weeks with amlodipine (5 or 10 mg), atorvastatin (10, 20, 40, or 80 mg), 8 combinations of the aforementioned amlodipine plus atorvastatin doses, or placebo. All-causality, treatment-emergent AEs are reported.
RESULTS: A total of 1660 patients with concomitant HTN/DYS (n=110-111 per treatment group) were included in the safety analysis. Overall, 663 (40%) patients reported AEs. Rates of discontinuation due to AEs were similar in the combination (5.6%), amlodipine alone (5.4%), atorvastatin alone (4.1%), and placebo (4.5%) groups. Most AEs were mild or moderate in intensity. Overall, the most common AEs were peripheral edema (overall 7.4%: amlodipine alone 12.2%, atorvastatin alone 1.1%, amlodipine plus atorvastatin 9.9%, placebo 2.7%), headache (6.2%), and respiratory tract infection (4.3%). The incidence of myalgia in combination-treated patients was low (1.6%) and similar to the amlodipine or atorvastatin alone and placebo groups (1.4%, 1.8%, and 1.8%, respectively). No increase in the incidence of AEs was observed with coadministered amlodipine 10 mg plus atorvastatin 80 mg (41.4%) versus amlodipine 10 mg alone (47.7%), and only a small increase versus atorvastatin 80 mg alone (37.3%).
CONCLUSION: Coadministered amlodipine plus atorvastatin is well tolerated in patients with concomitant HTN/DYS. Furthermore, AEs observed with coadministered amlodipine plus atorvastatin are similar in nature, severity, and frequency to those seen with amlodipine or atorvastatin alone.
Published in Am J of Hypertens 2005 18;(suppl 1):A92-A93.

395. Secondary prevention lipid clinic in collaboration with pharmacists addresses risk factors in a cardiology practice better than usual cardiology care. *Kim K. Birtcher, M.S., Pharm.D.*[1], Mehran Massumi, B.S.[2], Sujit S. Sansgiry, Ph.D.[1], Madjid Mirzai-tehrane, M.D.[2], Haroon-Ur Rashid, M.D., Ph.D.[2], Ali Mortazavi, M.D.[2]; (1)University of Houston College of Pharmacy, Houston, TX; (2)Kelsey-Seybold Clinic, Houston, TX.

PURPOSE: The National Cholesterol Education Program–Adult Treatment Panel III guidelines suggest using lipid clinics and collaboration with pharmacists to help patients reach lipid goals, but little is known regarding implementation of these strategies in a cardiology practice. A secondary prevention lipid clinic was started in a cardiology practice in March 2002 using 3 of 6 cardiologists and a pharmacist. This study compares results for cardiology patients treated in the lipid clinic to cardiology patients receiving usual care by a cardiologist.
METHODS: Medical records for 200 cardiology patients seen at least twice in 2003 were reviewed: 100 each from the lipid clinic (LC) and non-lipid clinic (NLC); and all had a history of coronary artery disease, hyperlipidemia, and documented LDL-C. Demographics, therapeutic lifestyle modification counseling, lipid levels, and medications were documented.
RESULTS: Baseline characteristics (gender, age, body mass index, revascularization procedures, diabetes, tobacco use) were statistically the same for both groups. LC patients had more clinic visits and were more often on combination therapy than NLC patients. LC patients were more often at goal for total cholesterol (91 vs. 71%), LDL-C (78 vs. 52%), and triglycerides (72 vs. 54%), but not for HDL-C (77 vs. 78%). LC patients had lower total cholesterol and LDL-C respectively (161 + 30 vs. 181 + 38; 86 + 23 vs. 100 + 34; p<0001). All LC patients received lifestyle modification counseling compared with NLC patients: diet (20%), exercise (18%), and tobacco cessation (50%). A stepwise forward selection regression model showed enrollment in the lipid clinic was a major predictor of achieving target total cholesterol and LDL-C (p<0.001).
CONCLUSIONS: The multidisciplinary approach, using a pharmacist in a cardiology-based secondary prevention lipid clinic, more effectively addressed risk factors and attained lipid goals than usual care provided by a cardiologist.

396E. Reduction in Framingham cardiovascular risk with concomitant treatment of hypertension and dyslipidemia with coadministered amlodipine and atorvastatin. *Richard A. Preston, MD*[1], J. Wouter Jukema, MD, PhD, FESC, FACC[2], Peter Harvey, MA, MB, BCHIR, MRCGP, DRCOG[3], Ottmar Herfert, MD[4], Gary Dykstra, DO[5], Franklin Sun, MPhil, MS[6], David Gillen, MD[6]; (1)Division of Clinical Pharmacology, Pharmacokinetics and Clinical Research Center, University of Miami School of Medicine, Miami, FL; (2)The Dept of Cardiology C5-P, Leiden University Medical Center, Leiden, Netherlands; (3)Crouch Oak Family Practice, Surrey, Addlestone, United Kingdom; (4)General Practice, Stuttgart, Germany; (5)Bluestem Cardiology, Bartlesville, OK; (6)Pfizer Inc, New York, NY.

PURPOSE: Recent guidelines have stressed the importance of the simultaneous management of multiple cardiovascular risk factors; however, the impact of such strategies has not been adequately tested by clinical trials. The Respond study investigated the efficacy of the concurrent treatment of concomitant hypertension and dyslipidemia.
METHODS: Respond is a multicentre, double-blind, placebo-controlled trial undertaken in 1660 patients with hypertension and dyslipidemia from 15 countries, randomized to 1 of 15 combinations of amlodipine besylate (placebo, 5, or 10 mg) and atorvastatin calcium (placebo, 10, 20, 40, or 80 mg). The main efficacy assessment was the mean change from baseline to end point in systolic blood pressure (SBP) and low-density lipoprotein cholesterol (LDL-C). A key clinical secondary end point was change from baseline to end point in Framingham risk score in patients without coronary heart disease (CHD) or risk equivalent (n=830).
RESULTS: At 8 weeks, combination-treated patients experienced dose-related and statistically significant reductions in SBP, LDL-C, and Framingham risk score, resulting in the estimated 10-year risk of developing CHD being reduced by 7.7-11.2 mean percentage point at end point from mean baseline levels of 15.8-18.5% in combination-treated patients. Overall, adding amlodipine to atorvastatin did not affect the LDL-C–lowering efficacy of atorvastatin. Adding atorvastatin to amlodipine did not affect the SBP-lowering efficacy of amlodipine.
CONCLUSION: Simultaneous treatment of concomitant hypertension and dyslipidemia with amlodipine and atorvastatin is a highly effective strategy for reducing Framingham risk score.
Published in Am J Hypertens 2005;18(5 suppl 1):A226.

397. Use of a risk screening tool (RST) and education to improve compliance with deep vein thrombosis (DVT) prevention practice guidelines. *Jay M. Mirtallo, M.S., RPh, BCNSP, FASHP*, Sara Damewood, B.S, Adam Rush, B.S., Jan Gatto, M.S., RN, David Bahner, M.D.; The Ohio State University Medical Center, Columbus, OH.

PURPOSE: Determine the effectiveness of a DVT risk screening tool and education in improving appropriate DVT risk assessment and prophylaxis.
METHODS: An RST was developed for patients at risk of developing DVT that included common risk factors, criteria for risk assignment to low, moderate, high or very high levels and recommended prophylaxis for each risk level. The content of the tool was extracted from the medical center's practice guideline. The tool was used to assess compliance with the guideline by evaluating each patient admission over a 5 week period in a general medicine unit at a tertiary teaching hospital (GM-U) as compared with a general medicine (GM-C) and orthopedic surgery (OS-C) unit in a community hospital. Compliance to the guideline was defined as the prophylaxis prescribed being in agreement with the risk level assignment done by review of the patient chart or interview with the patient and/or staff. In-service education was provided for medical and nursing staff on the GM-U unit. Also identified was frequency of risk factors occurring in this patient population pertinent to guideline.
RESULTS: There was a 61% compliance with the guideline in 285 patients evaluated. Compliance per unit was 55% (OS-C), 56% (GM-C) and 77% (GM-U). Compliance with the guideline was significantly improved in the group in whom in-service education was provided (GM-U, p<0.05). Guideline compliance was not affected by DVT risk level. The most common risk factors for DVT were age > 40 and obesity (BMI>30). Variables that influence anticoagulant dosing such as obesity (25% of patients) and impaired renal function (CrCl < 50 ml/min, 25%) as well as drug response; elderly (age > 65, 36%) were frequently present.
CONCLUSIONS: An RST and in-service education is effective in facilitating appropriate DVT prophylaxis. There are many variables present that influence anticoagulant response that requires further attention.

398. Evaluation of a metoprolol intravenous minibag administration pilot program at a community hospital. *Karen M. Whalen, B.S.Pharm, BCPS*, Deirdre Pierce, Pharm.D, BCPS, MaryRose Kott, MS, RN, NP, CNN, Dennis A. Ehrich, MD, FACC, AnneMarie Czyz, RN; St. Joseph's Hospital, Syracuse, NY.

PURPOSE: The administration of intravenous metoprolol by RNs in noncritical care areas was not permitted until a pilot program for intravenous minibag (IVMB) administration was launched. Prior to this all IV metoprolol doses had to be administered by an MD, NP or PA, usually as a bolus infusion. This program now allows nursing to administer metoprolol IVMB infusion with specific criteria on the telemetry floor.
METHODS: A panel of nurses, pharmacists and cardiologists was convened to outline the parameters of the pilot program. Education was performed prior to implementation. Patients were candidates for IVMB metoprolol if they were on chronic beta-blockers for chronic conditions and unable to receive medications enterally; exclusions included acute arrhythmia. Suggested oral to IV dose conversion was 2.5:1. For safety, the infusion was run over 60 minutes via infusion pump; all patients had telemetry monitoring and vital signs q15 minutes for 1 hour. The pharmacy sent an adverse reaction "ticket" with each minibag to prompt nursing to prospectively report adverse reactions.
RESULTS: A retrospective review of all patients receiving IVMB metoprolol on

a telemetry floor from 12/04 through 5/05 and discharged before 6/1/05 was conducted. Twenty-six patients received 201 of 231 scheduled doses. Only 11/26 met all inclusion criteria and some patients had one or more of the following: 14/26 had the exclusion criteria of acute arrhythmia, 8/26 were not on chronic beta-blockers and 6/26 could have received enteral metoprolol. Vital sign monitoring was performed for 61% of the doses with 73% of patients having at least half of their doses monitored per protocol. No prospective or retrospective adverse reactions were identified.
CONCLUSIONS: Nursing safely administered IVMB metoprolol even when all inclusion/exclusion criteria or vital sign monitoring were not met in this small patient population. Education will be enhanced to improve appropriate patient selection.

399. Implementation of a telephonic diabetes disease management program in a community-based primary care medical group. *Dawn Fuke, Pharm.D.*, Ginger Pape, Pharm.D., Jacquelyn Hunt, Pharm.D., MS, Joseph Siemienczuk, M.D.; Providence Medical Group, Beaverton, OR.

PURPOSE: Recent data demonstrate a low rate of ADA guideline-recommended diabetes treatment goal achievement and published evidence suggests improvements in care occur by incorporating pharmacists in the management of patients with diabetes. Furthermore, medication management often does not require an in office physical examination. The purpose of this program is to determine if the addition of a telephonic pharmacist diabetes program collaborating with clinics improve key diabetic parameters beyond clinic-based registry implementation.
METHODS: This is a prospective, randomized, non-blinded, controlled study in Providence Medical Group (PMG), a community-based primary care health system that has been utilizing an electronic medical record for the past eight years. Patients are included if they are active patients of a participating primary care physician, have the diagnosis of diabetes in their problem list and are at least 18 years of age. An active patient is defined as one with chart activity in the past three years. Randomization occurred at the clinic level. All clinics received the Diabetes Registry, a web-based disease management tool, at study start. Clinics in the pharmacist intervention arm obtained additional support that includes a medical assistant and clinical pharmacy specialist team. This team focuses on active telephonic cholesterol management, facilitates laboratory orders and office visits for diabetes follow-up. The primary outcome measure is percent low-density lipoprotein-cholesterol goal attainment (less than 100 mg/dL). Secondary outcomes include percent goal attainment of hemoglobin A1c (less than 7%), blood pressure (less than 130/80 mmHg) and aspirin use, patient and physician/staff satisfaction scores as well as healthcare utilization during the study period.

400. An international survey of critical care pharmacists. *Jaclyn M. LeBlanc, Pharm.D.*, Enrique C. Seoane-Vazquez, Ph.D., Joseph F. Dasta, M.Sc.; College of Pharmacy, The Ohio State University, Columbus, OH.

PURPOSE: The role of the intensive care unit (ICU) pharmacist has advanced in parallel to the clinical pharmacy movement, as described in a US survey (Crit Care Med 2004;32:A613). The purpose of this project was to describe the activities and responsibilities of ICU pharmacists in an international setting.
METHODS: The validated questionnaire of comprehensive hospital pharmacy activity in 2004-5 was placed on the web. A pharmacist from each country disseminated the information to members of the respective pharmacy societies or organizations. Descriptive statistics were used in analysis.
RESULTS: From the survey, a subset of 125 (12.4%) pharmacists from 18 countries were identified as ICU pharmacists (>50% time in the ICU). Response rate could not be calculated, as the number of ICU pharmacists in most countries was unknown. Countries represented in this sample were Australia (n=13, 10.4%), Canada (n=23, 18.4%), Thailand (n=12, 9.6%) and the UK (n=40, 32%), with 13 other countries comprising the remaining 29.6%. Pharmacists worked an average of 42.4 ± 9.5 hours/week (range 8-72). Patient care rounds were attended by 86 (68.8%) for an average of 9.8 ± 6.5 hours/week. Therapeutic drug monitoring was performed by 73 pharmacists (58.4%). Other specific activities are presented in Table 1. Table 1:

Specific activities of ICU pharmacists

Activity	n (%)
Intervene to change drug therapy when required	108 (86.4)
Monitor drug therapy for efficacy/adverse events	103 (82.4)
Develop or update ICU protocols	80 (64.0)
Assess suspected drug-related ICU admissions for causality	75 (60.0)
Evaluate all parenteral nutrition orders	53 (42.4)
Involved in ICU research	37 (29.6)
Provide written nutrition consults	28 (22.4)
Respond to resuscitation events	17 (13.6)

CONCLUSIONS: Many ICU pharmacists around the world provide a wide range of important clinical services. There are opportunities to increase clinical activities specifically in the areas of research involvement and participation in resuscitation events.

401. Evaluation of an intensive insulin protocol in critically ill patients. *Christopher K. Finch, Pharm.D.*, Bob L Lobo, Pharm.D.; Methodist Healthcare University Hospital, Memphis, TN.

PURPOSE: Intensive insulin protocols have been demonstrated to reduce morbidity and mortality in critically ill patients, but their use presents challenges to clinicians and health-care systems. We evaluated an intensive insulin protocol in critically ill patients to ensure that it effectively reduced hyperglycemia without an excess of hypoglycemia.
METHODS: Blood glucose measurements from critically ill patients treated with an intensive insulin protocol were retrospectively reviewed to determine how many were in the goal range of 80-130 mg/dl and how many were below 60 mg/dl. Blood glucose determinations were compared with those of other critically ill patients managed with a standard sliding scale insulin protocol.
RESULTS: There were 942 blood glucose measurements from 15 patients treated with the intensive insulin protocol and 353 blood glucose measurements from 15 patients managed with a standard sliding scale protocol. Blood glucose was in the goal range 47% of the time with the intensive insulin protocol versus 33% of the time with a standard sliding scale insulin protocol (P<0.001). Patients managed with the intensive insulin protocol were also more likely to be in an acceptable range of 60-130 mg/dl (53.1% vs. 35.8%; P<0.001). Hypoglycemia occurred in 2% of those managed with the intensive insulin protocol versus 1.4% of those receiving a standard sliding scale insulin protocol (P=NS).
CONCLUSIONS: Implementation of an intensive insulin protocol for critically ill patients improved the management of hyperglycemia compared to a standard sliding scale insulin protocol.

402E. Evaluation of venous thromboembolism prophylaxis in mechanically ventilated intensive care patients. *Abir O. Kanaan, Pharm.D.*[1], Jennifer Mazzola, Pharm.D.[1], Maichi Tran, Pharm.D.[2], Julie Drake, Pharm.D.[2], Frederick Spencer, MD[2]; (1)Mass College of Pharmacy and Health Sciences, Worcester, MA; (2)UMass Memorial Medical Center, Worcester, MA.

PURPOSE: Current guidelines from the American College of Chest Physicians recommend the use of either unfractionated heparin (UFH) or low-molecular weight-heparins (LMWH) for DVT prophylaxis in medically ill patients. To date, there are no formal recommendations for VTE prophylaxis in mechanically-ventilated intensive-care unit patients as this patient population is often excluded from clinical trials. We hypothesize that the incidence of hospital acquired VTE is greater than what is routinely reported for the "medically ill" patient (~15%). Our secondary endpoints are to evaluate the different modalities used in the prevention of VTE and bleeding events.
METHODS: A retrospective medical chart review was conducted in 500 consecutive patients at UMass Memorial Medical Center to evaluate the incidence of VTE and the prophylactic anticoagulant utilization in critically ill medical patients requiring mechanical ventilation for greater than 24 hours. Patients were included if they were 18 years or older, and had a non-surgical admission to the coronary or medical ICUs during study years 2001 through 2004. Patients with recent surgery (during the last 3 months) or those with VTE on admission will be excluded.
RESULTS: Two hundred charts have been reviewed and 85 patients have met inclusion criteria. The incidence of confirmed VTE via venography, CT, duplex, MRI or pathology, was 9% (n = 8). Of these patients, four did not receive VTE prophylaxis. The most common prophylactic anticoagulant utilized in the total population evaluated was UFH (29%) followed by pneumatic compression boots (28%), UFH in combination with pneumatic compression boots (19%) and enoxaparin (7%). Bleeding risk is currently under review.
CONCLUSIONS: We found the incidence of VTE in the medically ill, mechanically ventilated patient less than the incidence reported in the medically ill patient. A larger population needs to be further evaluated to confirm this result.
Presented at the 39th Midyear Clinical Meeting of the American Society of Health-System Pharmacists, Orlando, FL, December 5-9, 2004.

403. Development, implementation and evaluation of an erythropoietin alpha (EPO) program in trauma patients. *Karen O. Petros, PharmD*[1], Alison M. Wilson, MD[2], Maria Pompili, PharmD[3]; (1)West Virginia University Hospitals, Morgantown, WV; (2)West Virginia University, Morgantown, WV; (3)Monongalia General Hospital, Morgantown, WV.

PURPOSE: EPO was being increasingly utilized in our trauma population without sufficient evidence for dosing and efficacy. We observed a wide variation in EPO dosing, adjunctive therapy utilization and therapeutic monitoring.
METHODS: An anemia management program was undertaken to provide guidelines for patient selection for initiation of EPO, to encourage uniform laboratory monitoring, dosing, and adjunctive medication prescribing. A multidisciplinary team developed and implemented the program in August 2004 based on literature from other patient populations.

RESULTS: Twenty-one trauma patients (15 male, 6 female) received EPO from 8/2004 through 1/2005. The average patient age was 52yr (range 18-80) and weight was 88kg (range 52-149). All patients met criteria for initiation of therapy. Patients received from 1 to 25 subcutaneous doses (median 5.) The average hemoglobin (Hgb) at initiation was 8.03mg/dl (range 6.7-8.9) and 10.8mg/dl (range 9.2-13.3) at treatment end. Patients demonstrated an increase in Hgb from 1.1-6mg/dl and were appropriately monitored. Sixteen patients had ICU LOS > 5 days with 3 deaths prior to day 5. A loading-dose of 600u/kg was given to 12 patients (57%); a maintenance-dose of 150u/kg was given to all patients who received > one dose (N=19). Sixty-eight percent of patients received < 40,000 units/wk; 10% received 40,000 units/wk and 21% (N=4) received >40,000 units/wk- a common ICU dose. Baseline reticulocyte count, serum iron, folic acid and B12 levels were checked in 48%, 58%, 10% and 42%, respectively. Repeat labs were rare. All patients, except one, received iron supplementation. All patients received multivitamins, folic acid and cyanocobalamin.
CONCLUSIONS: The program successfully standardized dosing, route of administration, adjuvant medication prescribing and established initiation criteria. Weight-based dosing appears to be effective for increasing Hgb and may be more economical than standardized dosing even in an overweight population. Further education of appropriate laboratory monitoring is needed.

404. Development and implementation of a Web-based nonformulary documentation system. *Nannette M. Berensen, PharmD, BCPS*, Sabrina W Cole, PharmD, Kelli L Davis, PharmD, Holly M MacFall, PharmD, Liu H Jiang, PharmD, Paul W Bush, PharmD, MBA; Medical University of South Carolina, Charleston, SC.

PURPOSE: To develop and implement a nonformulary documentation system to improve formulary system compliance and increase operational efficiencies.
METHODS: A workgroup was convened to identify features and functional components of an automated nonformulary documentation system. The following characteristics were identified: electronic, user friendly, real-time submission capability, real-time notification of nonformulary requests to distribution center staff, minimize free-text fields, maximize the use of standardized statements for clinical justification, and generate nonformulary reports efficiently. The programmer worked closely with the drug information staff to develop, implement, and refine the system. Coldfusion Web programming language was used to build the request form. The system is composed of a Web page to collect requests, a Web page to report the details of each request, and a data storage table. Data are housed on a secure server. Education about the system was provided in October 2004, and the system was implemented in November 2004. A user satisfaction survey was distributed to 64 pharmacists in June 2005.
RESULTS: Thirty-six percent of surveys were returned (n = 23). Eighty-seven percent of respondents reported being very satisfied with the new system, and 13% reported being somewhat satisfied. Eighty-three percent of respondents reported that the system takes less time to complete nonformulary documentation. All respondents reported that the system was either very easy or easy to use. Forty-four percent of respondents reported improved formulary system compliance, whereas, 52% reported no change. Nonformulary documentation has increased 6%. The average number of documented nonformulary orders converted to formulary alternatives has increased from 12 to 25 per month. The average amount of time to produce a nonformulary report has decreased from about 16 to 4 hours. The real-time notification of distribution center staff has expedited procurement.
CONCLUSIONS: This system has improved formulary system compliance and operational efficiencies. Respondents identified future system enhancements.

405. Pharmacy student collaborative disease state management on an intermediate internal medicine unit. *Angela R. Thomason, Pharm.D.*[1], Manivannan Neelamegam, M.D.[2]; (1)McWhorter School of Pharmacy, Samford University, Birmingham, AL; (2)Tuscaloosa Veterans Affairs Medical Center, Tuscaloosa, AL.

PURPOSE: Student collaborative disease state management was implemented to improve patient outcomes, increase documentation, and reduce medication cost. Secondary purpose was to enhance pharmacy students' knowledge of assessment, treatment, management, and monitoring of disease states such as diabetes, hypertension, hyperlipidemia, anticoagulation, and various infection diseases on an internal medicine unit.
METHODS: Students completed an initial assessment on the patient upon admission including a patient interview, past medical history, admission medications, allergies, vitals, drug interactions, laboratory values, and renal clearance. Students were required to complete an assessment of current medication therapy; evaluate and set goals based on guidelines; recommend adjustments in medications to reach target goals; and set guidelines for monitoring and reevaluating. The evaluation was documented in a SOAP note format and presented to the supervising pharmacist for approval. After approval, the recommendations were presented to the interdisciplinary team, and the SOAP note was documented in the patient's medical chart. Students followed the patient's disease states based on the monitoring recommendations in the initial assessment and changes were documented with an abbreviated SOAP note.
RESULTS: Eight doctor of pharmacy students completed a 4-week rotation on the internal medicine unit during a 5-month time period. During the 5 months, 48 initial and 30 follow-up patient assessment SOAP notes were completed by the students. In addition, students helped the interdisciplinary team in reducing medication cost by 5,109 dollars per month. By the third week students were able to determine monitoring parameters, patient specific goals for various disease states, adjustment of medications, and appropriate documentation.
CONCLUSIONS: Student collaborative disease state management improved cost and documentation. Secondarily students had improved their knowledge in assessment, treatment, management and monitoring in areas such as diabetes mellitus, hypertension, hyperlipidemia, anticoagulation, and various infection diseases.

406. Initiating clinical pharmacy services in the State of Qatar. *Yolande Hanssens, PharmD(BEL)*, Noora Obaidan, BScPharm, MSc, PhD, Fathia Adheir, BScPharm, Aisha Alsulaiti, BPharm, Ghada Al-Mulla, BPharm, Noriya Al-Khuzaei, BScPharm, Banan Mukhalalati, BPharm; Hamad Medical Corporation, Doha, Qatar.

The State of Qatar is the peninsula bordering the Arabian Gulf and Saudi Arabia, and has an estimated population size of 744,000. Free healthcare for nationals and subsidized healthcare for residents form the cornerstone of the national healthcare program. Hamad Medical Corporation (HMC), a 1,600 bed tertiary referral center located in the capital Doha, opened in 1981 and provides service in all medical and paramedical specialties. The Pharmacy department applies a unit dose supply system, provides total parenteral nutrition, intravenous admixtures, outpatient dispensing, and has a drug and poison information center. In March 2004, a Clinical Pharmacy Services (CPS) unit was established in the pharmacy department, which is led by a PharmD(BEL) holder with 20 years of extensive clinical and drug information experience. The aim of the unit is to initiate and establish continuous CPS to all intensive care units (ICUs), in addition to the training of young Qatari pharmacists in the field of CPS. Currently, 4 Qatari pharmacists–all graduates from universities in the Middle East–are full-time involved and are integrated members of the clinical teams in medical, surgical and trauma ICU as well as the coronary care units. A fifth pharmacist joined in April 2005 to develop CPS in neonatal ICU. To meet Joint Commission International (JCI) standards, a 34-week training program for 12 Qatari pharmacists was scheduled to start in June 2005, in collaboration with an American consultant PharmD. Selected staff will proceed with overseas training in the field of CPS. The overall goal is to provide CPS throughout HMC at inpatient as well as outpatient level. Therefore, recruiting extra staff with the required level of experience and skills would allow expansion of the CPS, and provide continuity in service while Qatari staff embarks on their overseas training.

407. The development of patient and practitioner education materials for an HIV/AIDS clinic in Kenya. John Lock, PharmD, Eliza Smoker, PharmD, *Ellen M. Schellhase, PharmD*, Julie A. Everett, PharmD; Purdue University, Indianapolis, IN.

HIV/AIDS is a significant problem in Kenya, affecting 15% of the population. Moi Teaching and Referral Hospital and its affiliated rural clinics treat the largest number of patients with HIV in Kenya. With the increasing availability of antiretroviral therapy, there is a growing need for appropriate medication education. This is difficult due to lack of resources, lack of time for patient education, and inconsistent knowledge among providers. The purpose of this project was to provide educational resources for health care providers and patients. Pharmacy students developed a drug therapy education handbook for healthcare providers including information about the commonly prescribed antiretroviral drug regimens and ancillary medications. The resource was written in a standardized format and contains information such as dosing intervals, adverse effects, and contraindications. One-page patient education handouts were also developed for each of the medications. These include information and answers to commonly asked medication questions. The challenges of creating the provider education resource included understanding the cultural, fiscal, and therapeutic differences seen in Kenya. The stigma associated with HIV/AIDS and its treatment complicated the development of the patient education handouts. In the future, these resources will be translated into Swahili in order to reach a broader patient population. The education materials will be made available in all clinic areas and in the dispensing pharmacies.

408. Assessment of a "Rotation Fair" to increase awareness of select advanced pharmacy practice experiences. *Michelle Holt-Macey, RPh*, Edward

F. Foote, PharmD, FCCP, BCPS, Anne Lin, PharmD; Wilkes University, Wilkes-Barre, PA.

PURPOSE: A Rotation Fair was developed to enable students to gain a better understanding of available Advanced Pharmacy Practice Experiences (APPE). The purpose of our study was to assess its value and to measure its impact on the level of interest in select rotations.
METHODS: Preceptors of select rotations were asked to participate. Fourth year professional students (P4) on rotation at participating sites were required to prepare posters that highlighted their rotation activities, samples of their work, and what they've gained from the rotation. P3 students, who were about to begin the rotation selection process, were able to review the posters and talk to students and preceptors. Our "pre-selected" rotations, which students must be interviewed and chosen for, were highlighted. A web-based survey was sent to P4 students on rotation in November 2004 regarding the Fair held for them in January 2004 to assess the quality of the Fair. Interest in pre-selected rotations was measured by a count of interviews requested by students.
RESULTS: Two Rotation Fairs have been held to date (2004 and 2005). Thirty-five students completed the survey (response rate 51%). Students agreed or strongly agreed to the following statements: the information I received at the fair was helpful in making my rotation decisions (71%); the information provided was an accurate description of the rotation (90%); a poster presentation is the best format for the rotation fair (78%); and the rotation fair should be held every year (94%). The number of pre-selected rotations that students voluntarily interviewed for increased from 34 (2003, prior to implementing the Fair), to 63 (2004), and to 80 (2005).
CONCLUSIONS: Results from the survey suggest the Rotation Fair was well received by students. The increase in interviews for pre-selected rotations also suggests that the Fair increased interest in these excellent rotations.

409. Cost of a media fill test used to evaluate aseptic manipulation skills mandated in USP <797>. *Claudia A. Kaneshiro, Pharm.D.*, Steven D. Chretien, Pharm.D., Lucy S. Ung, Pharm.D.; VA Medical Center, Long Beach, CA.

PURPOSE: Good aseptic technique is a major component in the preparation of compounded sterile products (CSPs). Evaluation of this skill is a mandatory requirement of USP <797>. At the VA Medical Center in Long Beach, a large number of staff perform this skill: 16 pharmacists and 15 technicians prepare CSPs.
METHODS: We developed a media fill test to validate the aseptic technique of our IV personnel based on guidance outlined in USP <797>. We have analyzed the cost of using in-house resources compared to a commercially purchased media fill kit (Valiteq System, the RL-2 Kit). Our method employed the transfer of 3 sets of enriched soybean-casein digest broth between sterile evacuated vials resulting in a total of 21 manipulations per operator. The vials are sent to the microbiology lab and incubated in the Bactec 9000 Instrument for 14 days.
RESULTS: The estimated cost per operator for supplies (excluding syringes, needles, transfer sets) at the VA is $7 compared to the Valiteq kit $27 ($82 for 3 operators). The cost of annual testing (medium risk level) for our staff is $217 which is 75% savings over a commercially purchased kit.
CONCLUSION: Planned USP <797> physical plant requirements and the construction necessary to implement will be costly for most pharmacies that prepare CSPs. Minimizing the recurring cost of media fill tests is one way of reducing the anticipated cost of meeting the requirements of USP <797>.

410. Student preparedness for advanced practice experiences: preceptors' perceptions. *Lisa M. Lundquist, PharmD, BCPS*, Shirley Hogan, PharmD; University of Mississippi School of Pharmacy, Jackson, MS.

PURPOSE: The aim of this two-year evaluation is to assess the preceptors' perceptions of students' preparedness for advanced practice experiences in the fourth professional year, after completing the PBL curriculum in the third professional year.
METHODS: A survey was developed utilizing the PBL evaluation benchmarks for group performance. Preceptors were asked to rate the adequacy of students' preparedness in knowledge acquisition, self-directed learning, and clinical reasoning. The survey tool was then transferred to scantron readable format with a range of 1–5 with 1 = very well prepared and 5 = very poorly prepared. The survey was administered to all preceptors in attendance at the annual Mississippi Preceptors Conference held in March 2004 and March 2005.
RESULTS: Seventy-one of 141 current preceptors (50%) attended the conference and participated in 2004, and 72 preceptors (51%) participated in 2005. Preceptors reported students perform very well or well researching reputable and pertinent primary literature (90% in 2004, 91% in 2005), incorporating primary literature into patient care decision making (77%, 68%), efficiently retrieving current medical information (93%, 94%), evaluating drug regimen appropriateness (76%, 79%), and communicating with patients about medications or diseases (71%, 78%). Thirty percent or more of preceptors reported only average or poor performance in identifying and utilizing drug assistance programs (63%, 68%) identifying significant drug interactions (43%, 31%), and effectively communicating in writing with healthcare professionals (35%, 35%).
CONCLUSIONS: A majority of preceptors report PBL effectively prepares students to research and utilize current medical literature and tailor drug therapy regimens while incorporating information from a variety of disciplines. However, areas in need of further evaluation have been identified and will be addressed in future research initiatives for curricula development.

411E. Body mass index and bone mineral density: is there a link? *Lisa M. Lundquist, PharmD, BCPS*, Leigh Ann Ross, PharmD, BCPS, CDE; University of Mississippi School of Pharmacy, Jackson, MS.

PURPOSE: To assess body habitus as a predictor for osteoporosis risk.
METHODS: Bone mineral density (BMD) screenings were held at two shopping malls in ethnically diverse locations. Patient demographics of women greater than 18 years, including age, race, height and weight, were obtained and body mass index (BMI) was calculated. A nurse assessed osteoporosis risk by using the Achilles Express Bone Ultrasonometer. Results of the osteoporosis screening were reported at T-scores, which represent low bone mass, a risk factor for osteoporosis. A pharmacist or pharmacy student individually discussed osteoporosis prevention and treatment, and screening results with each patient. Patients were encouraged to discuss the results with their physician.
RESULTS: Seventy-one patients were screened. The mean age was 54.9 years; mean BMI was 28. The racial demographic was 27 African American (38%), 1 Asian (1.4%), and 43 Caucasian (60.6%). Of the total patients screened, mean T-score was -0.46 standard deviations (SD) from normal. Overall, 27 patients (38%) were at risk of osteoporosis based on their T-score > -1.0 SD from normal; mean BMI was 28.1. Of overweight and obese patients with BMI greater than 25 (n=51), 37.3% (n=19) were at risk of osteoporosis based on T-score (mean T-score -1.65). Of obese patients with BMI greater than 30 (n=25), 32% (n=8) were at risk of osteoporosis based on T-score (mean T-score -1.54).
CONCLUSIONS: Overall, 38% of women screened were at risk of osteoporosis regardless of race. Thirty-seven percent of overweight or obese patients screened were at risk of osteoporosis. Historically, women with a larger body habitus were thought to have higher BMD than women with a smaller frame, and have not been identified as high risk for developing osteoporosis. This data suggests that overweight and obese women may have low BMD at any age and may benefit from screenings and prevention strategies.
Presented at the Women's Health Update of The National Center of Excellence in Women's Health, Jackson, MS, June 9, 2005.

412. Race and bone mineral density: are African American women at risk for osteoporosis? *Lisa M. Lundquist, PharmD, BCPS*, Leigh Ann Ross, PharmD, BCPS, CDE; University of Mississippi School of Pharmacy, Jackson, MS.

PURPOSE: To determine whether African American women are at risk for osteoporosis based on bone mineral density.
METHODS: Bone mineral density (BMD) screenings were held at two shopping malls in ethnically diverse locations. Patient demographics of women greater than 18 years including age and race were obtained. A nurse assessed osteoporosis risk by using the Achilles Express Bone Ultrasonometer. Results of the osteoporosis screening were reported as T-scores, which represent low bone mass, a risk factor for osteoporosis. A pharmacist or pharmacy student individually discussed osteoporosis prevention, treatment, and screening results with each patient. Patients were encouraged to discuss the results with their physician.
RESULTS: One hundred thirty-four patients were screened. The mean age was 52.1 years (range 21 to 87); the mean T-score was -0.3 standard deviations (SD) from normal (range –2.6 to 3.1). The racial demographic was 65 African American (48.5%), 2 Asian (1.5%), and 67 white (50%). Overall, 47 patients (35.1%) were at risk of osteoporosis based on T-score > -1.0 SD from normal; mean age was 59.3 years (range 29 to 87). Of African American patients screened, 14 were at risk of osteoporosis based on T-score (21.5%); mean age was 55.3 years. Of white patients screened, 32 were at risk of osteoporosis based on T-score (47.8%); mean age was 61.8 years.
CONCLUSION: Over one-third of women screened were at risk of osteoporosis regardless of race. Of African American patients screened, 21.5% were at risk of osteoporosis. Historically, African American women were thought to have higher bone mineral density (BMD) and lower osteoporosis risk than white women at any given age. This data suggests that African American women may have low BMD at any age and may benefit from screenings and prevention strategies. Further investigation into osteoporosis risk in African American women is needed.

413. Implementation of continuous pharmacist code response in a large

academic medical center. *William Alvarez Jr., Pharm.D., BCPS*, Umbreen Idrees, Pharm.D., Keith Thomassett, Pharm.D., BCPS, Mike Veltri, Pharm.D., Connie Saltsman, Pharm.D., MBA, John Clark, Pharm.D., M.S., BCPS, Nauder Faraday, M.D., Elizabeth Hunt, M.D., Todd Nesbit, Pharm.D., BCPS, Carla Gill, R.Ph., MBA, Heather Robinson, Pharm.D., Julene McClary, M.C.P.; The Johns Hopkins Hospital, Baltimore, MD.

PURPOSE: To describe the development and implementation process for a continuous pharmacist code response program.
METHODS: On October 1, 2004, an institution-wide continuous pharmacist code response program was implemented in the oncology, medicine, surgery, and pediatric divisions of The Johns Hopkins Hospital, a 945 bed tertiary academic medical center. Implementation was endorsed by the hospital's Cardiopulmonary Resuscitation Committee. The goal of the program was to provide consistent pharmacist coverage to facilitate medication admixture and delivery, assist with medication selection, and provide additional drug information as needed. A plan for education and implementation was developed in conjunction with pharmacy administrative staff. Clinical pharmacy specialists developed both adult and pediatric educational sessions for pharmacists and pharmacy residents. Pharmacists were required to complete both didactic and practical sessions prior to attending codes. Reference materials were developed and provided to pharmacists. Continuing education, in the form of mock codes, is conducted periodically to ensure retention of skills. A computerized quality assurance tool was developed to track pharmacists' activities on codes. A survey directed to pharmacists, nurses and physicians will also be conducted.
RESULTS: In October 2004, pharmacists began attending all codes within the hospital on all shifts. Since this time, pharmacists have responded to over 350 codes, facilitating medication admixture and delivery, assisting with medication selection, and providing additional drug information. A summary of pharmacist activities on codes will be reported. Results from the aforementioned survey will also be reported.
CONCLUSIONS: Successful implementation of a continuous pharmacist code response service within a large academic medical center requires a detailed implementation plan, an extensive training program for pharmacists, development of reference materials, provision of continuing education, and use of a quality improvement tool.

414. Point-of-care testing to promote health. *Wendy I. Brown, Pharm.D.*, Norma Kiser-Larson, PhD, RN; North Dakota State University College of Pharmacy, Fargo, ND.

PURPOSE: To promote awareness of health for Native Americans by providing point-of-care testing. To enhance cultural awareness and social responsibility of pharmacy students by promoting public health.
METHODS: Recognizing the need of health services for underrepresented groups in the community, a multi-disciplinary ambulatory screening program was formed. The team included a clinic nurse, college of pharmacy preceptors, and students. Cultural awareness surveys were given to P4 pharmacy students before and after the screenings. Monthly screenings were conducted though Native American Programs from September to December 2003. The Cholestech LDX Analyzer was utilized to screen lipid levels and the Elite Glucose Monitor screened blood glucose. Along with providing point-of-care testing, pharmacy students offered drug reviews to participants. Nursing students assessed Body Mass Index, blood pressure, vision and completed questionnaires relating to cardiovascular, depression, and diabetes risk. Participants with abnormal values were encouraged to share results with their healthcare provider or had an appointment scheduled through a federally supported clinic to establish a healthcare provider.
RESULTS: As the months progressed, the average total cholesterol increased and the HDL decreased indicating that the population currently attending the screenings was at greater risk for developing chronic disease. The trend in results convinced community partners to continue funding for two years. Prior to the screenings students' comfort level on Native American culture was "neutral." Following the screenings student comfort level was "good." Students' averages showed 70% of the cultural experiences received were new, 28% re-enforced previous experiences, and two percent of the experiences did not provide any benefit. Pharmacy students indicated that 91% of the cultural experiences received would be applied to their future practice of pharmacy.
CONCLUSIONS: Providing students with multi-disciplinary, culturally sensitive, service learning experiences promotes public health through identifying patient at risk for developing chronic disease.

415. Developing and implementing an interdisciplinary educational conference series to improve organizational performance. *Nannette M. Berensen, PharmD*, Krystal L. Moorman, PharmD, C. Wayne Weart, PharmD, Mark H. DeLegge, MD, Ronald O. Nickel, PhD, Celeste O. Phillips, MN, Paul W. Bush, PharmD, MBA, Marilyn Schaffner, MSN, Odessa B. Ussery, MEd; Medical University of South Carolina, Charleston, SC.

PURPOSE: To develop and implement an interdisciplinary, educational conference series to improve the professional staff's knowledge of and compliance with organizational initiatives.
METHODS: A steering committee convened to discuss strategies to improve the professional staff's knowledge of and compliance with organizational initiatives (e.g., Centers for Medicare and Medicaid Services indicators). The committee chose an educational conference series approach and branded it Med-U-Way. The committee agreed that a non-industry-based sponsorship was important to promote objective presentations. Each Med-U-Way Conference is 1 hour and features a physician, pharmacist, and nurse speaker to address each discipline's unique practice issues. The interdisciplinary presentation format is used to facilitate communication and cooperation between disciplines. Hospital administration allocates funding to provide lunches for participants. The committee pairs the professional staff's learning needs with organizational priorities when selecting topics. Attendees receive continuing education credit at no charge. The Med-U-Way program coordinator is responsible for on-going program management. The committee has two planning meetings each year where topics are selected and prioritized. Speakers are chosen based on their expertise. Advanced notification of Med-U-Way Conferences occurs via broadcast e-mails and posted announcements in elevators. Presentation topics have included managing patients with community acquired pneumonia, heart failure, acute coronary syndrome, anemia, diabetes, stroke, and pain; safe and appropriate use of direct thrombin inhibitors, proton pump inhibitors, and atypical antipsychotics; fall prevention; tobacco cessation; and medication safety.
RESULTS: The first Med-U-Way Conference was held in January 2003. To date, there have been 25 Med-U-Way Conferences. Since the program began, 711 hours of pharmacy continuing education credit, 567 hours of nursing continuing education credit, and 26 hours of medical continuing education credit have been issued.
CONCLUSIONS: Med-U-Way Conferences are well-attended by nurses and pharmacists. The interdisciplinary presentation format is an effective mechanism to promote communication and cooperation among health care professionals.

416. Evaluation of pharmacy practice residency candidate self-assessment surveys. *Marlea G. Wellein, PharmD, BCPS*, Andrea M. Wessell, PharmD, BCPS, CDE, Dominic Ragucci, PharmD, BCPS, Melissa Blair, PharmD, BCPS, CDE; Medical University of South Carolina, Charleston, SC.

PURPOSE: This descriptive analysis summarizes self-assessment survey results performed by Pharmacy Practice residency candidates in order to determine the level of experience based upon a standardized list of skills important to general hospital practice, and what candidate-specific variables correlate with a higher level of experience.
METHODS: Self-assessment surveys were administered to Pharmacy Practice residency candidates during an on-site interview at the Medical University of South Carolina (MUSC) from 2003-2005. The survey assessed the applicants' level of experience with certain areas of general pharmacy practice, including patient care activities, drug information, and drug distribution/control, based on a five point Likert scale (1-no experience/never done to 5-very experienced/routinely done). Correlation statistics were performed with the candidates' self-reported level of experience and their class rank, clinical rotation experience, and year of interview. In addition, a series of ANOVA analyses were conducted between the variables.
RESULTS: One hundred and sixteen applicants from forty-one schools of pharmacy completed the survey from 2003-2005. The applicants described a greater level of experience with patient counseling (median = 5), pharmacy databases (median = 5) medications histories (median = 4), pharmacokinetics (median = 4), and outpatient dispensing procedures (median = 4). Least experience was noted with participation in medical emergencies (median = 1.5), parenteral nutrition (TPN) (median = 2), and intravenous (IV) admixture techniques (median = 2). Overall, there was no correlation between class rank, clinical rotation experience or year of interview with level of experience in any topic area.
CONCLUSIONS: Graduating pharmacy students interested in Pharmacy Practice residency training described the least experience with medical emergencies, TPN, and IV admixture techniques. ASHP-accredited residency programs can increase exposure to these areas and should be considered by graduating pharmacy students interested in general hospital pharmacy practice.

417. Pharmacists' involvement in TOPOFF 3 bioterrorism exercises. *Joseph A. Barone, Pharm.D., FCCP*[1], Lois Jessen, MS, Pharm.D.[1], Clifton R. Lacy, M.D.[2]; (1)Ernest Mario School of Pharmacy, Piscataway, NJ; (2)Robert Wood Johnson University Hospital, New Brunswick, NJ.

TOPOFF (Top Officials) is a series of exercises mandated by the Federal Government to strengthen this country's ability to prepare for and respond to large-scale terrorist threats. In April 2005, the U.S. Department of Homeland Security, along with other federal, state, and local agencies conducted TOPOFF-3 (T3), the third and largest multinational TOPOFF exercise. New

Jersey (NJ) was confronted by a simulated, deliberate pneumonic plague outbreak. The T3 exercise also involved Connecticut (simulated explosive and chemical threat), as well as the United Kingdom and Canada. Every hospital and every county in NJ participated in the exercise. NJ pharmacists were actively involved in T3, from planning through execution and after action analysis. Critical areas of pharmacist involvement included chairing the executive council of NJ's terrorism preparedness and response advisory committee; planning and participating in the pre-T3 Strategic National Stockpile exercise; identifying and designing processes for safe, effective, and efficient medication distribution; and staffing of the Points of Dispensing (PODs). The T3 exercise demonstrated the vital role that pharmacists would play in response to mass casualty and mass exposure events. Pharmacists are a valuable part of the team involved in disaster response planning, development of medication management and dispensing systems, and design of medication prophylaxis and treatment protocols. Pharmacists are also useful to assist other health care providers with general patient care activities. Although it has been almost 4 years since the 9/11 tragedy and the anthrax bioterrorism, the need to continually exercise and stress the response systems remains critical. Pharmacists should involve themselves in the many aspects of readiness training and thereby contribute to overall preparedness.

418. An evaluation of patients with diabetes followed by a pharmaceutical care clinic. *Marc A. Earl, Pharm.D.*, Jodie M. Fink, Pharm.D., Cari A. Cristiani, Pharm.D.; The Cleveland Clinic Foundation, Cleveland, OH.

PURPOSE: Prior studies have demonstrated that pharmacist-managed diabetes clinics can assist patients in obtaining better glycemic control. This study assessed the impact of the diabetes services provided by the pharmacist-run Medication Management Clinic at The Cleveland Clinic Foundation.
METHODS: Patients with an initial visit to the Medication Management Clinic between April 2002 and November 2004 and a hemoglobin A1c (HbA1c) > 7.5% were included in the analysis. The primary objective was to determine the change in HbA1c from baseline to 3-6 months after the pharmacist intervention. Secondarily, cardiovascular risk factors (low density lipoprotein (LDL) and blood pressure) were evaluated. The type of pharmacist intervention made, demographics, and baseline characteristics were also collected.
RESULTS: Fifty-five patients with type 2 diabetes were included in the analysis (60% male, mean age 60.5 years). The mean HbA1c was 10.1% at baseline and 8.2% after pharmacist intervention, resulting in a mean change in HbA1c of -1.9% ± 1.8% ($p<0.0001$). Regarding cardiovascular risk factors, at baseline 58% of patients had a blood pressure > 130/80 mmHg, and 49% of patients had a LDL value > 100 mg/dL. The most common pharmacist intervention involved maximizing doses of patients' current medications. Fifty-five percent of patients had an increase in oral diabetes medication and 47% of patients had the amount of total daily insulin increased. In contrast, only 15% of patients had another class of diabetes medication added to therapy.
CONCLUSION: Pharmacist intervention services resulted in a significant decrease in HbA1c in patients with poorly controlled type 2 diabetes. Opportunities also exist for future pharmacist intervention to assist in the control of other cardiovascular risk factors such as blood pressure and LDL.

419. The impact of a pharmacist CDE on nephropathy risk assessment in a community health center. *David Hughes, Pharm.D., BCPS, CDE*[1], Ken Loving, M.D.[2]; (1)University of Wisconsin-Madison School of Pharmacy, Madison, WI; (2)Access Community Health Center, Madison, WI.

PURPOSE: To determine the impact of a pharmacist CDE on nephropathy risk assessment of diabetic patients seen in a federally qualified health center (FQHC).
METHODS: Demographic and clinical data of all diabetic patients seen between January 2005 and June 2005 were collected using Cardiovascular/Diabetes Electronic Management System (CV-DEMS). This diabetes database system is used by FQHCs to summarize diabetes outcomes. Patients seen by a pharmacist CDE (Rx group) were compared with patients seen by usual care (UC group) with respect to blood pressure control, glycemic control, smoking status, cholesterol values, and drug therapy regimens (anti-hypertensive and anti-diabetic).
RESULTS: Seventy percent of diabetic patients in the Rx group (n = 43) were evaluated for risk of nephropathy with a microalbuminuria (MA) test compared to 11.6% of patients seen by UC (n = 138; $p<0.05$ by χ^2). Of the patients screened for MA, approximately 50% of patients in the Rx group (16 of 30) had normal MA compared to 60% of patients in the UC group (10 of 16; p=NS). Average blood pressure values were 122/76 mm Hg for patients in the Rx group compared to 127/75 mm Hg for the patients seen by usual care (p=NS). Mean A1c values for patients seen by a pharmacist CDE were 9.2% compared to 8.2% in patients seen by usual care ($p<0.05$ by χ^2). Angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs) were used in 39.5% of patients in the Rx group and in 43.5% of patients in the UC group (p=NS).
CONCLUSIONS: Pharmacist CDEs can assist clinicians in diabetic nephropathy risk assessment. Improved screening of patients may not ensure optimization of renally protective therapy such as ACEIs or ARBs. Strategies for increasing utilization of optimal therapy warrant further investigation.

420. Arkansas outreach program for the Medicare drug discount card. *Lisa C. Hutchison, PharmD, MPH*[1], Claudia J. Beverly, PhD[2], Sharay C Lovett, PharmD[1]; (1)University of Arkansas for Medical Sciences College of Pharmacy, Little Rock, AR; (2)University of Arkansas for Medical Sciences College of Nursing, Little Rock, AR.

PURPOSE: The Medicare Modernization Act of 2003 established Medicare-approved Prescription Drug Discount Cards to provide a temporary drug benefit to Medicare recipients from June 2004 through December 2005. Educational outreach through community based organizations was funded as a primary means for providing information to eligible beneficiaries. The purpose of our program was to educate seniors in Arkansas about the Medicare Prescription Drug Discount Card and assist with enrollment in the best card for their circumstances.
METHODS: The project began September 2004 and continued through May 2005. The project director, a clinical pharmacist, attended a national training program and subsequently provided 13 train-the-trainer programs at the rural Centers of Aging (COAs)which make up the Arkansas Aging Initiative (AAI) and are located throughout the state. Instruction was provided with Internet resources, CMS-developed Prescription Drug Discount Card materials and locally appropriate case studies. The COA Education Directors coordinated outreach in each county within their cachement area. General information was provided through radio and television public service announcements and newspaper articles. Exhibits, seminars and one-on-one assistance were provided to senior Medicare beneficiaries. Success with outreach programming was reported bi-weekly to the project director.
RESULTS: 387 staff and volunteers were trained to provide assistance with the Medicare Prescription Drug Discount Cards. Information about the card reached nearly 1 million Arkansans through the news media. Subsequently, 4205 Arkansas Medicare beneficiaries received assistance with enrollment in the drug discount card. Our original target for assistance was 4200 seniors. We estimate 1262 enrollees (30%) qualified for various levels of transitional assistance which translates to $729,150 in assistance for these lower-income elders.
CONCLUSIONS: Funding of educational outreach through the AAI infrastructure is an effective means to enroll Medicare beneficiaries into Prescription Drug Discount Cards. Lessons learned will be useful in educating seniors about the new Medicare Part D benefit.

421. Cardiovascular risk reduction in frail elderly nursing home residents with diabetes. *Barbara Zarowitz, Pharm.D.*[1], Kelly Hollenack, Pharm.D., CGP, FASCP[2], Steve Law, Pharm.D., CGP[3], Samuel Gurevitz, Pharm.D., CGP[3], Terry O'Shea, Pharm.D., CGP, FASCP[4]; (1)Omnicare, Inc., Livonia, MI; (2)Omnicare, Inc., Dublin, OH; (3)Omnicare, Inc., Indianapolis, IN; (4)Omnicare, Inc., Englewood, OH.

PURPOSE: Diabetes is present in 25% of residents admitted to nursing homes. A health management diabetes program was developed to achieve treatment goals established by the American Geriatric Society (i.e. glycated hemoglobin (A1c)<8%, blood pressure (BP)<140/80 mm Hg, low-density lipoprotein cholesterol (LDL)<100 mg/dL, and triglycerides <150 mg/dL).
METHODS: Comprehensive educational, assessment, monitoring and intervention tools were developed and then implemented by 800 pharmacists for over 1 million nursing home residents following telephonic, web cast, and live, training. Interventions for glycemic control, BP, antiplatelet, and lipid therapy management and medication safety were documented using proprietary decision-support software. Primary outcomes were % appropriately treated and % at goal values. Data were collected in time series nationwide, and as point prevalence in Indiana.
RESULTS: From 3Q2004 (beginning of intervention) through 1Q2005 (ongoing intervention) the mean number of unique nursing home residents with diabetes was 167,043/690,678 (24%). The % of diabetics receiving ACEI/ARB and lipid-lowering therapy increased from 49 to 51% and 32.8 to 36.4%, respectively, from 3Q2004 to 1Q2005. In Indiana, of 4125 nursing home residents evaluated, 756 (18.3%) were elderly diabetic residents with coincident coronary heart, carotid artery and peripheral artery diseases in 51.7%, 28.4%, and 13.8% of residents, respectively. Lipid-lowering agents were prescribed in 307 (41.7%) residents. Of those tested, 68.2% and 60% of residents achieved an LDL <100 mg/dL and serum triglyceride values <150 mg/dL, respectively. Forty-six and 68.9% of residents attained a blood pressure <130/80, and <140/80 mmHg, respectively. Aspirin or clopidogrel was prescribed in 55.6% of residents. A1c testing was performed in 71% of diabetic residents with resultant A1c<8% in 458/538 (85%) of residents tested. Nationwide A1c, LDL and BP results are pending.
CONCLUSIONS: It is possible to achieve or exceed national standards for management of diabetes in frail elderly nursing home patients with targeted

educational intervention.

422. Medication managment in the elderly: a home care pharmacy service to improve emergency preparedness and medication use. *Danielle L. Wiley, Pharm.D.*, Ivy O. Poon, Pharm.D.; Texas Southern University, Houston, TX.

PURPOSE: To describe a cognitive pharmacy service that: (1) provides education on emergency preparedness, (2) counsels on medication management in a cohort of community dwelling homebound elderly patients in the Houston area.
METHODS: This is a descriptive study to review the medication management program provided by Texas Southern University College of Pharmacy and Health Sciences, in collaboration with the Area Agency on Aging of Harris County, Houston Department of Health and Human Services. The program involves (1) providing emergency safety kits, (2) counseling on medication(s) and associated disease state(s), (3) assisting with medication assistance programs (if applicable), and (4) publishing quarterly newsletters on current geriatric issues. Descriptive statistics will be used to summarize the study findings.
RESULTS: From March 2004 to October 2005, pharmacy faculty and pharmacy students performed about 125 home visits. Each client received an emergency safety kit, medication counseling, and tips on better self-care. Of those, about 92% were on more than 4 medications, and automatic electronic medication dispensers were provided to improve compliance. Two newsletters were published and distributed to 1,500 elderly clients in the Houston area. About ten percent of those clients received assistance with medication programs provided by drug companies.
CONCLUSIONS: This study describes an innovative cognitive pharmacy service to improve emergency preparedness and medication management in a cohort of community dwelling elderly in Houston.

423. Pharmacy-managed rural health screening. *Donna G. Beall, Pharm.D.*, Brian L. Galbreth, Pharm.D.; The University of Montana, Missoula, MT.

PURPOSE: One of the healthcare challenges facing residents of rural communities is the ability to obtain disease-screening services. Rural communities also have limited access to innovative pharmacy services. The ImProving Health Among Rural Montanans (IPHARM) project meets these needs. The goals of the IPHARM project are to deliver health-screening services to rural Montanans and to serve as a model ambulatory care practice.
METHODS: Screening events are scheduled through community pharmacies, the Montana Primary Care Association, and other organizations. Tests offered include bone density, cholesterol, HbA1c and thyroid. These tests are chosen because they are CLIA waived, meet the goals of "Healthy People 2010" and address conditions that are often silent and can be moderated or treated. Clients are counseled on therapeutic lifestyle changes and are encouraged to share these results with their provider. The IPHARM Clinical Pharmacy Specialist (CPS) trains students prior to participation. Students perform the tests as well as counsel clients. At least two pharmacists attend each event and serve as role models and preceptors. Students complete an assessment/satisfaction survey after participation.
RESULTS: IPHARM has traveled 27,647 miles and performed 5785 tests on 3731 Montanans with an average of 1.57 tests per patient. Of the tests provided, 36.5% were categorized as abnormal. The breakdown of tests performed and percent abnormal are: bone density 2971 (43%), lipids 1625 (40.74%), HbA1c 948 (14.5%), spirometry 305 (21.64%), thyroid 24 (4.17%). Screening services have taken place in community pharmacies, firehouses, county fairs and clinics. Since the beginning of the project, 86 pharmacy students have participated in an IPHARM event. Results of the students' assessment/satisfaction survey reveal positive results.
CONCLUSIONS: Residents of rural communities can gain access to pharmacist-performed health screening services. The program also acts as a model rural practice site for pharmacy students to gain experience in providing direct patient care.

424. Shared medical appointments in a primary care clinic: a new model of care. *Jeff L. Hulstein, PharmD, CDE*, Monica D Robinson, PharmD, Muhammad A Nasir, MD, Annette Hawkins-Frost, PA-C; Parkland Health and Hospital System, Dallas, TX.

PURPOSE: Shared Medical Appointments (SMAs) are efficient delivery of quality medical care to a group of patients in a supportive environment in which each patient's unique medical needs are individually addressed. Within 90 minutes, 12 to 16 relatively stable chronically ill patients are seen for routine follow-up care. These visits are voluntary for patients and provide a secure but interactive setting in which patients have improved access to their physicians and the benefit of a health care team. The purpose of the shared medical appointment is to improve patient access to their provider, increase clinical team productivity and efficiency, while improving overall patient and staff satisfaction.
METHODS: Within the primary care clinics of Parkland Health and Hospital System, patients due for routine follow-up care are registered voluntarily for a 90-minute shared medical appointment. A series of one physician to one patient encounters, with observers, address the unique medical need of each patient. A behaviorist is present during the session to manage group dynamics, facilitate time management and guide patient interaction. The nursing staff is responsible for vitals, assisting with discharge and patient education. During the individual encounters, a pharmacist is present to educate the patient group regarding disease-state management, address medication topics and provide discharge prescription instructions.
CONCLUSIONS: SMAs are a new and innovative model for healthcare. The SMA model helps improve patient access, continuity of care, patient satisfaction, clinical team productivity and versatility of practice. SMAs allow patients the opportunity to spend more time with their physician while utilizing the group environment to ensure care and improve quality of life.

425. The effect of an automatic prescription refill service on medication adherence and clinical outcomes in patient with hypercholesterolemia. *Jocelyn Chan, Pharm.D.*[1], Rita Hui, Pharm.D., MS[2]; (1)University of California, San Francisco, San Francisco, CA; (2)Kaiser Permanente Medical Care Program, Oakland, CA.

PURPOSE: Landmark clinical trials have demonstrated the overall benefits of statins on survival. Previous research has shown that adherence with statins is low and decreases over time. Nonadherent patients are less likely to reach target lipid values and therefore less likely to achieve full benefit from therapy. San Francisco Kaiser Permanente outpatient pharmacy implemented an automatic prescription refill service, called the Autorefill program to promote better adherence among patients. The study was designed to assess how the implementation of an automatic prescription refill service affects medication adherence and LDL-cholesterol (LDL-C) levels.
METHODS: This is a retrospective matched case control study using electronic databases. The primary outcome measures were the change in medication adherence rate and the proportion of adherent patients. Secondary outcome measures were the change in LDL cholesterol level and the proportion of patients at target LDL cholesterol.
RESULTS: We enrolled 306 patients from the Autorefill program and matched them to a control of 1105 patients based on age, gender, index date, and baseline LDL cholesterol level. The continuous medication acquisition ratio for patients enrolled in the Autorefill program increased by 4% compared to usual care patients ($p<0.0001$). Autorefill patients are 2.4 times (OR 1.5-4.0, $p=0.0005$) more likely to be adherent to statins compared to usual care patients. There was no significant difference in change in LDL cholesterol level (-8.5 mg/dL vs. -5.9 mg/dL $p=0.10$) nor proportion of patients at target LDL cholesterol (OR 1.18, $p=0.27$). However, there was a trend that indicates a higher likelihood of reaching target LDL cholesterol level for those enrolled in the Autorefill program.
CONCLUSION: These findings confirm that an automatic prescription refill service can improve medication adherence so that patients can fully realize the clinical benefits of their medications.

426. Medication therapy management services in ambulatory care. Stacy M. Prutting, BS, PharmD, BCPS, CDE, Jennifer N. Mazur, BS, PharmD, CDE, *Melissa M. Blair, BS, PharmD, BCPS, CDE*, Andrea M. Wessell, PharmD, BCPS, CDE, Alisa K. Christman, PharmD, Kelly R. Ragucci, BS, PharmD, BCPS, CDE, Joli D. Fermo, PharmD, BCPS, CDE, Sarah P. Shrader, PharmD, Elizabeth E. Ashcraft, BS, PharmD; Medical University of South Carolina, Charleston, SC.

PURPOSE: The Medicare Modernization Act of 2003 (MMA 2003) provides an avenue for outpatient prescription benefits that include Medication Therapy Management Services (MTMS). MTMS is a proposed distinct billable service designed to optimize therapeutic outcomes and improve continuity of care for individual patients. In order to attain this recognition, documentation of the scope of clinical practice is necessary. The purpose of this study is to quantify the scope of clinical services provided by ambulatory care clinical pharmacists.
METHODS: Ambulatory care clinical pharmacists from 5 university-based sites captured daily MTMS through the documentation system, CliniTrend®. Services included scheduled patient visits and telephone encounters for disease-state management. Management primarily involved anticoagulation, diabetes, hypertension, hyperlipidemia, smoking cessation, osteoporosis, and immunosuppression. Other patient-related activities were categorized as medication review/history and patient counseling. Pharmacotherapeutic interventions including consults, treatment recommendations, and monitoring were documented, in addition to administrative tasks such as medication refills, formulary conversions, and patient scheduling. All services were recorded from January to April 2005, and the results were annualized.
RESULTS: An annual total of 12,897 patient encounters for disease-state management were documented. Additionally, a total of 8,835 other patient encounters, pharmacotherapeutic interventions, and administrative tasks were documented. Based on a total of 21,732 interventions, approximately

59% of services were devoted to direct patient encounters and 41% devoted to other patient-related activities, pharmacotherapeutic interventions, and administrative tasks.
CONCLUSIONS: Ambulatory clinical pharmacists engage in a multitude of MTMS to facilitate and improve pharmaceutical care for their patients. The MMA and proposed reimbursement for MTMS is an opportunity for pharmacists performing these activities. Documentation of all medication-related activities and patient encounters is necessary to establish recognition for pharmacists as providers.

427. Pharmacist-directed lifestyle weight management service: development of a primary care clinic service. *Larry Aull, Pharm.D., M.S.*, Chris Cook, Pharm.D., Ph.D.; University of Georgia College of Pharmacy, Athens, GA.

PURPOSE: To describe the development of a pharmacist managed weight-loss clinic that uses lifestyle counseling and education to achieve weight loss.
METHODS: Responding to a need expressed by primary care clinic physicians for weight management counseling, two clinic pharmacists became certified as Lifestyle Counselors through the American Association of Lifestyle Counselors. Patients were recruited from northeast Georgia through physician referral and radio advertising promotion beginning in March 2004. Upon patient enrollment, the pharmacists perform baseline measures of height, weight, body mass index, body fat percentage, and blood pressure. Patients receive a pedometer, calorie counting guide, and a LEARN Program manual. The LEARN program emphasizes a modest, healthy 1-2 pounds per week weight loss through lifestyle, exercise, attitude, relationships, and nutrition changes. Daily caloric intake was determined for each individual based on height, weight, age, gender, and current level of physical activity. Patients could choose to meet weekly in either individual or group sessions for weigh-ins and discussions of the LEARN weekly lessons. Additionally, the pharmacists assisted patients to resolve medication-related issues while enrolled in the program.
RESULTS: Of 21 participants enrolled, 17 (80.9%) completed the program. Results are based on an intent-to-treat analysis. Mean baseline weight was 212.2 pounds. Mean weight loss was 10.7 pounds. The mean weight lost for patients completing the program was 12.2 pounds whereas for patients not completing the program was only 4 pounds. Individual weight loss ranged from one pound gained to 25.5 pounds lost. Additional benefits of improved blood pressure, lipid profile, and diabetes control were documented. Patients who have completed the program report maintaining or continuing their weight loss upon follow-up.
CONCLUSION: A pharmacist managed weight-loss program that focuses on gradual lifestyle modifications can successfully help patients lose weight in a healthy, sustainable manner.

428. Clinical pharmacy involvement in meeting American Diabetes Association (ADA) standards of care in a group-visit model. *Stephanie Barud, Pharm.D.*, Jennifer Chonlahan, Pharm.D., Todd Marcy, Pharm.D.; University of Oklahoma College of Pharmacy, Oklahoma City, OK.

PURPOSE: This study describes an innovative approach to meeting ADA standards of care through a multi-disciplinary group visit model in diabetic patients.
METHODS: Patients are scheduled for a modified drop-in medical group appointment (DIGMA). The first phase of the DIGMA is a pre-visit chart review. During the review the following standards of care are assessed: weight, blood pressure, dilated funduscopic eye examination, Hgb A1c, lipid profile, fasting plasma glucose, microalbuminuria screening, serum creatinine, pneumococcal and influenza vaccinations, anti-platelet therapy, and documentation of a foot examination. The second phase of the DIGMA is an individual component in which a physical examination is completed by a physician. A clinical pharmacist performs a detailed medication history, foot examination, and point-of-care (POC) laboratory. Billable POC laboratory is available to measure blood glucose, Hgb A1c, fasting lipid profile, and qualitative microalbuminuria. The third stage is the group component. A clinical pharmacist provides a 15-30 minute education session for the group of 5-15 patients. The physician then discusses individual patient needs. Further education and medical intervention is provided. Clinical pharmacists participate in the discussion and make recommendations. Finally, billing paperwork is completed. The pharmacy portion of the service is supported by billing G0109 codes.
RESULTS: An innovative process of care has been developed and has successfully improved compliance with ADA standards of care in the patients seen the DIGMA. Data collection that will quantify interventions is incomplete and will be reported at a later date.
CONCLUSIONS: DIGMA visits provide a model of care in which pharmacists contribute toward improved compliance with ADA standards of care.

429. Utilization of med kits for an HIV-positive population in Kenya. Julie A. Everett, PharmD, *Ellen M. Schellhase, PharmD*; Purdue University, Indianapolis, IN.

Moi Teaching and Referral Hospital consists of a 350-bed hospital and one on-site clinic located in Eldoret, Kenya's fifth-largest city (population 400,000). An additional seven rural clinics sites are located between 30 and 50 km from Eldoret. These clinics provide care to over 3,000 HIV + patients. Many of these patients need medications other than anti-retrovirals but are unable to afford the needed medications. In the U.S. at many long term care facilities, there are med kits containing medications that may be retrieved by the nursing staff when a new prescription has been written and has not been received from the outside pharmacy. It was identified that developing a program based on the med kit concept would impact the care of many HIV patients. The purpose of the med kits is to ensure patients receive medications needed to treat common ailments seen in the HIV + population. Medications for the med kit were chosen based on common health conditions seen by practitioners at the clinics, as well as price. Each of the 8 clinics is provided with an adult and a pediatric med kit. Grant support allows patients to receive the medications at no charge. Med kits are returned daily, refilled and redistributed on the next clinic day. Medications dispensed are tracked to monitor utilization as well as the need to order more drug supply. Weekly educational flyers concerning appropriate prescribing of these medications are placed in the med kits. In order to optimize the med kits, utilization data will be used to modify the med kit contents. Based on physician feedback and utilization, the med kits are having an impact on providing optimal HIV patient care.

430. Evaluation of a risk assessment approach to venous thromboembolism (VTE) prophylaxis in medically ill patients. *Michael P. Rivey, M.S.*, Douglas R. Allington, Pharm.D., J. Bradley Mathis, Pharm.D.; University of Montana Skaggs School of Pharmacy, Missoula, MT.

PURPOSE: The use of a risk assessment intervention to enhance use of venous thromboembolic (VTE) disease prophylaxis in medically ill patients was evaluated in the medicine unit of a small community hospital.
METHODS: Patients at risk of VTE with an anticipated hospital stay of at least 3 days were prospectively identified and assessed for VTE risk. Data regarding patient diagnosis, risk factors, and the use VTE prophylaxis was collected for a pre-intervention period and compared to results from a post-intervention period after implementation of a Clinical Pharmacy Note that provided a VTE risk assessment and treatment recommendations according to American College of Chest Physicians (ACCP) guidelines.
RESULTS: Use of recommended VTE prophylaxis by physicians increased from 28.6% (10 of 35 patients) in the pre-intervention group to 37.9% (33 of 87 patients) in the post-intervention group ($p>0.05$). Patients in post-implementation group (n=87) were an average 73.1 years of age with a mean 3.1 risk factors/patient; 77.0% had at least 3 risk factors for VTE. Use of the Clinical Pharmacy Note risk assessment intervention resulted in initiation of prophylaxis in 17 of 54 patients (31.5%), resulting in an overall use of VTE prophylaxis in 50 of 87 patients (57.5%) in the post-intervention group ($p<0.005$ compared to pre-intervention group). The most common VTE risk factor present in the post-intervention group was age > 75 years (40 patients), followed by pneumonia (39 patients), congestive heart failure (27 patients) and COPD (26 patients).
CONCLUSIONS: The Clinical Pharmacy Note intervention augmented use of VTE prophylaxis to a modest extent, due to limited physician acceptance. Our experience suggests a risk assessment/prophylaxis recommendation approach is insufficient to measurably affect a change in the use of VTE prophylaxis in medically ill patients.

431. Tenofovir-induced nephrotoxicity: recognizing incidence and determining risk factors in the first year of therapy. *Brooke Y. Patterson, PharmD*, Kathryn DeSilva, PharmD, Jodie L. Guest, PhD, David Rimland, MD; Atlanta VA Medical Center, Decatur, GA.

PURPOSE: To identify patients who have experienced nephrotoxicity while receiving a tenofovir (TFV)-containing antiretroviral regimen and to identify potential risk factors for the development of nephrotoxicity. Design: A retrospective chart review of HIV+ patients followed by the Infectious Disease Clinic was conducted at the Atlanta VA Medical Center. All patients who had received TFV prior to September 2004 were evaluated. Serum creatinine and phosphates were collected as follows: baseline and follow-up creatinine at 6 week, 3, 6, 9, and 12-month intervals after initiation. Data was also collected on co-morbidities, medication usage, and previous antiretroviral exposure.
METHODS: The primary endpoint was a composite of nephrotoxicity. Renal insufficiency was defined as a decline of ≥50% in calculated creatinine clearance from baseline. Hypophosphatemia was defined as a single serum phosphate ≤2.0 mg/dL during the treatment period.
RESULTS: Two hundred twenty-two patients were included. At baseline, patients had normal renal functioning (mean baseline SrCr 0.99 (± 0.31) mg/dL, mean baseline creatinine clearance 99 (± 31.15) mL/min), were highly treatment experienced (8 naive (4%)), and had an AIDS diagnosis (188 patients (84.6%)). After 1 year of therapy, 38 patients (17.12%) developed

nephrotoxicity. Of those 38 patients, 9 (4%) developed renal insufficiency and 29 (13%) developed hypophosphatemia. IV drug users had an increased risk (RR 3.94 (1.05-14.778), p=0.0329) of developing renal insufficiency. Treatment-naive patients were at an increased risk (RR 11.78 (3.49-39.69) p<0.0001) of developing renal insufficiency and of developing the composite endpoint. Patients with a prior history of amphotericin B exposure were at an increased risk (RR 3.08 (1.31-7.26) p=0.0305) of developing the composite endpoint.
CONCLUSIONS: The incidence of nephrotoxicity in our cohort in the first year of therapy was higher than previously reported in other cohorts. IV drug use, treatment naivety, and prior amphotericin B exposure were identified as risk factors.

432E. Pilot study of once-daily (QD) quad therapy with Trizivir (ABC/3TC/ZDV) and efavirenz (EFV). Peter Ruane, MD[1], Joseph Lang, MD[2], Edwin DeJesus, MD[3], Daniel S. Berger, MD[4], Robin Dretler, MD[5], Allan E. Rodriguez, MD[6], Doug Ward, MD[7], *Michael L. Lim, PharmD*[8], Qiming M. Liao, PhD[8], Sunila Reddy, PharmD[8], Marty H. StClair, PhD[8], Mark S. Shaefer, PharmD[8]; (1)Tower ID, Los, Angeles, CA; (2)ID Consultants, Charlotte, NC; (3)Orlando Immunology Center, Orlando, FL; (4)Northstar Medical Center, Chicago, IL; (5)ID Specialists, Atlanta, GA; (6)University of Miami, Miami, FL; (7)Dupont Circle Physicians Group, Washington DC, DC; (8)GlaxoSmithKline, Research Triangle Park, NC.

PURPOSE: Trizivir (TZV) + EFV is a potent quad regimen. QD dosing of ABC, 3TC, and EFV are each supported by PK and clinical data. At the time this study was designed, ZDV QD was under investigation. This pilot study explored the feasibility of TZV QD + EFV.
METHODS: Prospective, open-label trial of subjects initially receiving TZV BID + EFV QD with viral load (VL) <50 c/mL for ≥3 months. Subjects randomized to switch to TZV QD + EFV QD (QD arm) or continue current treatment (BID arm) for 24 weeks.
RESULTS: 36 subjects (89% male, median CD4+ count = 521 cells/mm3) randomized. One was lost to follow-up (BID arm); one did not take all study drugs (QD arm). At 24 weeks, 17/18 (94%) in QD arm and 16/18 (89%) in BID arm maintained VL <50 c/mL by intent to treat, missing = failure (p=1.0). As treated, 17/17 (100%) in QD arm and 15/16 (94%) in BID arm maintained VL <50 c/mL. One subject (QD arm) met virologic failure (confirmed VL≥120 c/mL); genotype showed M184V, later revealed to not have taken EFV. At 24 weeks, median CD4 count was 522 cells/mm3 (QD arm) and 500 cells/mm3 (BID arm). Adverse events (AEs) were similar between arms; no HSR or AE withdrawals occurred.
CONCLUSIONS: In this pilot study of subjects suppressed on TZV BID + EFV, switching to TZV QD + EFV (3 tablets QD) was associated with similar rates of virologic suppression and tolerability, compared to continued TZV BID + EFV.
Presented at the 7th International Congress on Drug Therapy in HIV Infection, Glasgow, UK; 14–18 November 2004.

433E. HIV adherence-pharmacology unit coordinates pharmacotherapy and clinical research. *Naomi Boston, Pharm.D.*[1], Linda Catanzaro, Pharm.D.[1], Judianne Slish, Pharm.D.[1], Kathleen Walsh, MSW[2], Adel Suliaman, M.D.[2], Chui-Bin Hsiao, M.D.[2], Gene Morse, Pharm.D.[1]; (1)University at Buffalo School of Pharmacy and Pharmaceutical Sciences, Buffalo, NY; (2)Erie County Medical Center, Buffalo, NY.

PURPOSE: An Adherence-Pharmacology Unit has been established in an urban HIV clinic utilizing pharmacists in the management of pharmacotherapy and promotion of medication adherence. Identifying patients for enrollment in clinical trials provides the opportunity for improving individual HIV therapy management.
METHODS: Patients are referred for adherence counseling prior to initiation of or change in antiretroviral therapy. Pharmacists also review all patients with viral load increases of > 0.5 log and interpret all resistance test results on a weekly basis. Potential candidates for active protocols are discussed with the provider and offered the opportunity to participate. New protocols and patients on current protocols are reviewed with a multi-disciplinary clinical research staff bi-weekly.
RESULTS: As of 5/28/05, a total of 1,057 patients are currently seen at the HIV clinic. Between June 2004 and May 2005, a total of 163 patients were seen in the Adherence-Pharmacology Unit, 177 viral load assessments and 116 resistance test interpretations have been performed. Active enrollment in studies began in 2003, and is still in place. There are four active research protocols in which the Adherence-Pharmacology Unit interfaces research with patient care. A total of 101 patients have been referred to these studies. Common reasons for referral include: virologic or treatment failure, suspected toxicity, suspected non-adherence, and drug-drug interactions.
CONCLUSIONS: The Adherence-Pharmacology Unit is an integral component of an urban clinic which provides various novel academic services to a diverse patient population facilitating pharmacotherapy management and clinical research.
Presented at the 9th Annual United States Conference on AIDS, Atlanta, GA, October 1-4, 2005.

434E. Therapeutic drug monitoring (TDM) in patients coinfected with HIV and hepatitis C (HCV). *Judianne Slish, Pharm.D.*[1], Naomi Boston, Pharm.D.[1], Angela Redlinski, Pharm.D.[1], Linda Catanzaro, Pharm.D.[1], Chui-Bin Hsiao, M.D.[2], Adel Suliaman, M.D.[2], Gene Morse, Pharm.D.[1]; (1)University at Buffalo School of Pharmacy and Pharmaceutical Sciences, Buffalo, NY; (2)Erie County Medical Center, Buffalo, NY.

PURPOSE: The purpose of this study is to examine TDM of antiretrovirals (ARVs) in patients co-infected with HIV/HCV and determine what portion of patients with co-infection have ARV plasma concentrations outside of the target range.
METHODS: A web-based mechanism has been established for collection and reporting of ARV concentrations in HIV/HCV co-infected patients. Samples were collected between 12/11/2002 and 02/22/2005, and assayed by a certified HPLC technique. ARV dosing regimens, demographics, concurrent medications, toxicity information, and laboratory data were acquired. Expected trough concentrations were defined using available primary literature sources. Concentrations were normalized to FDA recommended doses and identified as higher, within or lower than the expected range.
RESULTS: Fifty-seven trough concentrations were obtained from 51 samples. Seventy percent of subjects were male, 41% black, 43% white, and 16% Hispanic. Mean CD4 count was 376 cells/mm3 (range 69-1200), and 61 had undetectable (<50copies/ml) viral loads. Twelve percent of subjects received HCV treatment at the time of TDM with either weight-based interferon and ribavirin, or pegylated interferon and ribavirin therapy. Thirty-one concentrations were within, 12 higher, nine lower than the expected range, and two were unable to be determined. Possible factors contributing to concentrations outside of the defined range: nine drug interactions, three malabsorption, 12 hepatic decompensations, and nine undetermined. Nine subjects were on adjusted doses to counteract hepatic dysfunction or avoid drug interactions.
CONCLUSIONS: Our subset of HCV co-infected patients exhibited large interpatient variability with respect to TDM concentrations. Our findings demonstrate that using TDM in this subset of co-infected patients is useful to adjust doses.
Presented at the 45th Interscience Conference on Antimicrobial Agents and Chemotherapy of the American Society for Microbiology, New Orleans, LA, September 21-24, 2005.

435. Evaluation of vaccination practices in an ambulatory HIV clinic. *Thomas W. F. Chin, BScPhm, PharmD*, Phu Lam, BSc, Kevin Gough, MD, FRCPC; St. Michael's Hospital Toronto, Toronto, ON, Canada.

PURPOSE: HIV infected people are at risk for co-infection with hepatitis viruses. Recommendations for prevention include immunization against Hepatitis A virus (HAV) and Hepatitis B virus (HBV). Compliance with these recommendations are variable and not well reported. To evaluate the screening and vaccination practices for HAV and HBV in an inner city HIV Clinic to determine compliance with current recommendations.
METHODS: A retrospective study of vaccination records of HIV-positive patients was conducted. Alternate records from an alphabetized list were selected for review. Subjects were included if they were first screened in 1998 or later, a time when this particular information was to be collected and recorded systematically at the clinic. Non-compliance was defined as screening blood tests for HAV and HBV not performed or not recorded, or respective vaccination series not completed or not recorded. Factors associated with non-compliance to recommendations were examined.
RESULTS: A total of 357 subjects (77% males) were enrolled; mean age was 40.3 ± 10.3 years, baseline mean CD4 was 292 ± 227 cells/μL and and HIV-viral load was 4.8 ± 5.1 log10. Overall compliance was 47.9% for HAV and 69.8% for HBV. Screening rates for HAV and HBV serology were 71.2% and 88.2% respectively. For patients with negative serology requiring vaccination, the compliance rate was 5.9 % for HAV and 54.7 % for HBV. Additional analysis will be conducted to determine predictive factors and to review clinic practices/procedures affecting compliance.
CONCLUSIONS: Preliminary results suggest that overall compliance with recommendations regarding HBV is higher than for HAV. Improvements are needed to increase compliance rates in this patient population. Additional information on predictive factors and clinic practices may help improve compliance to the recommended guidelines.

436. Development and provision pf clinical pharmacy services at a university based coinfection clinic. *Renata O. Smith, Pharm.D.*, Mariela Diaz-Linares, Pharm.D., Timothy J. Doyle, RN., BS., Maximo Brito, MD.; University of Illinois, Chicago, IL.

PURPOSE: To describe clinical pharmacy services (CPS) developed and provided to HIV and hepatitis co-infected patients at a university based clinic.

METHODS: The HIV and hepatitis co-infection clinic was established one year ago to serve patients from our eight HIV clinics which provide medical services to underserved areas of Chicago. Approximately 30-40% of all our patients are co-infected with the hepatitis B and/or C virus. Funding was pursued and approved for this clinic and a multi-disciplinary team (MDT) consisting of an ID physician, a Hepatologist, an HIV certified nurse, and a pharmacist was created. A protocol was developed and implemented by the MDT to treat and monitor these patients. CPS were developed to promote patient education and to monitor adherence and outcomes of the antiviral therapy. The pharmacist also identifies and manages adverse drug reactions and drug-drug interactions, coordinates medication access and refills. Due to a large number of indigent patients the pharmacist also has to facilitate patient enrollment in medication assistance programs and provide drug samples. In addition to patient services, the pharmacist provides academic teaching to pharmacy students, residents and fellows.
CONCLUSIONS: As the complexity of caring for co-infected patients increased a dedicated clinic was created of which CPS are an important component. Services have been met with a high level of acceptance by the MDT and patients. CPS have been and will continue to be supported by external funding from various sources.

437. Antibiotic prescribing pattern in a medical intensive care unit in Qatar. *Yolande Hanssens, PharmD*, Bassam Ismaeil, MBChB, Ahmed Kamha, MD, Sittana Elshafie, MBBS, FRCPath, Fathia Adheir, BPharm, Thoraya Saleh, MBBS, MRCPath, Dirk Deleu, MD, PhD, FAAN, FRCP; Hamad Medical Corporation, Doha, Qatar.

PURPOSE: The objectives were to evaluate the current usage of anti-microbial agents in the MICU of Hamad Medical Corporation (HMC) in Doha (State of Qatar) and to correlate this with the infectious disease pattern as well as with the isolated microorganisms and their sensitivity pattern.
METHODS: Prospective study covered a two-month period from February 8 through April 7, 2004, including all patients admitted to the medical intensive care unit (MICU) for a minimum of 48 hours, and receiving a systemic antibiotic.
RESULTS: From the 71 eligible patients admitted, 54 (76%) were treated for presumed or proven infections and received antibiotics, corresponding with 280 (89%) of the 313 patient days. Respiratory infections accounted for 57%. A total of 159 antibiotics (134 intravenously and 25 orally) were administered to 54 patients during their stay in MICU, corresponding with an average of almost 3 antibiotics per patient. Ceftriaxone was prescribed in 31 patients (57%) as initial therapy. Throughout the study period, a total of 385 microbiology samples for culturing were taken, corresponding with almost one sample per patient per day. Fifty-two percent of patients had a microbiologically-proven infection (MPI): 18% with community-acquired pneumonia (CAP), 18% ventilated-acquired pneumonia (VAP), and 11% with hospital-acquired pneumonia (HAP). In the group of bacterial MPI sensitivity pattern resulted in change in empirical antibiotic therapy in 12 of 23 patients (52%). In the group of patients with non-MPI, antibiotherapy was changed in 5 of the 26 patients (19%). No antibiotic course was discontinued because of negative culture results while many patients were transferred to other units before the microbiological results became available.
CONCLUSIONS: This study highlights the urgent need for updated empiric and treatment guidelines as well as the monitoring of the antibiotic usage.

438. Outpatient antibiotic therapy (OPAT): our Singapore General Hospital (SGH) experience. *Winnie HL Lee, B, Pharm*, MeiChi Kwek, B Pharm, Germane Lee, B Pharm, Joyce Lim, B Nursing, BanHock Tan, MBBS; Singapore General Hospital, SIngapore, Singapore.

PURPOSE: To report the efficacy and safety outcomes of the OPAT service offered in the SGH since its inception in June 2003.
METHODS: Medical records of all patients on OPAT between June 2003 and Mar 2005 were reviewed. Patients' general demographics, types of infections, laboratory markers and antibiotic therapy were collected. Outcome measures were microbiological eradication (ME), clinical signs of improvement, number of adverse events (AE) and patients' daily cost savings.
RESULTS: 80 patients (equivalent to 90 OPAT courses) were reviewed. Their mean and median age were 49.3 ± 16.6 years and 51 years respectively. Bone and joints were the most common sites of infection (32.2%). The most frequent type of infection was abscesses (16.7%), followed by osteomyelitis (15.6%) and meliodosis (8.9%). Gram-positive bacteria were more common (54.0%) than gram-negative bacteria (29.9%). The more common antibiotics were vancomycin (25.6%) and cephalosporins (45.6%). The mean total length of antibiotic therapy was 31.2 ± 18.5 days, of which, approximately 64.1% were completed on OPAT (20.0 ±15.0 days). 91.1% of 82 evaluable OPAT cases achieved ME presumably while clinical improvement was documented in 83 (92.2%) cases. 11 (12.2%) cases developed AE, with leucopenia (54.5%) being the most common complication. Rehospitalization was required for 18 (20%) cases due to infection relapse (38.9%), complication relating to therapy (33.3%) and others (27.8%) eg. falls. Cost savings of up to $227.00/day were attained for OPAT patients.
CONCLUSIONS: The OPAT provides an attractive alternative to hospitalization for patients who require prolonged antibiotic treatment but are otherwise well. For OPAT to be successful, all criteria should be met before patients are admitted into this scheme. Regular monitoring of patients' outcomes and satisfaction level is needed to further improve this service.

439. Methicillin resistant staphylococcus aureus (MRSA) prosthetic valve endcarditis treated with daptomycin and rifampin. *Christian Cheatham, Pharm.D.*, David Cox, M.D.; St. Francis Hospitals and Health Centers, Beech Grove, IN.

Prosthetic valve endocarditis (PVE) is a serious complication following surgical valve replacement with significant mortality rates. Medical management alone for PVE may have higher mortality and complication rates than medical plus surgical interventions. Prosthetic valve infections include pathogens that cause bacteremia such as staphylococcus aureus. For methicillin resistant staphylococcus aureus infections (MRSA), the standard medical care has been vancomycin possibly combined with gentamicin and/or rifampin. We report a case of prosthetic valve endocarditis and posterior annular abscess with MRSA. The patient was deemed not to be a candidate for surgical intervention. The patient was initiated on antibiotic therapy with vancomycin, gentamicin, and rifampin, but continued to clinically deteriorate and remained persistently bacteremic while on therapy. The antibiotic regimen was changed to daptomycin (6.2mg/kg) every 48 hours and rifampin with subsequent clearance of the MRSA bacteremia. Repeat transesophageal echocardiogram demonstrated minimization/resolution of the vegetation and reduction of the abscess. The patient completed antibiotic therapy and was discharged home. In cases of MRSA PVE, such as ours, when surgical intervention is not an option and there is clinical failure of vancomycin combination therapies, daptomycin combination therapy was shown to be an alternative treatment.

440. A novel team approach to antibiotic streamlining. *Kevin D. Mills, Pharm.D.*, Marisa P. Rahn, Pharm.D., Corstiaan Brass, M.D.; Mount St. Mary's Hospital, Lewiston, NY.

PURPOSE: A quality improvement initiative was implemented in a 100-bed community hospital to demonstrate the impact of a unique team approach to antibiotic streamlining.
METHODS: Upon demonstration by a feasibility study of the utility of streamlining, an antibiotic streamlining program was implemented. Utilizing a clinical pharmacist, the antibiotic orders of patients were reviewed within 48 hours of admission. Appropriateness, dose and route of antibiotics were assessed, using established guidelines. Recommendations were made by the clinical pharmacist. Response to the recommendations was evaluated by the clinical pharmacist, an infectious disease physician and nurse case managers and follow-up was initiated. All interventions and clinical and pharmacy data were collected on an ACCESS database.
RESULTS: Of 1577 patients discharged in the first fiscal quarter, 432 were reviewed. Recommendations were made in 370 instances. Recommendations were accepted and implemented within 24 hours of the recommendation in 83.7% of the cases. Inappropriate antibiotics represented 41% of the recommendations. The conversion from intravenous to oral therapy represented 42%. Actual saving to the pharmacy was $25,264.90, but when corrected for the increase in patient census, the corrected savings was $30,770.57, which was 98% of predicted savings from the feasibility study. Reduction of length of stay was demonstrated to be 0.88 days/per patient overall. Reduction of stay for infectious DRGs as the primary diagnosis was 1.47 days per patient. These patients represented 21% of discharges.
CONCLUSIONS: This report represents evidence of direct and indirect hospital savings accomplished through the collaboration of case managers, a clinical pharmacist and an ID physician. This represents the first report of collaboration with case managers to demonstrate that optimization of care can result in reduction in length of stay. The data would suggest that the influence of the clinical pharmacist on patient care may extend beyond the impact on antibiotic therapy.

441. Quantifying the potential impact of antibiotic management services through prospective evaluation. *Kevin D. Mills, Pharm.D.*, Corstiaan Brass, MD, Marisa P. Rahn, Pharm.D.; Mount St. Mary's Hospital, Lewiston, NY.

PURPOSE: The inappropriate and unnecessary use of antibiotics is an important problem in the hospital setting. The goal of this assessment was to prospectively evaluate the extent of antibiotic misuse at a community hospital, and to realistically quantify the potential reduction of direct and indirect hospital costs if an antibiotic management service were employed.
METHODS: A 3-week prospective observational study was performed at a 100 bed secondary care facility. During the study period, all antibiotic use at the facility was captured by a residency-trained antibiotic streamlining pharmacist. Appropriateness of antibiotic therapy was assessed based on

infection diagnosis and supporting evidence for the presence of active infection. The extent of inappropriate antibiotic use, as well as the potential direct and indirect hospital cost of sub-optimal antibiotic utilization, was estimated using a customized database.
RESULTS: Of a total of 149 patients who received antibiotic therapy during the study period, 116 were evaluated and actively followed by the streamliner. A total of 137 potential interventions were identified. Seventy-four of the potential interventions involved antibiotic change or discontinuation, while 44 involved change from IV to oral therapy. An estimated $8,354 in potential drug cost savings was identified ($144,807 annually). Also, a minimum cumulative reduction of 23 patient days could have been achieved by earlier conversion to oral therapy, accounting for an additional $5,750 in potential cost savings to the facility ($99,750 annually).
CONCLUSIONS: Based on the results of this observational study, the annual cost savings for the facility that could be achieved through optimization of antibiotic therapy is approximately $244,000. We intend to initiate an antibiotic management program at this facility beginning in 2005. Once this program has been established, we will be able to evaluate the accuracy of our methods for determining the potential cost savings of antibiotic management services.

442. West Nile Virus public awareness and education: collaboration between Pharm.D. students and the county public health department. *Anne M. Fulton, Pharm.D.*, Susan L. Ravnan, Pharm.D., Allen Shek, Pharm.D.; University of the Pacific, Stockton, CA.

PURPOSE: West Nile Virus (WNV) was first isolated in 1937 and in 1999 was identified in New York City. The virus has spread across the United States and in 2002 the CDC reported 4156 documented human cases of WNV in 44 states. By 2005, peak outbreaks of WNV were predicted to occur in California. Therefore the San Joaquin Public Health Department (PHD) began educating the public surrounding the emergence of the WNV. Pharm.D. students during their advanced experiential learning period assisted in educating the public about the transmission and prevention of the WNV. To describe the collaboration between pharmacy students and the Public Health Department in increasing the awareness of WNV epidemic and to identify the most effective route for disseminating timely health information to the public.
METHODS: Public service announcements focusing on the transmission, prevention and infection identification of the WNV were broadcasted within San Joaquin County. Radio, television, and newspaper announcements were provided by the PHD. In addition, educational posters and flyers were strategically placed throughout the community. Pharmacy students educated patients about the transmission, prevention and infection identification of the WNV. The pharmacy students asked a series of questions to assess the effectiveness of the educational material and the routes used to disseminate the information.
RESULTS: 808 patients were surveyed. Of those patients, 87% identified the mode of transmission and 73% understood how to protect themselves from the virus. The most common modes of communication were via the newspaper or television. However patients who reported receiving information from health care workers, churches and schools retained more accurate information.
CONCLUSIONS: Timely and accurate dissemination of public health information is critical in combating community outbreaks. Pharmacy students can play a vital role in facilitating timely and accurate information to the public.

443. Impact of a restricted antibiotic formulary on utilization of piperacillin/tazobactam in a tertiary care teaching hospital. *Roy Guharoy, Pharm.D.*[1], Donald Blair, M.D.[1], Frederick Rose, MD[2]; (1)SUNY-Upstate Medical University, Syracuse, NY; (2)SUNY-Upstate Medical University, Syracuse, NY.

PURPOSE: Objective of our presentation is to evaluate impact of restriction of broad spectrum antimicrobials on piperacillin/tazobactam utilization and resistance trend in our institution. Pharmacy is an integral part of the infectious disease management team and utilization of all restricted agents are prospectively monitored by the team daily. Piperacillin/tazobactam is the only unrestricted agent in our formulary.
METHODS: Hospital database warehouse was utilized to determine the usage of piperacillin/tazobactam and other broad spectrum agents in 2002,2003 and 2004. Resistance rates were also compared during the same period
RESULTS: Defined daily dose per patient day for piperacillin/tazobactam included 1.19 in 2002, 1.28 in 2003and 1.15 in 2004. Top five restricted agents were vancomycin, ceftriaxone, ceftazidime, fluconazole and azithromycin. The utilization of restricted agents decreased from 2002–2004. Piperacillin/tazobactam sensitivity against Pseudomonas aeruginosa included 84% in 2002, 81% in 2003 and 93% in 2004. Piperacillin/tazobactam sensitivity against Klebsiella pneumonia included 93% in 2002, 83% in 2003 and 95% in 2004. Piperacillin/tazobactam sensitivity against Enterobacter aerogens included 55% in 2002, 59% in 2003 and 61% in 2004. Oxacillin sensitivity to Staphylococcus aureus included 58% in 2002, 61% in 2003 and 60% in 2004.
CONCLUSIONS: Unrestricted use of piperacillin/tazobactam led to decreased use of restricted broad spectrum agents in our institution. It also resulted in decreased rate of resistance.

444. Evaluation of patient-centered pharmacotherapy management in a managed care organization. *Erin M. Sabia, Pharm.D.*[1], Nicole Paolini, Pharm.D.[1], Gregg Broffman, M.D.[2], Gene D. Morse, Pharm.D., FCCP, BCPS[1]; (1)University at Buffalo School of Pharmacy and Pharmaceutical Sciences, Buffalo, NY; (2)Lifetime Health Medical Group, West Seneca, NY.

PURPOSE: The University at Buffalo Department of Pharmacy Practice has partnered with a local health maintenance organization to evaluate pharmacist-guided medication management in a case control comparison of medication adherence, medication management strategies, and disease state monitoring outcomes.
METHODS: An IRB-approved protocol was put into place that allowed for enrollment of patients receiving more than 6 chronic medications, patients over the age of 70, or patients identified by their healthcare provider as having a complex medication regimen. Patients meeting at least one of the above criteria were enrolled into the study once consent was obtained. Self-referral was also permissible. Thorough medication, social, and disease state histories were taken and the patients received education and counseling tailored to their needs. The recommendations of the pharmacist were subsequently forwarded to the appropriate healthcare provider for review and implementation.
RESULTS: Between February 2004 and April 2005, 66 patients were enrolled. The most common reasons for enrollment were diabetes education and blood glucose monitoring (35%), complex medication regimen management (28%), and drug regimen evaluation (15%). Many patients were enrolled for multiple reasons. The mean age upon enrollment was 67.3 years which includes 5 pediatric patients. The mean number of medications upon enrollment was 9.7 and 56.1% of patients were female. The most common recommendations were patient education (100%), additional or alternative agents recommended (69.9%), and recommendation of non-pharmacologic therapy (50%). A follow-up session was required by 77.3% of patients.
CONCLUSIONS: Preliminary data suggests that there is a need for more pharmacist-guided medication management programs. The use of selected entry criteria provides a mechanism for protocol implementation and recruitment of patients with complex regimens that benefit from study participation.

445. Clinical impact of a pharmacist managed lipid clinic in a managed care setting. *Joy N. Ezidinma, Pharm.D*, Jennifer J. D'Souza, Pharm.D, Amie D. McCord, Pharm.D., BCPS, CDE; Midwestern University–Chicago College of Pharmacy, Downers Grove, IL.

PURPOSE: It has been supported in the medical literature that pharmacists can play an important role in improving cholesterol management. Pharmacists in these clinics are responsible for reviewing medical history, monitoring laboratory values, selecting therapies, and educating patients regarding their disease and drug therapies. The goal of the lipid disease management clinic is to establish a service that aims at reducing the patient's risk of cardiovascular disease by optimizing pharmacotherapy, patient education, and medication compliance.
METHODS: Collaborative agreements were established with physicians in the Internal Medicine and Family Practice groups. Lipid management for the enrolled patients was documented from February 16, 2004 to February 28, 2005. Data collection included age, sex, number of risk factors, CHD or CHD risk equivalents, and fasting lipid panels at baseline and follow-up.
RESULTS: During the time period, 75 patients were enrolled in the program. Of those, 45 patients returned for follow-up. At baseline, the patient population was 55% male with a mean age of 53 years; 13% were documented smokers, 27% of the patients had CHD or CHD risk equivalents. The percentage of patients with LDL goals of < 100, < 130, and < 160 mg/dl were 35%, 27%, and 39% respectively. Patients who met their goal at baseline for each group were 8%, 5%, and 24% respectively. At follow-up, 29% in the < 100mg/dl group, 64% in the < 130 mg/dl, and 86% in the < 160 mg/dl group were at goal.
CONCLUSIONS: The clinic made considerable improvement in LDL reduction. We also found some areas for future improvement such as addressing poor follow-up and minimal number of referrals. Future goals for the clinic are: 1) targeting more high-risk patients through auto-referrals, 2) enhancing patient follow-up by generating letters, postcards, or phone calls, and 3) stimulating physician interest using public relations.

446. Documenting provision of preventive medicine by a clinical pharmacist in the acute care setting. *Jennifer E. Stark, Pharm.D., BCPS*; University of Oklahoma College of Pharmacy, Oklahoma City, OK.

PURPOSE: Preventive medicine focuses on preventing disease and promoting health of individuals and the community. Preventive medicine is an integral part of many pharmacists' daily interventions. However, the focus of documenting interventions in the acute care setting often focuses less on events that were circumvented (preventive care) and more on those events that did occur and how they were addressed (problem-oriented interventions). The objective of specifically recording preventive medicine is to better document the range of services provided by pharmacists in the acute care setting.
METHODS: A standardized data collection form was used to record the preventive care provided during a 3-month period in a 300 bed teaching institution. A clinical pharmacist rounding with an internal medicine team provided pharmaceutical care on a daily basis, six days per week. All interventions were documented and categorized as preventive medicine or other pharmaceutical care.
RESULTS: Specific preventive medicine strategies included immunizations, screening and assessing risk of preventable diseases, discrepancy reconciliation, and patient education on medications as well as appropriate lifestyle modifications. Specific examples of preventive care will be described and quantified as well as projected economic benefits.
CONCLUSIONS: A wealth of data exists affirming that preventive medicine not only improves patient care, but also is economically sound. This study further supports the benefit of clinical pharmacists in the acute care setting.

447. Medication reconciliation upon admit using an electronic medical record. *Douglas D. DeCarolis, Pharm, D*, Murray C. Leraas, Pharm, D, Connie Rowley, BS; Minneapolis VA Medical Center, Minneapolis, MN.

PURPOSE: Medications are a leading cause of adverse events. Literature reports demonstrate problems with accurate medication ordering upon admission to a hospital. Difficulties with obtaining an accurate medication list play a significant role. These issues have led the Joint Commission of Health Care Organization (JCAHO) to adopt medication reconciliation as a 2005 National Patient Safety Goal. This study was performed to compare the current process of ordering medications upon admit to the hospital versus a systematic medication reconciliation process.
METHODS: Within 24–48 hours of admission, a medication history was obtained from patients to ascertain a true medication list. This list was compared to the computerized outpatient medication profile and to initial inpatient orders. Order discrepancies were clarified with the provider and classified as intended or non-intended. After collecting baseline data, a medication reconciliation pilot system was put in place. Pharmacists were notified of admissions in real time, tailored the computerized profile to a user-friendly version, and provided analysis to alert prescribing physicians of potential medication problems. This "Drug List upon Admit" was documented in the electronic record and made available as a tool in obtaining the initial medication history. Discrepancies between this list and the initial medication history were reconciled by an addendum to the note in the electronic record.
RESULTS: Baseline data revealed the computerized profile to be inaccurate in 71% of patients, medication histories by providers not routinely performed, and unintended order discrepancies in 58% of patients. The medication reconciliation system reduced the number of patients with unintended discrepancies by 43%. The number of unintended discrepancies per patient decreased by 53%. We also noted the system to increase initial medication history taking by 75%.
CONCLUSIONS: A medication reconciliation system using pharmacist analysis of computerized profiles and documentation before initial inpatient orders significantly decreased potential medication errors.

448. Evaluation of potential medication errors in a neonatal intensive care unit. *Carla M. Christensen, PharmD*[1], Kelly K. Nystrom, PharmD[1], Pamela A. Foral, PharmD[1], Estella M. Davis, PharmD[1], Angela Ward, BSPharm, MBA[2], Lisa R. Strasheim, MSN, APRN[2]; (1)Creighton University Medical Center–School of Pharmacy and Health Professions, Hixon-Lied Sceince Building, Omaha, NE; (2)Alegent Health–Bergan Mercy Medical Center, Omaha, NE.

PURPOSE: Medication errors in the neonatal intensive care unit (NICU) often result in high morbidity and mortality compared to the adult population. Our 18-bed unit recently increased to a Level 3 NICU. Because of this change in acuity, identifying potential medication errors prior to their occurrence has become a top priority. Evaluation of the medication process can help focus efforts in preventing errors from reaching the patients.
METHODS: A quality concern form was developed to enhance the reporting of potential medication errors: a medication incident which never reaches the patient, therefore resulting in no apparent injury. Potential errors were evaluated by concern, medication involved, and origination. Concerns included incorrect medication, dose, route, rate, patient, or time of administration. Concern origination was classified as written order, verbal/telephone order, computer entry, dispensing, or label.
RESULTS: From March 2004 to May 2005, there were 105 quality concerns reported. Over half of the concerns involved an incorrect dose (48%) or medication (24%). The top five most frequent medication therapies reported included continuous fluid infusions (36%) and continuous medication drip infusions (29%), indomethacin (9%), furosemide (6%) and caffeine citrate (6%). The origination of these concerns most frequently derived from written orders (40%), followed by computer order entry (32%), dispensing (24%), and labeling (14%).
CONCLUSIONS: Several areas in which the implementation of changes could greatly reduce the potential for medication errors have been identified. Writing and interpretation of the orders are areas of greatest concern. The origination of concerns is concentrated most in the areas of order writing and computer order entry. Due to these results, the order process is being streamlined to meet neonatal medication needs. This includes the revision and implementation of standing order sets and predefined computer order sets. Finally, staff education of health care professionals is essential for quality improvement.

449. Evaluation of the impact of clinician order entry on medication errors in an inpatient oncology unit in a community teaching hospital. *Dianne M. Brundage, PharmD*, Kelly Becicka, PharmD, Judy Wilson, RN, Amy Sticha, RN; Methodist Hospital/Park Nicollet Health Services, Minneapolis, MN.

PURPOSE: Clinician order entry (COE) should decrease medical errors. Methodist Hospital has 51 beds for patients with cancer, an on-line system of self-reporting adverse events, and electronic medication administration records. This study examines medication errors that could be prevented by COE during a 1-year baseline period, and medication errors attributable to COE for 1 year after implementation. Standardized paper order sets are used for TPN, epidurals and chemotherapy throughout the period.
METHODS: Adverse medication events were extracted from the Quality Resources database for a 1-year period prior to COE and 1 year after COE implementation. Medication events that could be prevented by or attributed to COE were separated from all other events. Two pharmacists independently reviewed events to determine if the event could be prevented by COE (baseline) or attributed to COE (COE phase). Patient days were obtained from Quality Resources.
RESULTS: During the baseline period of 17,008 patient days, 99 medication events were considered preventable by COE (5.8 per 1000 patient days). Twenty COE-related medication events occurred in the first year of COE (1.2 per 1000 patient days). Drug categories associated with preventable events (baseline) were: miscellaneous (17), opioids (15), antiinfectives (15), while categories in the COE phase were highest for fluids/lytes (4) and miscellaneous (4). Changes were developed during the COE phase to prevent additional events from occurring.
CONCLUSIONS: COE decreases medication errors that occur in an inpatient oncology unit.

450. Evaluation of medication safety interventions documented by pharmacists in ambulatory care. *Kathy E. Fit, PharmD*, Jill S. Burkiewicz, PharmD, BCPS, Brooke L. Sweeney, PharmD; Midwestern University–Chicago College of Pharmacy, Downers Grove, IL.

PURPOSE: Medication safety is a major concern in primary care as prescribing medications is the most common intervention performed. Pharmacists are able to improve safety by identifying and resolving drug-related problems (DRPs). The primary objective of this study is to describe types of medication safety interventions performed by pharmacists in an urban ambulatory care clinic. The secondary objectives are to determine predictors of specific DRPs and to describe physician acceptance rates.
METHODS: This six-month prospective study documents interventions performed by pharmacists in an ambulatory care clinic. A PDA documentation system was developed specific for ambulatory care. Patient demographics and physician acceptance rates were documented. Descriptive statistics were employed to describe the type and frequency of interventions and physician acceptance rates. Multivariate logistic regression analysis was used to determine significant predictors for pre-selected DRPs.
RESULTS: Over six months, 965 interventions were documented. The mean patient age was 61.8 (± 15.51) years, the mean number of medications was 7.1 (± 3.95) per patient, and 72.3% were female. The most common interventions were lab monitoring (56.2%), patient education (14.5%) and drug therapy (12.4%). Medications most commonly involved in interventions included anticoagulants (56.8%, n=548) and cardiac drugs (9.4%, n=91). The use of antihypertensive agents was a predictor for dosing-related problems, specifically dose too high and dose too low ($p=0.001$ and $p=0.003$, respectively). Of the applicable interventions, 89.8% (246/274) were accepted by the physician.
CONCLUSIONS: Pharmacists in this urban ambulatory care clinic offer a variety of recommendations which are well received by physicians. Identification of predictors of DRPs will 1) focus the pharmacist's time in particular areas to allow maximum benefit from limited resources and 2)

provide implications for education to physicians and other health care professionals.

451E. Survey of topical oral solutions for the treatment of chemotherapy induced oral mucositis. *Alexandre Chan, Pharm.D.*, Robert J. Ignoffo, Pharm.D., FASHP, FCSHP; University of California, San Francisco, San Francisco, CA.

PURPOSE: The objectives of this study were to 1) describe the usage of topical oral solutions in patients experiencing chemotherapy induced oral mucositis (CIOM); 2) survey the care of oral mucositis provided to patients by clinical oncology pharmacists in institutional settings.
METHODS: Surveys were distributed to institutional pharmacists in the United States between December 2004 and February 2005. Pharmacists were asked to provide the components of their "Magic Mouthwash" and to identify the potential side effects of the mouthwash. Other questions included whether an institutional mucositis management guideline is available and what is the involvement of clinical pharmacy in mucositis care.
RESULTS: Forty institutions returned surveys during the study period. The top five ingredients used to compound the "Magic Mouthwash" are diphenhydramine, viscous lidocaine, magnesium hydroxide/aluminum hydroxide, nystatin and corticosteroids. Eighty percent of the institutions compound their "Magic Mouthwash" with three ingredients. Most institutions administer the mouthwash every 4 hours (36%) or every 6 hours (36%). The most frequently reported side effect of the mouthwash to the pharmacist is taste disturbance (49%). Furthermore, 33% of the surveyed institutions currently possess guidelines for the management of CIOM.
CONCLUSION: Most institutions in the country formulate their topical solution, or "Magic Mouthwash" with a variety of ingredients. There is a need to standardize the ingredients used to compound the "Magic Mouthwash," in order to fully evaluate the efficacy of the solution to manage CIOM. Maximizing the efficacy of "Magic Mouthwash" is essential in order to provide better care for patients who are suffering from CIOM.
Presented at the Western States Conference, Pacific Grove, CA, May 15-18, 2005.

452. Validation of methodologies used to detect erythropoietin receptor expression in tumor cells. *Steve Elliott, PhD*[1], Michael B Bass, BS[1], Chris Spahr, BS[1], Hsieng Lu, PhD[1], Leigh Busse, BS[1], Ildiko Sarosi, MD[1], Angus M Sinclair, PhD[1], Monkyoung Um, PhD[2], Gwyneth Van, PhD[1], C Glenn Begley, PhD[1]; (1)Amgen Inc., Thousand Oaks, CA; (2)Whitehead Institute for Biomedical Research, Cambridge, MA.

PURPOSE: Some publications report overexpression of erythropoietin receptor (EpoR) in tumor versus non-tumor cells based on immunoblotting and immunohistochemistry experiments, suggesting EpoR expression is involved in tumor-cell survival/proliferation and raising concerns about use of erythropoietic agents in cancer settings.
METHODS: We tested the specificity of the anti-EpoR antibodies used in those studies. We generated positive and negative control samples including: extracts of cells over-expressing recombinant Human EpoR, extracts and tissues from EpoR+/+ and EpoR-/- mice, and extracts of cells expressing high (UT-7/Epo) and low (769P) endogenous levels of EpoR.
RESULTS: We confirmed that antibodies detected overexpressed rHuEpoR in immunoblots, with a size of ~59kDa. However, larger proteins were evident (66-78kDa) that were the focus of those reports and were reported to be EpoR by the antibody manufacturers and investigators. One polyclonal antibody, C-20 (SantaCruz Inc.), showed no differences in abundance of these larger proteins in immunoblots of control SH-SY5Y cells versus SH-SY5Y cells treated with EpoR siRNA, nor in UT-7/EPO versus 769P cells. However, a difference was detected in abundance of the 59kDa protein in these same cells using M-20 (SantaCruz Inc.), an anti-murine EpoR antibody. With M-20 and C-20 antibody preparations, there were no differences in either immunostaining of EpoR+/+ versus EpoR-/- tissues, or in immunostaining of 769P versus UT-7/Epo cells. Amino-acid-sequence analysis of peptides eluted from preparative gels confirmed that the 59kDa protein was EpoR while the larger proteins were not. While the larger proteins shared some sequence similarity to the C-terminus of EpoR (the antigen used to raise the C-20 polyclonal antibodies), competition experiments with peptides from these larger, non-EpoR proteins confirmed the specificity of C-20 for the non-EpoR proteins.
CONCLUSIONS: The failure of these antibodies to specifically recognize EpoR in immunoblot and immunohistochemistry assays substantially limits their utility, raising questions about earlier studies using these antibodies.

453. Evaluation of pediatric discharge prescriptions. *Dawn M. Niedermeier, PharmD*, Sandra S. Garner, Pharm.D., Gautham K. Suresh, M.D.; Medical University of South Carolina, Charleston, SC.

PURPOSE: The available literature concerning pediatric medication errors focuses on hospitalized patients. In this setting, medication orders are subject to an extensive system of error-prevention checks by various health professionals. Discharge prescriptions are subject to fewer checks with one concern being the lack of patient data available to the outpatient pharmacist to verify the choice and dose of medication. Our objective was to measure and characterize errors in pediatric discharge prescriptions to guide the development of an improved discharge medication process.
METHODS: We evaluated 135 pediatric discharge prescriptions dispensed from the Medical University of South Carolina outpatient pharmacy between 12/1/04 and 4/30/05. Two pediatric pharmacists evaluated each prescription for medication errors, defined as the absence or inaccuracy of any component required by law or the criteria of an ideal prescription described by the Institute for Safe Medication Practices and American Academy of Pediatrics. Prescriptions were also evaluated by comparison to final inpatient medication administration record (MAR), discharge diagnoses, discharge orders, patient allergies and weight.
RESULTS: The frequencies of missing components required by law were: correct dosage form: 20%, drug strength: 9%, and instructions for use: 6%. The frequencies of deviations from the ideal prescription were: missing patient weight: 93%, missing patient allergies: 88%, missing indication: 67%, impractical dosage volumes: 24%, vague instructions: 10%, and illegibility: 1.5%. Of prescriptions containing decimal points, 4% had errors related to decimal usage and 16% of prescriptions with abbreviations had abbreviation-related errors. There was a disagreement with final MAR for no apparent reason in 26% and with discharge orders in 14%. Other errors were wrong dosing schedule (17%), overdose (9%), underdose (7%), and prescription for contraindicated medication (1.5%).
CONCLUSIONS: Medication errors commonly occur in pediatric discharge prescriptions. The results of this evaluation will be used to design an improved pediatric discharge medication process.

454. Continued decrease of pharmacy-related medication use process error reports after introduction of a neonatal intensive care unit pharmacist. *Ronald A. Floyd, Pharm.D., BCPS, FCCP*, Pauline Chan, MBA, BCPP, FASHP; Sharp Mary Birch Hospital for Women, San Diego, CA.

PURPOSE: After implementing most published recommendations, guidelines and actions for prevention of medication error in pediatrics, we decided in 2002 that the pharmacy-related reports of variances in dispensing and delivery of medications could be further substantially reduced only by introducing a dedicated pharmacist knowledgeable about neonatal pharmacology and pharmacotherapy into daily practice in our NICU. Previously we reported that addition of an NICU pharmacist was associated with a significant decrease in medication use process pharmacy-related error reporting. The purpose of this study was to determine whether this decrease was maintained for a second consecutive year, 2004.
METHODS: Data documenting deviations from established medication use processes were collected and analyzed previously from Quality Variance Reports for the years 2001 and 2002 (baseline), and 2003. For the present report, data were similarly collected and analyzed for the year 2004. At SMBHW, QVR's are analyzed, categorized and tracked by a group outside the clinical departments. Only reports generated from within NICU and citing pharmacy as a primary or secondary cause of deviation were included.
RESULTS: Previously we were able to show that the average number of medication use process variances decreased significantly (t test, $p<0.05$) from baseline (2.9 per month) to 2003 (1.7 per month) for any pharmacy-related variance from standard medication use processes within the NICU. This decrease was maintained throughout 2004 with an average of 1.8 variances being reported per month. The two areas that showed the most discernable decreases in reporting were for medication turn-around-times that exceeded usual or policy-mandated times and for intravenous fluids not being delivered before the hanging container was completed.
CONCLUSIONS: Addition of a pharmacist dedicated to serving the needs of the NICU patients, nurses and physicians was associated with a decreased rate of reporting by others of pharmacy-derived medication use process errors.

455E. Medication assistance programs: true savings for low-income patients. *John T. Johnson, Pharm, D.*; University of Georgia College of Pharmacy, Athens, GA.

PURPOSE: To develop and implement a viable service to help patients obtain medications through Medication Assistance Programs and receive information about the proper use of their medications.
METHODS: A business was developed to help low income individuals that do not qualify for Medicaid or prescription drug insurance, obtain medications through Medication Assistance Programs. A program that did not utilize grant money was developed primarily to easily duplicate this model in community pharmacies. Drug interaction and information reports were developed and provided to each individual.
RESULTS: Annual savings for patients utilizing our services compared to prices obtained from www.drugstore.com and www.medicare.gov averaged $2040 per person or $2,244,392 overall. After 13 months in business, the

company is making a profit. The average number of applications submitted is 3 per person, with the average number of medications taken by each patient being 8. Medications not obtained through our assistance program include generics and controlled substances.
CONCLUSIONS: Many people do not take their medications or do not take them properly due to the inability to pay for medications. A business was developed to assist people obtain their medicines. This service can be implemented by pharmacists to help low income citizens obtain some of their more expensive medications. Medications that are not obtained through the program and over the counter products still need to be filled somewhere. By offering this service, other business may be gained. Many physicians would like to offer this service for their patients, but do not have or want to spend the resources that are required. By having a pharmacist verifying that the right medication and dose was sent, this reduces errors. Providing drug interaction and information reports increases the likelihood that patients are taking their medications properly and without the potential for an adverse reaction.
Published in the Journal of the American Pharmacists Association 2005;45(2):238–239.

456E. Calculation of defined daily doses in retrospective database analysis. Pamela C. Heaton, Ph.D., R.Ph.[1], Charles J. Moomaw, PhD[2], *Robert J. Cluxton Jr., PharmD*[1]; (1)University of Cincinnati College of Pharmacy, Division of Pharmacy Practice, Cincinnati, OH; (2)Institute for Health Care Policy and Health Services Research, Cincinnati, OH.

PURPOSE: Special problems arise in retrospective database research when calculating drug utilization. The first problem involves ascertaining the equivalency of drug usage within drug classes rather than within individual medications. While the World Health Organization has defined DDDs for many medications, five commonly used anti-asthmatic drugs in the United States do not have established DDDs: Triamcinolone MDI; Flunisolide MDI; Albuterol MDI and solution for inhalation; Metaproterenol solution for inhalation; Levalbuterol inhalation solution The second situation involves the calculation of drug usage in the presence of artificial date boundaries. The purpose of this poster is to discuss these two situations and provide solutions.
METHODS: We reviewed the literature to obtain therapeutic equivalencies for drugs which did not have DDDs, and used those equivalences, along with the existing DDD values for similar drugs, to calculate DDDs for the drugs which did not have an established DDD. We also developed algorithms to allocate drug usage across artificial date boundaries.
RESULTS: Using data about a hypothetical patient from one of our research projects, we present an example of an application of both the defined daily doses algorithms and date boundary algorithm. For instance, we show that a patient who received two 20gm inhalers of triamcinolone MDI received approximately the same number DDDs of inhaled corticosteroids as a patient who received one 13 gm inhaler of fluticasone 110mg MDI. We use the hypothetical patient data to explain how the newly defined DDDs and date boundary algorithms can be applied in database research.
CONCLUSIONS: We have addressed important methodological issues that arise when calculating defined daily doses. Simply counting prescriptions or adding up number of units dispensed is not sufficient to accurately capture patient drug use. With improved database research methods, the results from database research studies will continue to be valid and reliable.
Presented at the Midyear Clinical Meeting of the American Society of Health-System Pharmacists, Boston, MA, June 14, 2005.

457. The impact of a computerized order entry form on gabapentin prescribing in a veterans affairs medical center. *Randall Rowen, Pharm.D.*[1], S. Scott Sutton, Pharm.D.[1], John Voris, Pharm.D.[1], Cynthia Voris, Pharm.D.[2]; (1)University of South Carolina, Columbia, SC; (2)WJB Dorn VA Medical Center, Columbia, SC.

PURPOSE: Gabapentin accounts for the third highest drug expenditure in the Veterans Administration Healthcare System (VHA). This expenditure is primarily due to prescriptions for off-label indications. The purpose of this intervention is to reduce inappropriate prescribing of gabapentin in a Veterans Administration Medical Center (VAMC) utilizing a computerized order form.
METHODS: In April 2004 our VAMC identified gabapentin as a high volume, high cost medication, with the potential for misuse. Review of pharmacy data indicated gabapentin was being prescribed primarily for non-FDA approved uses. With support of the medical staff, an evidence-based algorithm was created and implemented in October 2004 as a computerized Gabapentin Order Form (GOF). From June 2004 through March 2005 the number of patients prescribed gabapentin and monthly gabapentin expenditures was collected. To assess effectiveness of the GOF, a comparison of gabapentin data between our VAMC and seven other facilities in our Veterans Integrated Service Network (VISN) was completed.
RESULTS: In June 2004 we had 1272 patients receiving gabapentin at a cost of $147,415.00. In March 2005 we had 703 patients receiving gabapentin at a cost of $43,755.00. This was a 43% decrease in the number of patients receiving gabapentin and a 70% reduction in expenditures for gabapentin. The VISN averaged a -16% change in the number of patients receiving gabapentin and a 50% reduction in gabapentin expenditures.
CONCLUSION: Implementation of a computerized GOF is an effective intervention to reduce gabapentin prescriptions and expenditures.

458. Clinical interventions and outcomes utilizing an internally developed documentation system. *Morton P. Goldman, PharmD, BCPS*, Michael A. Militello, Pharm.D., BCPS; The Cleveland Clinic Foundation, Cleveland, OH.

PURPOSE: Documenting clinical interventions is an important part of justification of clinical pharmacy services. It is quite necessary to show the importance of these interventions on effectiveness, safety and cost of patient care. We describe the clinical pharmacy interventions performed by clinical pharmacy specialists and clinical staff pharmacists at the Cleveland Clinic Foundation in 2004.
METHODS: An internally developed clinical documentation system has been in place at CCF since 2003 and will be described elsewhere. Clinical interventions are systematically documented and categorized. Data is extracted from this system and analyzed using a web based reporting system and Excel.
RESULTS: More than 19,000 clinical interventions were documented in the system in 2004. Interventions related to order processing (order clarification for legibility, abbreviations, allergy checks, therapeutic interchange, etc.) are not included in this system. The most common interventions consisted of drug information requests, discontinuation of therapy, dosing changes, nutrition and IV fluid changes, initiation of drug therapy and laboratory test requests. 35% of the documented outcomes impact on prevention of toxicity or side effects, with 25% impacting on improving efficacy and 15% removing unnecessary therapy. The most common classes of drugs intervened on were antimicrobials, cardiovascular agents, gastrointestinal agents, and anticoagulants. There was a $233,000 documented direct cost savings with a cost avoidance (calculated from a previous published study) of more than $1.9 million. Major limitations include the voluntary nature of reporting (~70% of relevant interventions are documented) and the modeling of cost avoidance.
CONCLUSIONS: Documenting clinical interventions is a vital piece of continued justification for clinical pharmacy services. Documentation systems must be user friendly, have the capability to calculate cost savings, have easy to use report functions to categorize intervention types and impact, and should ultimately be tied to the patient specific pharmacy profile or medical record.

459. Alterations in usage of atypical neuroleptics resulting from an educational series at a VA hospital and clinic. *John Voris, Pharm.D.*[1], Randall C. Rowen, Pharm.D.[1], S. Scott Sutton, Pharm.D.[1], Helen Woods, RPh[2], Rachel Sharpe, Pharm.D.[2]; (1)University of South Carolina, Columbia, SC; (2)Dorn Veterans Medical Center, Columbia, SC.

PURPOSE: This study documented the effects of an educational series conducted by a clinical pharmacist designed to illuminate the side effect profile and maximize use of cost efficient dosing strategies (e.g. split tabs, logical dose selection) of all atypical neuroleptics.
METHODS: The use of each atypical neuroleptic was recorded for twelve months (1 month prior and 11 months post) after institution of an organized, monthly Pharm.D.-led educational program. Weight scales and Body Mass Index tables were placed in each prescriber's offices to facilitate compliance with suggested monitoring parameters. Hospitalization rates of a sample of patients were also followed.
RESULTS: The Medical Center realized a savings of $14,000/month in drug acquisition cost (4.8% decrease), while the number of prescriptions/month increased 12.6% (259/month) and the patient load increased 12.0%. The largest changes occurred with olanzapine (34.5% decrease), aripiprazole (increased 5-fold), and quetiapine 25 mg (33% decrease). No significant change in the rates of hospitalization occurred during the time period.
CONCLUSIONS: A clinical pharmacist-directed educational series resulted in alterations in usage of atypical neuroleptics. During the study period, atypical neuroleptic pharmacotherapy becomes more cost efficient without negatively impacting hospitalization rates.

460. An evaluation of clinical pharmacists impact on drug utilization of traditional NSAIDS and selective COX-II inhibitors. *S. Scott Sutton, Pharm.D.*[1], John Voris, Pharm.D.[1], Randall C. Rowen, Pharm.D.[1], Joe C. Blizzard, RPh, Ph.D.[2]; (1)University of South Carolina, Columbia, SC; (2)Wingate University, Wingate, NC.

PURPOSE: To evaluate the effectiveness of drug utilization criteria developed by clinical pharmacists for non-steroidal anti-inflammatory drugs (NSAIDS) and cyclooxygenase-II inhibitors (COX-II inhibitors) on pharmacy utilization in a Veterans Affairs Medical Center.
METHODS: This was an analysis that evaluated the utilization of NSAIDs and

COX II inhibitors (percentage of patients utilizing medications and drug costs) from April 2004–March 2005. Criteria for the utilization of COX-II inhibitors were developed and instituted by clinical pharmacists. Each patient must have met the criteria defined in the guidelines to be eligible for treatment with COX-II inhibitors. Data was then compared to national trends in COX-II inhibitor utilization rates.
RESULTS: The average number of patients/month prescribed NSAIDS or COX-II inhibitors was 3,202 (range 2806-3431). The average utilization rate for traditional NSAIDS was 92.4% (range 90.7%–95.0%) and 7.4% (range 5.0%–9.3%) for COX-II inhibitors. The cost per month for traditional NSAIDS was $2.60–$7.10 compared to $47.69–$95.37 for COX-II inhibitors. National utilization rates for NSAIDS and COX-II inhibitors from 2002 were 39% and 61% respectively. Incorporating drug utilization criteria led to a lower utilization rate of COX-II inhibitors compared to national data (61% versus 7.4%), which will also lead to lower pharmacy drug costs.
CONCLUSIONS: Drug utilization criteria developed by clinical pharmacists for non-steroidal pain medications can influence the prescribing patterns of traditional NSAIDS and COX-II inhibitors. Utilizing traditional NSAIDS in appropriate patients can lead to a lower utilization rates and pharmacy drug cost compared to COX-II inhibitors.

461. The impact of a pharmacist driven automatic fluconazole intravenous to oral step-down policy in a teaching hospital. *Manuel M. Horvitz, Pharm.D.*; New York University Hospital Center, New York, NY.

PURPOSE: This project was designed to compare patient outcome and overall cost of drugs to the institution as a result of the automatic fluconazole intravenous (IV) to oral (PO) step-down interventions versus patients prescribed fluconazole IV not automatically stepped-down.
METHODS: New York University Hospital Center "Drug Study Lists" between October 1, 2002 and October 31, 2002 were reviewed to identify patients started on fluconazole IV and when eligible for step-down (PO or tube feeding, functioning GI tract) automatically stepped-down by the clinical pharmacist via prior authorization from the Pharmacy & Therapeutics Committee. Patients prescribed fluconazole IV prior to October 1, 2002 and eligible for step-down were not automatically stepped-down. Patients in this group had required calling the physician.
RESULTS: Twenty-one of twenty-one (100%) patients in the automatic step-down group and eligible for step-down were automatically stepped-down by the clinical pharmacist with a total cost savings of $21,189. Five of twelve (42%) patients in the not automatically stepped-down group and eligible for step-down were stepped-down with a total cost savings of $3,465. There were positive patient outcomes (clinical/microbiolgic cure) for all patients in both groups.
CONCLUSION: Pharmacy driven automatic fluconazole IV to PO is a safe, effective method of step-down. It was performed by the clinical pharmacist and had a favorable economic impact to the institution.

462. Correlation between antibiotic utilization and resistance rates within a hospital system: results of the Antimicrobial Resistance Management (ARM) Program. *John G. Gums, PharmD*; University of Florida, Gainesville, FL.

PURPOSE: Antibiotic use is one of the major drivers of resistance. However, restricting one drug to reduce resistance among microorganisms can result in increased resistance among others. Studies have suggested that specific types and volume of antimicrobial agents used can play key roles in determining resistance rates. Development of a program to correlate how usage of specific antibiotics affects changes in resistance patterns can help address issues of significance to clinical pharmacy.
METHODS: ARM is an ongoing program to document trends in antibiotic use and resistance rates. Total number of isolates compared nationally (1990-2005) is 28.4 million. Institutions enrolling in ARM provide at least 3 years of antibiogram data. Participants receive a customized analysis of antimicrobial susceptibility trends within their hospital/system. The trends are benchmarked against national, regional, and state comparators. While this analysis identifies that a resistance problem may be occurring, it does not address what may be driving such resistance.
RESULTS: Working with a hospital system, ARM developed a pilot utilization review program to help evaluate the effect of antimicrobial use on antimicrobial susceptibilities. In addition to antibiograms, each hospital in the system provides at least 3 years of gross amount of drug used. Total drug use per year is determined and the percentage change in use of each antibiotic from year 1 to year 2 and year 2 to year 3 is calculated and correlations between usage and changes in resistance patterns determined. These correlations are currently being analyzed.
CONCLUSIONS: ARM utilization review data can be used to address clinical pharmacy issues within a hospital system by identifying modifications to infection control measures and proactive changes to the antimicrobial formulary. This utilization review program can easily be adapted to any clinical pharmacy setting and has the potential to have a significant effect on local resistance rates.

463E. Variable blood pressure (BP) response to verapamil by KCNMB1 genotype. *Amber L. Beitelshees, Pharm.D., M.PH.*[1], Yan Gong, Ph.D.[1], Rhonda M. Cooper-DeHoff, Pharm.D.[2], Jim Moss, Ph.D.[1], Carl J. Pepine, M.D.[2], Julie A. Johnson, Pharm.D.[1]; (1)Department of Pharmacy Practice, University of Florida, Gainesville, FL; (2)College of Medicine, Division of Cardiology, University of Florida, Gainesville, FL.

BACKGROUND: The gain-of-function Glu65Lys mutation in the KCNMB1 potassium channel subunit was found protective against diastolic HTN in a Spanish population. We sought to determine whether Glu65Lys or Val110Leu was associated with variable verapamil response in a substudy of the INVEST trial.
METHODS: Genetic samples were obtained from 611 (170 untreated and 441 stable background therapy) INVEST patients in whom the addition of verapamil was the only change to their antihypertensive treatment. Codons 65 and 110 were genotyped by pyrosequencing. The GLM procedure, controlling for age, BMI, baseline BP, and race, was used to compare BP response to verapamil at 6 weeks by genotype.
RESULTS: Minor allele frequencies were 0.12 and 0.09 for codon 65 and 110, respectively. No differences in BP response to verapamil were present by genotype in the entire population. However, when compared only in patients untreated at baseline, codon 65 and 110 variant allele carriers exhibited trends toward significantly greater SBP reductions to verapamil at 6 weeks than non-variant allele carriers.

Codon 65 genotype	Treatment SBP	Codon 110 genotype	Treatment SBP
Glu65Glu	139 (137, 142)	Val110Val	139 (136,141)
Lys65 carrier	132 (124, 140)*	Leu 110 carrier	133 (125, 141)**

Estimated adjusted means (95% confidence intervals), *p=0.07, **p=0.1

CONCLUSION: Our data suggest that codon 65 and 110 genotype may play a role in variable SBP response to verapamil monotherapy. Our data also suggest that background antihypertensive therapy may confound or influence pharmacogenetic associations.
Published in Clin Pharmacol Ther 2005;77(2):P97.

464. Implementation of a practical report of estimated free phenytoin concentration. *Lih-Jen Wang, Pharm.D., BCPS, FASHP*, Boyce Baker, PharmD, Ann Kathryn Rhodes, PharmD, Bob Wetherell, MT (ASCP), Kelly Kunkle, MT (ASCP); Columbus Regional Healthcare System, Columbus, GA.

Phenytoin is a commonly used anticonvulsant. Due to inter-patient variability and nonlinear elimination of the drug, doses are traditionally customized to the individual patient based on serum concentrations, therapeutic range, toxicities, and seizure control. Phenytoin is highly (90%) protein bound, primarily to albumin, with 10 % available to exert therapeutic effect. Factors that increase the free fraction of phenytoin could have both profound therapeutic and/or toxic effects. Therapeutic drug monitoring of free phenytoin concentrations is more accurate than monitoring total phenytoin concentrations. This study established a correlation between measured and estimated free phenytoin (Pearson Coefficient = -0.56), established the correlation between albumin and free phenytoin, and evaluated the cost of send out and in-house measured free phenytoin concentrations. In 43 % of patients in the study, the total phenytoin concentration did not accurately portray the active free phenytoin concentration as anticipated. The measurement of free phenytoin and the calculated free phenytoin concentration were comparable. An increase in measured free phenytoin concentration coincided with low albumin concentration, and higher serum creatinine (greater than 2.4 mg/dL), but not measured total phenytoin concentration. Based on these results, the pharmacy and laboratory departments collaboratively implemented a practicable report that includes measured total phenytoin concentration, albumin concentration, and calculated estimate of free phenytoin when a phenytoin concentration is ordered by clinicians. A costly send-out lab was avoided, and the results of phenytoin concentration were reported in a timely fashion. This report provided a useful tool for physicians and pharmacists to manage patients receiving phenytoin therapy more safely and effectively while providing a timely estimate of a reported phenytoin concentration.

465. Success in the prevention of potential medication errors within a forensic state hospital. *Julie M. Alizio, PharmD*; McKesson Medication Management, Bridgewater, MA.

PURPOSE: To prevent potential medication errors resulting from orders that are not prospectively reviewed by pharmacy
METHODS: Institute an After Hours Pharmacist Review Service at a central location off site. This includes notification of physicians of all potential drug interactions prior to initiation. Limited amount of medications in night cabinets and limited number of personnel with access to this area, who are trained in the verification process, prior to obtaining the dose. Ongoing

analysis of medication orders written after hours and indication of urgency.
RESULTS: Analysis of the data indicated a decrease in number of orders written and required for immediate dosing needed before the pharmacy opened. A comparison was also done on the number of new orders versus the number that were submitted for after hours pharmacist review. It demonstrated that this service was not being utilized as much as it should be by the nursing department. However direct contact with physicians did indicate that this information was of value and changes in therapy or additional monitoring parameters were noted.
CONCLUSIONS: It can be concluded that this program can be effective in preventing potential medication errors. However work still needs to be done to encourage the nursing staff to recognize its importance and to take advantage of this service.

466. Establishing a pharmacy presence in the emergency department. *Kyle A. Weant, PharmD*, Emily Sterling, PharmD, P. Shane Winstead, PharmD, Armitstead John, MS; University of Kentucky, Chandler Medical Center, Lexington, KY.

Currently the Department of Pharmacy Services at the University of Kentucky Chandler Medical Center does not have a consistent presence in the Emergency Department (ED). Although distribution is facilitated through a central pharmacy and an automated dispensing system, limited clinical pharmacy services are provided upon special request and/or emergency situations. Nevertheless the ED is the entry point for approximately 40% of all patients admitted to the hospital and is where several medication therapies are selected and initiated. Most patients that visit the ED are not admitted to the hospital, but are discharged without a pharmacist having an opportunity to provide pharmaceutical care directly to the patient. The opportunity for a clinical pharmacist to intervene and impact clinical pharmacotherapy decisions made in the ED may translate into an enhanced quality of care and a cost savings for the institution. To evaluate this hypothesis, an innovative rotation was established at the University of Kentucky for the two critical care residents in the Emergency Department over a two month period. All pharmacy interventions were documented as well as an evaluation of the time from urgent medication prescribing to medication administration. Approximately 75% of the residents' time was equally divided between obtaining medication histories, dosing medications, and providing pharmacotherapy consults. The average time from medication prescribing to medication administration was found to be approximately 60 minutes. The greatest delay in time appeared to result from entry into the pharmacy computer system to delivery to the emergency department. Overall the residents were well received by the medical staff and requests have been made for a continuous pharmacy presence. This rotation will continue to be offered for advanced PGY2 pharmacy residents, the goal being to provide full-time pharmacist services in the Emergency Department, as well as continuing to provide an innovative rotation for future pharmacy residents.

467. Utilization of surveys and staff education to improve medication documentation in the electronic medical record of an internal medicine department. *Sarah M. Westberg, Pharm.D., BCPS*[1], Kathrine A. Beeksma, RN[2], James N. Jorgenson, MD[2]; (1)University of Minnesota College of Pharmacy, Duluth/St. Mary's Duluth Clinic, Duluth, MN; (2)St. Mary's Duluth Clinic, Duluth, MN.

PURPOSE: This initiative was started to improve the medication documentation in the electronic medical record of an internal medicine department, with the goal that every patient's medication record will be 100% accurate at the conclusion of an encounter in the department.
METHODS: Initially a survey was developed and given to clinical assistants, registered nurses, and credentialed providers in the department to determine the existing barriers for achieving accurate medication documentation and to receive input on ideas for improvement. The results were used to develop new procedures and formed the basis for educational inservices for staff.
RESULTS: Surveys were completed by 100% of clinical assistants and nurse clinicians, and 69% of credentialed providers. The survey results indicated that major barriers toward achieving an accurate medication list included patients who do not know which medications they were taking (100%) and staff not having enough time to gather the information (60%). Clinical assistants were more likely to agree that the current medication documentation is 100% accurate compared to credentialed providers (p=0.0059). Three discussion sessions were held with the credentialed providers to present the survey results and to discuss necessary new procedures. Two mandatory one-hour inservices are planned and currently being implemented for departmental staff, including registered nurses and clinical assistants. These inservices have been designed to specifically address the concerns and deficiencies that were apparent based on survey results. In addition, the necessity for improved procedures has been recognized and implementation is pending.
CONCLUSIONS: The use of surveys and discussion hours was productive in identifying the challenges associated with keeping the medication documentation in an electronic medical record accurate and up-to-date. These tools were helpful in defining educational needs and procedural improvements. We expect that fulfilling these needs and improving procedures will result in increased accuracy of medication documentation.

468. Using a commercial intervention reporting system to track clinical transformation of staff pharmacists in a rural hospital system. *Renee R. Trewyn, Pharm.D.*, R. Craig Campbell, B.S.; Mercy Health System—Kansas, Fort Scott, KS.

PURPOSE: Determine if reports generated by commercial clinical intervention software may be used to track the clinical transformation of staff pharmacists.
METHODS: Routine use of a commercial reporting system was implemented in December 2003, as part of a corporate initiative for a pharmacy clinical transformation. Pharmacists were trained in the use of the software, and expected to document clinical interventions as part of their daily routine. The clinical coordinator periodically prepared reports generated from the software reporting features to be shared with hospital staff. At the end of the first year, a retrospective review of the data was conducted, and the results analyzed. To illustrate the clinical transformation of pharmacists, the intervention frequency was compared over time to the intervention complexity as determined by the hospital system.
RESULTS: Therapeutic interventions increased from 14% to 30%, patient safety interventions increased from 11% to 29%, and antibiotic interventions increased from 5% to 15% of total number logged. Switches from IV to PO fluctuated between 3% and 1.7% of total interventions. In the patient safety category, requests for clarification of abbreviations varied from 1% to 10% of all safety interventions while requests for clarification of handwriting decreased from 3% to 1% of the same. Not all interventions desired by the system could be documented in the commercial software. Intervention complexity showed little change over time.
CONCLUSIONS: The change in the type and number of interventions logged over time implies an increased clinical emphasis by the pharmacists. Adding intervention categories to the commercial system may allow better tracking of clinical transformation of staff pharmacists.

469. Assessment of pharmacist documentation in the medical record. *Sarah K. Ford, PharmD*, Melissa M. Blair, PharmD, Joseph E. Mazur, PharmD; Medical University of South Carolina, Charleston, SC.

PURPOSE: Little is published regarding documentation in medical records by clinical pharmacists. Therefore, this investigation was designed to measure the quantity and quality of pharmacy notes in medical records of patients at an academic medical center.
METHODS: Two hundred patient charts were randomly selected from services covered by a pharmacy clinical specialist in the adult, pediatric, and psychiatric inpatient hospitals, and ambulatory care clinics. Charts were retrospectively reviewed to determine the percent of medical records with documentation of pharmacy clinical services. Identified pharmacy notes were evaluated for quality based on essential elements (identification of patient, reason for encounter, relevant medications and history, relevant labs, assessment, goals of therapy, plan, monitoring, and follow-up) and quality indicators (legibility, clarity and completeness of message, need for inclusion in the medical record, and use of appropriate format).
RESULTS: Pharmacy notes were identified in 10% of medical records in the adult and children's hospital, 20% in the psychiatric hospital, and 100% of medical records of patients seen by ambulatory care pharmacists. Mean quality rating scores were 12.1, 12.9, 10.4, and 14 on a 15-point scale for the adult hospital, children's hospital, psychiatric hospital, and ambulatory care clinic, respectively, indicating notes of very good quality.
CONCLUSIONS: Education on the need for documentation in the medical record is warranted and should be undertaken to increase pharmacist awareness.

470E. Documentation of clinical activities using a Web-based application within a nine-hospital integrated health care system. *Robert T. Adamson, PharmD*, Heather Halama, RPH, Indu Lew, PharmD, Scott Mathis, PharmD, George Shehata, RPH; Saint Barnabas Health Care System, West Orange, NJ.

PURPOSE: Documentation of clinical activities is central to the practice of pharmacy. We have recently implemented a commercially available, modifiable, web based application for the documentation of clinical interventions. This system was used to document the first twelve months of clinical interventions and activities by a healthcare system pharmacy department after implementation of the new software.
METHODS: HealthProLink, a web based application was purchased and implemented in October 2002. A consensus was obtained by the system pharmacy department for the development of global intervention categories which included: automatic therapeutic substitutions (ATS), order clarification, education, IV to oral therapy, laboratory analysis, quality assurance, renal dose adjustment and therapeutic interventions. The

interventions of the healthcare system's pharmacists were tracked from January to December 2003. During the course of the study period, the intervention fields and associated costs, using actual contract pricing, were modified as needed by the healthcare system clinical pharmacy administrator.
RESULTS: A total of 30,769 interventions and activities were documented during the study period. Total documented cost savings were $611,801. The percentages of clinical intervention by global categories were: ATS (47%), order clarification (8.9%), education (5.3%), IV to oral therapy (5.7%), laboratory analysis (5.1%), quality assurance (17%) renal dose adjustment (7%) and therapeutic interventions (4%). The cost savings by global categories were: ATS ($128,479), IV to oral therapy ($189,658), renal dose adjustment ($116,242) and therapeutic interventions ($177,422).
CONCLUSIONS: This tool is an easy to use and convenient method of documenting clinical activities and interventions in real time with corresponding cost savings for a pharmacy department within an integrated healthcare system.
Presented at the 39th Mid-Year Clinical Meeting of the American Society of Health System Pharmacists, Orlando, FL, Decemeber 4-8, 2004.

471. Economic and clinical impact of a pharmacy-driven renal dose protocol. *John Noviasky, PharmD*, David Coriale, PharmD; St Elizabeth Medical Center, Utica, NY.

PURPOSE: This study was designed to evaluate the economic and clinical impact of a pharmacy renal dosing protocol in our community hospital. This protocol allows Pharmacy driven dose adjustments and ordering of serum levels for patients taking select medications.
METHODS: Interventions for one month were evaluated and data collected including patient age, gender, diagnosis, and length of stay. Physician override of dosage adjustment were noted and calculated savings are based upon clinitrend estimates.
RESULTS: There were a total of 51 clinical interventions for the month of March 2005. The average of patients was 77.5yo ± 10.7 years, of which 39.2% were male. The most common dose adjustments were for levofloxacin (n= 26), medications for gout (n=8) famotidine (n=4). There were 13 serum digoxin levels ordered during this time period, 1 of which was supratherapeutic and required change in dosage. No physicians override of dosage alteration and no upward dosage adjustments due to improvement in renal function occurred. The average savings per intervention was $110 with total savings of $5610. The amount of time saved by pharmacist driven protocol rather than traditional method of physician contact is estimated at 20 minutes per encounter or 17 hours per month.
CONCLUSIONS: Numerous medications have the potential to cause harm if they accumulate due to renal impairment. This program reduces costs by tailoring the amount of drug required to each patient's condition and avoids cost incurred with iatrogenic toxicity.

472. Effectiveness of electronic consult-based narcotic renewal program at the Minneapolis Veterans Administration Medical Center. *Kevin D. Burns, Pharm.D.*, Elzie J. Jones, Pharm.D., Robert W. Patridge, Pharm.D., Jill C. Hansen, LPN, Donald Weinshenker, M.D.; Minneapolis Veterans Affairs Medical Center, Minneapolis, MN.

PURPOSE: Develop a process whereby patients that are stable in their pain management regimen can request narcotics without having a monthly clinic visit. The Minneapolis Veterans Affairs Medical Center's outpatient clinics provide over 500,000 outpatient clinic visits annually. Of these visits, 22,189 patients are seen in the four distinct primary care clinics with 68 providers (MD/NP/PA) utilizing the program. There are 581 patients enrolled in the Narcotic Renewal Program.
METHODS: Patient Enrollment: Patient identified as stable requiring maintenance narcotic for pain management (may be on chronic "prn" administration). Electronic consult sent to reviewer requesting enrollment into program. Active enrollment is easily identifiable in electronic chart. Pain management agreement is reviewed and signed by patient during enrollment. Patient sent follow-up letter with instructions how to order medications. Patient reviewed at clinic visits to assess efficacy and appropriateness for this program and consults must be renewed annually. Dispensing: Narcotic request via direct dial telephone w/voicemail option. Nurse prints corresponding consult and reviews to determine next fill date. Consults forwarded to primary care provider for signature/dating; consult then becomes legal prescription for pharmacy to dispense. Prescriptions may be picked up on-site with 24-hour notice (every 30 days) or mailed with delivery tracking (every 28 days).
RESULTS: Resource utilization: This program requires approximately 1.5 FTE nursing & 0.2 FTE pharmacist support. Demographics: Number of patients per provider; Average number of prescriptions/patient; Average number of dosage changes/patient; Number of fills/patient/year; Trends of use by generic active ingredient. Feedback: Survey providers and pharmacy staff to discern satisfaction and elicit areas for improvement. Significant reduction in handwritten prescriptions. 95% of prescriptions are delivered via mail.
CONCLUSIONS: We developed an effective and reproducible narcotic renewal process, freeing up time for pharmacists and clinic staff to spend toward other patient care activities.

473. Survey of the members of the Clinical Administration PRN. Lih-Jen Wang, Pharm.D., BCPS, FASHP[1], Todd Nesbit, Pharm.D., BCPS[2], Susan Miller, PharmD, BCPS[3], Herb Pettit, PharmD, BCPS[4], Emilie Karpiuk, PharmD, BCOP[5], *John Noviasky, PharmD*[6]; (1)Columbus Regional Healthcare System, Columbus, GA; (2)The Johns Hopkins Hospital, Baltimore, MD; (3)MUSC, Fayetteville, NC; (4)Central Baptist Hospital Pharmacy, Lexington, KY; (5)Covenant Healthcare, Milwaukee, WI; (6)St Elizabeth Medical Center, Utica, NY.

PURPOSE: To characterize the members of the clinical administration PRN and to gauge their clinical, professional and research interests.
METHODS: A request to participate in an on-line electronic survey was sent to all members of the Clinical Administration PRN.
RESULTS: 62 individuals responded to request to participate in survey, of which 28 (47%) were female. Most respondents (n=32,53%) have been in the practice of pharmacy for more than 15 years and have PharmD Degrees (92%). The size of the clinical departments vary from having more than 15 clinical personnel (n=13) to only 1 to 2 (n=12) or no other clinical staff (n=5). Members are involved in many committees including P&T (n=53, 93%), JCAHO Preparation (n=34,60%), Medication Errors (n=33, 58%), Infection control (n=28,49%) and others. Their activities include Clinical Intervention reporting (n=55,90%), Adverse Drug Reaction Reporting (n=53,87%), Formulary Review (n=49,80%) and Personnel Issues (n=48,79%). An overwhelming majority are directly involved with teaching students and/or residents (n=52,85%), spending between 1 to 4 hours a day (n=27) in this duty. Most of the membership is either somewhat satisfied (n=19,32%)or satisfied with usual workload(n=26,43%) and somewhat satisfied (n=17,28%), satisfied (n=29,48%), or very satisfied (n=10,16%) with annual salary. Most of the members (94%) would recommend their job to another pharmacist for various reasons (unique, challenging, creative, interesting, rewarding, etc). A few respondents said they would not recommend their job because of excess responsibilities and lack of direction. Responses to inquiry about greatest accomplishment or project in the past year included publications, systems improvements, patient safety initiatives, and educational initiatives.
CONCLUSIONS: The Clinical Administration PRN is a dynamic group which has multiple responsibilities. This group is engaged in teaching, clinical- and service-related activities. These results will be used to shape the charges for the Clinical Administration PRN for the next year.

474E. Analog classroom study of amphetamine and atomoxetine in girls with ADHD. Joseph Biederman, MD[1], Sharon B. Wigal, PhD[2], Thomas J. Spencer, MD[1], James J. McGough, MD[3], *David A. Mays, PharmD, MBA, BCPS*[4]; (1)Harvard University and Massachusetts General Hospital, Boston, MA; (2)Child Development Center, University of California Irvine, Irvine, CA; (3)David Geffen School of Medicine at UCLA, Los Angeles, CA; (4)Shire Pharmaceuticals Inc., Wayne, PA.

PURPOSE: The objective of this study was to compare the efficacy and safety of mixed-amphetamine salts extended release (MAS XR) with those of atomoxetine in girls with ADHD.
METHODS: A subanalysis from a randomized, double-blind, multicenter, parallel-group, forced-dose–titration, analog laboratory classroom study of children aged 6–12 years with ADHD was undertaken to assess the efficacy, safety, and time course of effect of MAS XR vs atomoxetine in girls with ADHD.
RESULTS: Of the 57 girls in the ITT population, 26 were randomized to receive MAS XR and 31 to receive atomoxetine. Symptom severity at baseline was similar between treatment groups based on Clinical Global Impressions-Severity of Illness (CGI-S) scores. Mean SKAMP attention subscale scores at baseline were similar at baseline for both groups. Endpoint scores revealed a greater improvement in attention in the MAS XR group compared with the atomoxetine group. Mean SKAMP attention subscale scores by week revealed consistently greater improvement in attention with MAS XR than with atomoxetine. The time course of medication effect for attention demonstrated the 12-hour efficacy of MAS XR vs atomoxetine. Mean change from baseline throughout the study day revealed consistent, continued improvement in attention in the MAS XR group, and varied improvement in the atomoxetine group throughout the 12-hour analog classroom assessment period. Significant differences were seen at all these time points in the MAS XR group [P=0.009]; however, no significant differences compared with baseline were observed in the atomoxetine group for any of the time points. The total number of reported treatment-emergent AEs was similar for both groups.
CONCLUSIONS: The results from this analog classroom study suggest that MAS XR demonstrates greater reduction than atomoxetine in ADHD inattention in school-aged girls. Improvement in this ADHD symptom was significantly greater for girls receiving MAS XR than for girls receiving

atomoxetine.
Presented at the Annual Meeting of the American Psychological Association, Atlanta, GA, May 24, 2005.

475E. Antidepressant medication management in depression patients: a role for clinical pharmacists. *Troy A. Moore, Pharm.D., M.Sc.*[1], Cynthia A. Mascarenas, Pharm.D., M.Sc., BCPP[1], Christopher R. Frei, Pharm.D., M.Sc., BCPS[2]; (1)The University of Texas College of Pharmacy, UT Health Science Center at San Antonio, South Texas Veterans Health Care System, San Antonio, TX; (2)The University of Texas Health Science Center, San Antonio, TX.

PURPOSE: The purpose of this study is to determine if a pharmacist-run depression clinic (PRDC) can: 1) improve depression outcomes; 2) improve achievement rates of the Veterans Administration performance measure; and 3) impact medication costs.
METHODS: Data extracted from the electronic medical record system at South Texas Veterans Health Care System (STVHCS) from 06/01/04 to 12/10/04 included visit history; diagnosis; service connection; prescription information including medication, dosage, cost, and quantity; and Quick Inventory of Depressive Symptomatology Self Report (QIDS-SR) scores. Patients with a new diagnosis of a depressive disorder between 06/01/04 and 9/16/04, who had received a new prescription for an antidepressant medication 30 days prior to through 14 days after diagnosis, and no prior antidepressant prescriptions for at least 90 days, were included. Patients with psychiatric or substance abuse admissions, or who died, during the 12 week retention period were excluded. All consult patients seen in PRDC were included in pertinent outcomes analyses.
RESULTS: Three hundred and twenty-nine charts were examined (PRDC group, N=136; Non-PRDC group, N=159); 34 patients were excluded from analysis. The population was 84% male with a median age of 52 years (p=ns). The newly diagnosed PRDC patients: a) met the visit measure 60% vs. 22% in NON-PRDC group (p<0.0001); b) met the 12 consecutive weeks medication 43% vs. 33% in NON-PRDC group (p=0.2904); and c) met total measure 26% vs. 9% in NON-PRDC group (p=0.0103). Matched-pairs *t*-test comparing QIDS-SR baseline to endpoint scores, weighted for length of time between tests, showed a 4.0 point reduction (p<0.0001) for PRDC patients. The median medication cost initiated in PRDC was $9.51/month versus $29.97/month for other providers (p=0.006).
CONCLUSIONS: The STVHCS PRDC improved VHA depression performance outcomes, which has not been demonstrated in the literature previously. PRDCs contribute to improved depression outcomes with statistically significant reductions in medication costs.
Presented at the Annual Meeting of the College of Psychiatric and Neurologic Pharmacists, Orlando, FL, March 10-13, 2005.

476E. Response of mixed amphetamine salts and atomoxetine in ADHD treatment naive subjects. James J. McGough, MD[1], Sharon B. Wigal, PhD[2], Scott H. Kollins, PhD[3], *David A. Mays, PharmD, MBA, BCPS*[4]; (1)David Geffen School of Medicine at UCLA, Los Angeles, CA; (2)Child Development Center, University of California Irvine, Irvine, CA; (3)Duke University Medical School, Durham, NC; (4)Shire Pharmaceuticals Inc., Wayne, PA.

OBJECTIVE: The objective of this study was to compare the efficacy and safety of MAS XR with atomoxetine in treatment-naive children with ADHD.
METHODS: A subanalysis from a randomized, double-blind, multicenter, parallel-group, forced-dose–titration, analog laboratory classroom study of children 6–12 years of age with ADHD was conducted to assess the efficacy, safety, and time course of effect of MAS XR vs atomoxetine in treatment-naive patients with ADHD. Treatment-naive patients were defined as those who had never been prescribed medication to treat ADHD, either on- or off-label. The primary efficacy measure was the SKAMP deportment rating scale. Secondary efficacy measures will be presented. Safety was assessed based on spontaneously reported adverse events (AEs) recorded at each visit. Vital signs were measured at baseline and at each classroom visit.
RESULTS: Of the treatment-naive patients in population, 83 were randomized to receive MAS XR and 78 were randomized to atomoxetine. Baseline and demographic characteristics were similar. The mean change from baseline in SKAMP deportment scores for the MAS XR group was significantly greater (P=0.002) than that for the atomoxetine group. Mean change from baseline in SKAMP attention subscale scores was significantly greater (P<0.0001) at each week for the MAS XR group. At week 3, the mean change in SKAMP attention scores was –0.50 for the MAS XR group compared with –0.09 for the atomoxetine group. The percentage of patients considered improved or very much improved at endpoint on CGI-Improvement (CGI-I) was 70.9% in the MAS XR group and 34.2% in the atomoxetine group (P<0.001). Most of the reported AEs were mild to moderate in severity.
CONCLUSIONS: The results from this subanalysis of treatment-naive patients from the analog classroom study suggest that MAS XR demonstrates greater improvement in behavior and a greater reduction in inattention than atomoxetine in treatment-naive patients diagnosed with ADHD.
Presented at the Annual Meeting of the American Academy of Child and Adolescent Psychiatry, Toronto, ON, Canada, October 18–23, 2005.

477. The effect of patients' beliefs about medicines on adherence to antidepressants in Saudi depressed patients. Joza F. Al-Sabhan, Bsc[1], *Ola O. Al-Omran, PhD*[2]; (1)Al-Amal Hospital, Riyadh, Saudi Arabia; (2)King Saud University, Riyadh, Saudi Arabia.

PURPOSE: The objective of this study was 1) to assess adherence of depressed patients towards their antidepressant medication 2) to evaluate patients' beliefs about medicines in general, and about antidepressants in particular 3) finally, to assess the relationship between medication adherence in depressed patients and their beliefs about medicines.
METHODS: One hundred and twenty four depressed patients completed both the Medication Adherence Report Scale (MARS-5) and the Beliefs about Medicines Questionnaire (BMQ) . All patients were diagnosed with major depressive disorder according to DSM-IV criteria, and were recruited from an out-patient clinic in a large ministry of health hospital in Riyadh, Saudi Arabia.
RESULTS: Sixty three percent of the depressed patients were non-adherent to their antidepressant medications according to the MARS-5 scale. These patients held two types of beliefs about medicines in general; these beliefs were related to the overuse of medicines and their harmful effects. Two beliefs were also held for antidepressant medications in particular; the belief about the necessity of antidepressants and the belief about the need for concern about these medications. There was a statistically significant correlation between the general harm belief and adherence (p<0.001), and between specific concern beliefs and adherence (p<0.001).
CONCLUSIONS: Non adherence to antidepressants was high in Saudi depressed patients. Results of this study imply the importance of the beliefs about medicines, especially harm and concern beliefs on the overall adherence of patients to antidepressant medication.

478. Coverage of benzodiazepines under Medicare Part D: a multidisciplinary policy paper prepared for the 2005 DHHS Primary Health Care Policy Fellowship Program. *Nicole S. Culhane, PharmD, BCPS*[1], Stacy Barnes, MGS[2], Renee Crichlow, MD[3], Daniel Swagerty, MD, MPH[4]; (1)Wyoming Valley Family Practice Residency Program; Wilkes University, Wilkes-Barre, PA; (2)Marquette University, Milwaukee, WI; (3)Montana Family Medicine Residency Program, Billings, MT; (4)Landon Center on Aging, Kansas City, KS.

PURPOSE: The Centers for Medicare and Medicaid Services (CMS) has guidelines recognizing safe and appropriate use of benzodiazepines. Medicaid currently pays for benzodiazepines for dually eligible Medicare and Medicaid recipients. Beginning in January 2006, Medicare Part D will assume prescription coverage for Medicare patients, including the dually eligible, and has excluded this class of medication. This would affect more than 200,000 nursing home residents and at least 1.7 million of the 6.4 million dually eligible older adults.
METHODS: The 2005 Department of Health and Human Services (DHHS) Primary Health Care Policy Fellowship consisted of 35 primary care professionals, organized into seven multidisciplinary teams. Our team, consisting of a geriatrician, pharmacist, gerontologist, and family physician, focused its policy work on Medicare Part D legislation, namely exclusion of benzodiazepines. In addition to six months of examining federal legislation and policy development, our team reviewed pertinent literature regarding the implementation of Medicare Part D and the potential consequences of excluding benzodiazepines from coverage. Our policy paper underwent two peer review processes and was presented to DHHS.
RESULTS: If benzodiazepines are excluded from coverage through Medicare Part D, other higher cost and potentially riskier alternative drugs would be prescribed such as atypical antipsychotics and antihistamines. Atypical antipsychotics are not FDA approved for anxiety or sleep disorders. In older adults with dementia, atypical antipsychotics are associated with a three-fold increase in stroke and a two-fold increase in mortality. Antihistamines should be avoided in older adults due to increased risk of falls and confusion. Antidepressants, despite higher costs, are safer alternatives for anxiety. However, benzodiazepines often need to be administered for a short-term transitional period because anti-depressants take 4-8 weeks to achieve maximum effects.
CONCLUSIONS: Coverage of benzodiazepines under Medicare Part D must be maintained to achieve quality care and cost savings for older adults.

479. Treatment of sexual dysfunction in female sexual trauma survivors: an integrated approach of research, education and clinical practice. *Tracy Danielle Baher, Pharm.D.*[1], Laurie C. Ivey, PsyD[2], Kenton Voorhees, M.D.[2], Rocsanna Namdar, Pharm.D.[3]; (1)University Of Wyoming, School of Pharmacy, Laramie, WY; (2)Swedish Family Medicine Residency Program, Littleton, CO; (3)University of New Mexico Health Sciences Center, College of Pharmacy, Albuquerque, NM.

PURPOSE: Studies have shown that as many as 25% of female patients in primary care are survivors of either childhood sexual abuse and/or adult sexual assault, and only a small minority of these patients disclose this fact to their physician. Because of the sensitivity of this topic, particularly for this population, sexual dysfunction is likely under-diagnosed. A multidisciplinary approach to identify, treat and educate these patients is explored.
METHODS: Patients are referred to the clinical psychologist in a Family Medicine Residency Program. Integration of assessment, diagnosis, treatment and education is demonstrated with collaboration between three disciplines, the family physician, the doctors of pharmacy and the psychologist. The role of the clinical pharmacist is to provide evidence based recommendations for pharmacologic agents to treat female sexual dysfunction.
RESULTS: Collaboration is identified as a means of optimizing treatment for female sexual trauma survivors. This research reviews key points for assessment, diagnosis, treatment and education of sexual dysfunction in this population, and outlines psychological and pharmacologic modalities for treatment intervention. Pharmacologic agents such as hormone replacement therapy (HRT) and Sildenafil (Viagra®) are examples of aids for helping female sexual dysfunction. The clinical pharmacist was identified as being an integral member of this multidisciplinary group of practitioners and can make valuable treatment recommendations in this difficult to treat population.
CONCLUSION: A multi-disciplinary approach is a valuable method to assess, diagnose, treat and educate female patients with sexual dysfunction. Further research is needed to optimize care in this population.

480E. The use of erythropoetin and darbepoetin alfa in the treatment of anemia of chronic kidney disease. *Rhonda L. Martin, Pharm.D.*[1], Ted Walton, Pharm.D.[2], Andrew Howe, Pharm.D.[2]; (1)Mercer University Southern School of Pharmacy, Atlanta, GA; (2)Grady Health System, Atlanta, GA.

PURPOSE: To develop and evaluate treatment guidelines incorporating both epoetin alfa (EPO) and darbepoetin alfa for anemia of Chronic Kidney Disease (CKD) stages three through five; to measure the percent change of hemoglobin and hematocrit after conversion to darbepoetin alfa; and to evaluate the impact of pharmacist interventions in the management of anemia in CKD.
METHODS: A retrospective review was performed on all CKD patients in the Grady Health System Renal Clinic. Guidelines for anemia of CKD were developed to include both EPO and darbepoetin alfa by an interdisciplinary team. Patients receiving EPO were managed by a pharmacist for three months then converted to darbepoetin and followed for an additional three months.
RESULTS: Evaluation of current practice showed that there was a 45% compliance rate with clinic visits with majority of patients outside the target hematocrit range. Thirty patients were initially enrolled in this study and eleven were lost to follow-up. A total of nineteen patients were evaluated per protocol analysis on the EPO arm. Nine patients were lost during the conversion phase leaving ten patients who received darbepoetin. The mean baseline hematocrit was 32.3 ± 5.6 %. After the pharmacist intervention phase the mean hematocrit was 34.3 ± 3.5 %. Mean baseline EPO dose was 5526 ± 4741 units per week compared to 7158 ± 5002 units per week after pharmacist interventions. Three months after conversion to darbepoetin alfa, there was no change in mean hematocrit from the end of the interventions phase on EPO. The mean dose of darbepoetin at the end of the study was 45 ± 14.1 µg every other week.
CONCLUSION: The implementation of guidelines in the treatment of anemia of CKD by a clinical pharmacist has been shown to increase the number of patients within the target hematocrit range when receiving EPO therapy.

535. Impact of a team weight loss challenge on blood pressure, weight and health habits in an employee group. *Christine K. O'Neil, Pharm.D., BCPS, FCCP and Hildegarde J Berdine, Pharm.D., BCPS*; Mylan School of Pharmacy, Duquesne University, Pittsburgh, PA.

PURPOSE: Workplace health promotion programs have proven successful in reducing healthcare costs and improving employee health in a number of large US corporations. The purpose of this study was to determine the impact of a pharmacist-coordinated team challenge on weight loss, blood pressure and attitudes toward healthy lifestyles among employees in an urban university setting.
METHODS The study was a single-cohort, 12-week, observational study, to determine the impact of an educational intervention and team competition (weight loss challenge) on specific biomarkers (weight, blood pressure, body mass index or BMI) and attitudes regarding healthy lifestyles. Study participants included university employees,men and women, over age 18 years of age. Participants formed teams by self-selection. Blood pressure and weight were checked four times during the challenge. Participants completed a brief survey of health habits upon entry and completion of the study. Body mass index (BMI) was determined upon entry and completion with a chart using self-reported height. Printed information on healthy eating and exercise was provided; optional attendance at informational sessions on these topics was encouraged. Participants were not required to follow a specific diet or exercise program. The team with the greatest percentage weight loss per member won the challenge.
RESULTS: One hundred ninety-seven employees representing 43 teams were recruited. Over 1050 pounds was lost by the population, collectively, during the 12-week challenge. Data (demographics, risk assessment and screening results and follow-up) will be presented to determine the impact of pharmacist intervention on blood pressure, weight and changes in health habits in the target population.
CONCLUSION: This pharmacist-coordinated workplace health promotion project successfully recruited a large segment of the university workforce and resulted in considerable overall weight loss. Post-program surveys indicate a high level of satisfaction with the program.

STUDENT, RESIDENT, FELLOW RESEARCH IN PROGRESS

These papers describe original research by students, residents, and fellows in therapeutics, pharmacokinetics, pharmacodynamics, pharmacoeconomics, and pharmacoepidemiology in which the research effort is still on-going. The abstract title and authors are published in *Pharmacotherapy*; the full abstract will be published in the meeting program book.

481. The assessment of the accuracy of reported iodine allergies at the Western New York Veteran's Administration Medical Center (VAMC). *Elizabeth Scott-Ramsay, PharmD*[1], Edward M Bednarczyk, PharmD[1], Ken Kellick, PharmD[2]; (1)State University of New York at Buffalo, Department Of Nuclear Medicine, Buffalo, NY; (2)Western New York Veterans Administration Medical Center, Buffalo, NY.

PURPOSE: Use of iodinated contrast media as diagnostic adjuncts can improve the diagnostic accuracy of radiographic imaging procedures. In many patients, the presence of vague or poorly documented allergies may preclude the use of iodinated contrast. The primary objective is to determine the accuracy of reported allergies and to delineate between an anaphylactoid reaction, in which iodine should not be used and intolerance.
METHODS: Retrospective chart review of patients seen by the WNY VAMC with a noted allergy to "iodine," "contrast dye," ditrizoate or meglumine in their chart. After review of the patients chart, the patients were contacted and a detailed history of the initial event or reaction, especially the nature and time course of the allergy and any other allergies were noted.
RESULTS: 306 patients were identified from the VA system as having an iodine type allergy. 36 patients receive treatment from a WNY VA facility. 35 patients were male and 1 female. 2 male veterans had died. A total of 34 patients were contacted by phone and ~50% (14) have responded to date. Of those that responded 80% (11pts) were found to have intolerances, 7% (1pts) had no allergy and 15% (2pts) had a reported an anaphylactoid reaction.
CONCLUSIONS: In the general population an anaphylactoid reaction to iodine was found in <1%; however, we found that the rate of iodine allergy was higher (3%) in the WNY VA population. Currently, due to our response rate we are unable to make any conclusions with certainty; however, we found that there is a trend in the WNY VA system to label intolerances as allergies. This may erroneously exclude patients from having the appropriate imaging studies for optimal management. Further analysis is underway, including follow-up studies to assess the influence of charted allergies on the actual use of these agents in imaging procedures.

482. Hypertensive patients' satisfaction and adherence improved by pharmacist monitoring in northeast Thailand. *Phayom Sookaneknun; R. Michael E.Richards; Jaratbhan Sanguarnsermsri;, Pharm.D., Ph.D., Dr.rer.nat*; Faculty of Pharmacy, Chiang Mai University; Mahasarakham University; Thailand.

PURPOSE: This novel study was to investigate the effects of pharmacist monitoring on hypertensive patients' satisfaction and adherence in primary care settings in North East Thailand.
METHODS: A randomized control group, treatment group, pre test, post test design was used with hypertensive patients willing to enroll in the study. The research pharmacist provided pharmaceutical care consisting of drug counseling, patient education and medication review to the treatment group, in addition to their usual care, while the control group continued to receive the usual care provided for hypertensive patients. The 12-month study was undertaken in Mahasarakham University community pharmacy in the municipal area and in two nearby rural primary care units.
RESULTS: Two hundred and thirty five patients were enrolled in the study (118 in the treatment and 117 in the control group). Cronbach's alpha for the 16-item pro forma was 0.79. Patient overall satisfaction in the treatment group was greater than for the control group, $p < 0.05$. Patient adherence in the treatment group was also higher than in the control group, 66% and 34% respectively, $p < 0.05$, and significant improvement within groups after 12

months was found only in the treatment group, p <0.05.
CONCLUSIONS: The results indicate that pharmacist monitoring of hypertensive patients in the primary care setting in Northeast Thailand increases patient satisfaction and improves patient adherence.

483. Is the cholesterol lowering response to a statin and cholesterol absorption inhibitor inversely related?: a prospective, randomized, cross-over design study. *Rebecca J. Cheung, Pharm.D.*[1], Matthew K. Ito, Pharm.D.[2], Robert R. Henry, MD[3]; (1)Loma Linda University School of Pharmacy, Loma Linda, CA; (2)Oregon State University College of Pharmacy, Portland, OR; (3)VA San Diego Healthcare System, San Diego, CA.

PURPOSE: Studies have shown that cholesterol synthesis and absorption are negatively related. We hypothesize that there is an inverse relationship between LDL-c responses to simvastatin and ezetimibe, and patients with greater than expected LDL-c reduction to simvastatin will have less than expected LDL-c reduction to ezetimibe and vice versa.
METHODS: Participants with LDL-c levels ≥ 130 mg/dL were randomized to ezetimibe 10 mg daily or simvastatin 10 mg daily for four weeks and crossed over to the alternate medication for four weeks after a four week washout period. Serum lipid, liver function tests, and high-sensitivity C reactive protein (hs-CRP) levels were measured before and after each four week treatment period. D-simvastatin and D-ezetimibe, defined as LDL-c % change per manufacturer labeling minus individual LDL-c % change due to respective medications, were calculated. Linear Regression analysis was performed using D-simvastatin as the dependent variable and D-ezetimibe as the independent variable. A sample size of 26 patients will have approximately 80% power to detect r ≥ 0.5 with a level of a < 0.05. The study is likely to be completed by December 2005.
RESULTS: To date, 13 of 26 patients (46% male, mean of 51 years) have completed the study. Simvastatin reduced mean LDL-c levels from 162.9 ± 10.4 mg/dL at baseline to 112.0 ± 11.1 mg/dL at follow-up, resulting in a 31% reduction (P<0.001). Ezetimibe reduced mean LDL-c levels by 22%, from 161.9 ± 11.7 mg/dL at baseline to 124.5 ± 7.5 mg/dL at follow-up (P<0.001). Mean hs-CRP did not significantly change with either therapy. D-simvastatin and D-ezetimibe were negatively associated [D-simvastatin = 3.9–0.6 (D-ezetimibe) (r = -0.53, p=0.06)].
CONCLUSIONS: Although only half of the study population has completed the study, there is a strong trend toward a negative correlation between LDL-c response to simvastatin and ezetimibe.

484. Impact of a protocol on the safe and effective administration of nesiritide. *Shaunta Martina, Pharm.D.*, Kimi S. Vesta, Pharm.D., BCPS; University of Oklahoma College of Pharmacy, Oklahoma City, OK.

PURPOSE: The purpose of this study is to implement a nesiritide standardized protocol, to determine the impact of this protocol on the safe and effective administration of nesiritide and to evaluate the outcomes of nesiritide therapy at OU Medical Center.
METHODS: This project involved both retrospective and prospective chart review of patients given nesiritide for a 6-month period prior to and following implementation of a protocol. Patients were included if they received nesiritide as part of standard medical treatment. Data recorded included the patients' demographic information, nesiritide use (indications, contraindications, dose, administration, duration, monitoring), and outcomes (adverse effects, length of hospital and ICU stay, readmission). Following initial data collection the protocol was developed. Implementation of this protocol included educational sessions to physicians, nursing and pharmacy regarding heart failure, indications for nesiritide, proper dosing, administration and monitoring. Following implementation, a prospective chart review is being conducted. This will be compared to initial data to determine the impact of the protocol.
RESULTS: Seventeen patients were identified in the initial chart review. Of these patients 100% had proper indications and none had documented contraindications. Of patients receiving a bolus dose, 83% received the appropriate dose. The correct infusion dose was received by 88% of patients. Infusion duration exceeded 48 hours in 47% of patients and was started within 24 hours of hospital admission in 58% of patients. Recommended blood pressure monitoring was not done in 100% of patients. There was one documented episode of hypotension.
CONCLUSIONS: The final chart review is currently in progress. With implementation of a standardized protocol, we would expect to find that all patients will meet indication criteria, no patients will have contraindications, and more patients will receive the correct dosage and monitoring. We would expect improved outcomes such as decreased incidence and severity of adverse events.

485. Randomized trial evaluating the safety and efficacy of intermittent versus continuous intravenous furosemide. *Margaret R. Thomson, PharmD*, Jean M. Nappi, PharmD, BCPS, FCCP, Adrian Van Bakel, MD; Medical University of South Carolina, Charleston, SC.

INTRODUCTION: Aggressive diuresis in patients with symptomatic heart failure may be associated with increased mortality. Preliminary data also suggest that continuous infusions of furosemide are as effective as intermittent dosing and may possess a better safety profile.
OBJECTIVE: The objective of this study is to compare continuous versus intermittent furosemide dosing in patients requiring intravenous diuretic administration with respect to safety and efficacy.
METHODOLOGY: This is a prospective, randomized, stratified, parallel-group study assessing continuous furosemide infusion compared with intermittent furosemide in patients admitted to the hospital for heart failure exacerbations. Patients are stratified based upon initial serum creatinine. Patients included in this trial have decompensated heart failure requiring an anticipated extended (24 hours or longer) IV diuresis. They are excluded if they receive greater than 2 doses of IV furosemide prior to randomization. The primary efficacy outcome is net urine output. The primary safety outcome is the need for electrolyte replacement and hypotension. Other outcomes evaluated include daily weights, additional diuretics required, length of stay, and changes in markers of renal function.
RESULTS: Research is currently in progress. To date, 8 patients have been enrolled. Three patients have received continuous infusion, and 5 have received intermittent dosing of furosemide. Net urine output has been normalized for the amount of furosemide the patient received per day. The continuous infusion group had an average daily net urine output of 13.2 ml/mg furosemide/day while the intermittent dosing group had an average net output of 7.4 ml/mg furosemide/day. The continuous infusion group required an average of 500 mg magnesium and 50 mEq of potassium supplementation per day, while the intermittent dosing group required 371 mg of magnesium and 20 mEq of potassium per day. Additional sites are participating. Data collection is on-going and further results will be presented.

486. A comparison of cardiovascular outcomes in patients with diabetes: angiotensin converting enzyme inhibitors vs. angiotensin II receptor blockers. *Brian C. Sedam, Pharm.D.*, Julie M. Koehler, Pharm.D.; Butler University/ Clarian Health Partners, Indianpolis, IN.

PURPOSE: The objective of this study was to determine if angiotensin converting enzyme inhibitors (ACEI) and angiotensin II receptor blockers (ARB) offer similar cardiovascular protection in patients with diabetes mellitus (DM).
METHODS: This study was a retrospective chart review assessing patients with DM from January 2001 to November 2004. Patients were included in the study if they had a diagnosis of type 1 or type 2 DM, were ò 50 years of age, receiving an ACEI or ARB, and if they had a history of coronary artery disease, stroke, heart failure, or peripheral vascular disease plus hypertension or dyslipidemia. The primary outcome measurements included myocardial infarction (MI), stroke, death from cardiovascular causes, and the composite of the three outcomes. Unstable angina, heart failure exacerbation, and coronary revascularization were also assessed.
RESULTS: Of the study population (n=573), 442 received an ACEI and 131 received an ARB. Fewer patients in the ACEI group, in comparison to the ARB group, reached the primary outcomes of MI (8.1% vs 9.2%, CI -0.065, 0.041), stroke (4.1% vs 6.8%, CI -0.069, 0.013), death due to a cardiovascular cause (6.1% vs 7.6%, CI -0.063 vs. 0.033), and the composite of the three outcomes (18.3% vs 23.6%, CI -0.131 vs 0.024). Fewer patients in the ACEI group, in comparison to the ARB group, reached the secondary outcomes of hospitalization due to unstable angina (12.9% vs 15.3%, CI -0.090, 0.043), hospitalization for a heart failure exacerbation (10.4% vs 13.7%, CI -0.095, 0.028), and coronary revascularization (10.6% vs 12.2%, CI -0.077, 0.045).
CONCLUSION: ACEI and ARB appear to offer similar cardioprotective benefit in patients with DM at high risk for cardiovascular complications.

487. Effect of early cessation of nimodipine in the treatment of subarachnoid hemorrhage. *Emily A. Durr, Pharm.D.*, Eljim P. Tesoro, Pharm.D., Jeffrey J. Mucksavage, Pharm.D.; University of Illinois at Chicago, Chicago, IL.

PURPOSE: This study evaluated the effect of early discontinuation (≤15 days) of nimodipine in patients with subarachnoid hemorrhage (SAH) on the incidence of vasospasm and outcomes on discharge.
METHODS: A retrospective review of medical records was conducted for patients admitted between January 1, 2002 and October 31, 2004 to the Neurosurgical Intensive Care Unit (NSICU). Patient demographics, Fisher score, length of nimodipine therapy, reason for discontinuation, vasospasm incidence, length of hospital stay, discharge disposition, and Glasgow Outcome Scale (GOS) at discharge were documented.
RESULTS: Of the 129 patients included to date, nimodipine was discontinued early in 50% of patients. Of these, 40% experienced vasospasm (vs. 41% in the full course group). Upon discharge 25% were transferred to another facility and 66% went home (vs. 58% and 42%, respectively, in the full course group). Hypotension/bradycardia resulted in nimodipine discontinuation in

34% of patients in the short course group. More patients in the full course group were admitted with a Fisher Grade IV SAH (28% vs. 14%). Patients that received full course nimodipine had, on average, a 9 day longer hospitalization with 6 additional days in intensive care.
CONCLUSIONS: The incidence of vasospasm does not appear to be affected by duration of nimodipine therapy. The severity of SAH correlates more to hospital length of stay and patient outcomes than does nimodipine duration. The majority of patients in the short course group did not receive a full course of nimodipine as their hospital stay was less than 21 days, indicating a more rapid recovery. Short course nimodipine does not appear to negatively impact patient outcomes at discharge, as more patients were discharged home despite an abbreviated therapy. GOS is currently being calculated and these results will be presented at the poster session. All data collection and analysis will be completed by October 2005.

488. Implementation of a personal digital assistant documentation system in an academic ambulatory care setting. *Sarah E. Christiansen, Pharm.D.*[1], Teresa B. Klepser, Pharm.D., BCPS[2], Vicki J. Delgado, Pharm.D., BCPS[2]; (1)KCMS/MSU/Ferris State Universtiy, Kalamazoo, MI; (2)Ferris State University, Kalamazoo, MI.

PURPOSE: The role of the pharmacist in academic and clinical practice settings has greatly evolved in recent years. Further progression of the profession requires improved methods of clinical intervention documentation. The importance of documentation should be addressed in pharmacy school curriculums to enable the development of a routine that will be carried into professional careers. Along with verification of the clinical impact of pharmacists, documentation also provides a method to report financial value of the interventions. In comparison to traditional methods of documentation, the use of personal digital assistants (PDAs) is a more efficient and convenient method.
METHODS: Ferris State University pharmacy students and pharmacy residents provide clinical pharmacy services in an academic ambulatory care setting which served as the site for implementation of the project. Pharmacy students and residents were provided a PDA to track interventions during the two months they provided services to the clinic. Each PDA contained an identical data collection form authored with PenDragon® software. Interventions were entered into the PDA concurrent with the patient visit. Data from the PDAs was downloaded weekly into a Microsoft Access database to allow for pharmacy student evaluation and to identify educational topics for the medical residents. The collection of interventions was also analyzed for financial impact.
RESULTS: The development of the documentation tool is complete. Pharmacy students and residents are currently utilizing the PDA documentation program in their interactions at the ambulatory care clinic.
CONCLUSION: This method of documentation is expected to allow the pharmacy preceptors and academic clinic to evaluate the benefit of pharmacy students and residents. In addition, this project affords pharmacy students and residents early exposure to a new method of clinical documentation. Analysis of pharmacy services and preliminary results on the financial impact of pharmacy interventions are anticipated by September 2005.

489. An evaluation of microbiology coursework requirements at U.S. schools of pharmacy. *Lisa Pitrolo, B.S., Pharm.D., candidate*, Douglas Slain, Pharm.D., BCPS; West Virginia University School of Pharmacy, Morgantown, WV.

PURPOSE: To assess microbiology coursework requirements at US schools of pharmacy and the satisfaction of infectious diseases clinical faculty with microbiology education within their curriculum.
METHODS: An 18-question survey was administered to a single instructor of infectious diseases therapeutics at 69 US pharmacy schools. Information was collected about the school, faculty, and microbiology coursework requirements. In addition, faculty were asked six likert-style questions about the adequacy of microbiology requirements at their school and their interest in a supplemental online microbiology course or textbook tailored to pharmacy. Responses to likert-style questions were also analyzed for differences among disparate programs. A second survey will be sent to students at schools with diverse microbiology experiences to compare their assessment of their microbiology education.
RESULTS: Twenty-nine schools completed the survey. Seventeen (59%) schools offered 3-4 year professional programs and 12 (41%) schools offered 6-year programs. Microbiology coursework was part of the professional (final 3-4 years) curricula at 45% of schools. Another 45% of schools have microbiology only as a prerequisite. Only 57% of respondents' schools require a laboratory experience with microbiology coursework. Time between microbiology and infectious diseases therapeutics varied from being taught more than 3 years prior to being taught within the same course. Only 34% of respondents agree (0% strongly agree) that their current microbiology requirement prepares pharmacy students well for understanding antimicrobial therapeutics. 73% of faculty agree or strongly agree that a microbiology textbook tailored to pharmacy students would be a valuable addition to their curriculum. The only statistical difference between disparate programs was that instructors in the 6-year programs believed that the volume of microbiology material covered in the pharmacy curricula was less adequate for preparing students (p=0.006).
CONCLUSIONS: There appears to be great variability and room for improvement in microbiology coursework requirements at US pharmacy schools.

490. Effect of pioglitazone in combination with stable statin therapy on lipid levels in older subjects aged ≥65 years with type 2 diabetes and dyslipidemia after treatment conversion from rosiglitazone. *Charles Kelly, PharmD*[1], Mehmood Khan, MD[1], Alfonso Perez, MD[2], Robert Spanheimer, MD[1]; (1)Takeda Pharmaceuticals North America Inc., Lincolnshire, IL; (2)Takeda Global Research and Development Center, Lincolnshire, IL.

More than 20% of patients aged ≥65 years have type 2 diabetes (T2DM). In this population, it is especially important to reduce cardiovascular risk factors, such as dyslipidemia, in addition to achieving glycemic control. This subanalysis from an open-label study, "COMPLEMENT," was designed to determine whether lipid differences observed in a recent randomized, head-to-head, placebo-controlled study in the absence of concomitant lipid-altering therapies would be similar when older subjects were converted from rosiglitazone to pioglitazone therapy while maintaining constant doses of existing statins and other lipid-altering therapies.
In this multicenter, single-arm, open-label study, patients underwent 1 week of screening and 17 weeks of treatment with 30 mg QD pioglitazone (titrated to 45 mg QD at investigators' discretion) after conversion from rosiglitazone. All patients continued stable statin therapy. The primary outcome variable was change in triglycerides after conversion from rosiglitazone to pioglitazone. The data presented here are based on a subgroup of patients aged ≥65 years (55 male, 24 female) with T2DM and dyslipidemia (triglycerides ≥200 mg/dL but <1000 mg/dL). The primary outcome measure was fasting triglycerides.

Parameter, mg/dL	Baseline Mean (SD) (n=79)	% Change Mean at Week 17 (SE) (n=76)	P Value
Triglycerides	313.1 (169.3)	-16.6 (3.8)	<0.001
Total Cholesterol	197.1 (43.6)	-7.0 (1.6)	<0.001
LDL-C	99.1 (36.9)	11.0 (5.8)	0.063
HDL-C	41.9 (9.5)	6.7 (1.6)	<0.001

After treatment conversion from rosiglitazone to pioglitazone, patients aged ≥65 years with T2DM showed significant improvement in triglycerides, total cholesterol, and HDL-C levels over 17 weeks while maintaining stable statin therapy. LDL-C levels increased marginally. These lipid changes were independent of glycemic control.

491. Impact of a pharmacist-run diabetic clinic on attainment of american diabetes association goals. *Luba A. Kielbasa, Pharm.D.*, Karen P. Daniel, Pharm.D., CDE, Wallace A. Marsh, Ph.D., MBA; Nova Southeastern University, Ft. Lauderdale, FL.

PURPOSE: The objective of this study is to evaluate the impact of a pharmacist-run diabetes clinic on the achievement of American Diabetes Association (ADA) goals.
METHODS: A retrospective chart review is being conducted to assess the impact of a pharmacist-run diabetes clinic at Nova Southeastern University in achieving ADA guideline goals. Eligible patients were enrolled in the pharmacist-run diabetes clinic for at least 6 months from 2000-2005. Data collected include demographic data, A1C, fasting glucose, post-prandial glucose, blood pressure, cholesterol panel, and weight. Frequency of antiplatelet, ACE inhibitor and/or ARB use, as well as yearly proteinuria, eye, and foot evaluation referrals is also being assessed. Magnitude of change and ADA goal attainment at 6 months and 1 year following the initiation of management will be examined. Appropriate statistics will be used on the completed data set.
RESULTS: Preliminary results for twenty-six patients are subsequently described as magnitude of change from baseline and percent of patients at ADA goal attainment (GA) at 12 months. Glycemic results include an A1C reduction of 1.4 % and GA in 43 % of patients, as well as a fasting glucose reduction of 34 mg/dL and GA in 71 % of patients. Cholesterol results include an LDL reduction of 25 mg/dL and GA in 72 % of patients, HDL increase of 4 mg/dL and GA in 58 %, as well as TG reduction of 54 mg/dL and GA in 75% of patients. It is anticipated another 24 patients will be included.
CONCLUSION: Preliminary results indicate a beneficial effect of a pharmacist-run diabetic clinic on the achievement of ADA goals.

492. Preliminary findings of a pharmacotherapy management program aimed at increasing continuity of care in patients discharged from a county hospital. *Heather Spanbauer, Pharm.D.*, Gina M Zurick, Pharm.D., Cori A Wyman, Pharm.D., CDE, Antonia J Redhead, MD, William J Fiden, MD, Gene

D Morse, Pharm.D., FCCP, BCPS; University at Buffalo School of Pharmacy and Pharmaceutical Sciences, Buffalo, NY.

PURPOSE: Few studies evaluate the role of clinical pharmacy in regards to continuity of patient care. The University at Buffalo Department of Pharmacy Practice has implemented a multi-center study evaluating the impact of pharmacotherapy management on health and economic outcomes. This report describes the implementation of this protocol at a Family Medicine practice and teaching site and addresses these outcomes in relation to continuity of care.
METHODS: This program allows health care providers and/or pharmacists to identify patients at risk for medication complications, those with complicated medication regimens, and/or those whom it is deemed need additional pharmacist education during hospitalization. Outpatient pharmacist visits, at a nearby community health center, provide additional medication and compliance education, as well as continual follow-up after discharge. Pharmacists have access to patient charts and provide written recommendations to physicians, allowing for pharmacist interventions during all stages of care.
RESULTS: Early enrollment (including a pilot period) has included 14 patients, with initial data showing interesting trends. The two most common inclusion criteria met have been greater than four chronic medications prior to admission (21%) and at discharge (26%), with cardiac related conditions most prevalent (42%). General prescribing trends were identified. Most frequent medication management contributions were related to medication regimen problems (medications with no indication, duplicate therapy and suboptimal therapy). Patient specific follow-up visits occur as deemed necessary by the patient, provider and/or pharmacist, with data updated, as necessary, based on electronic medical records.
CONCLUSIONS: Pharmacist contributions to medication management can be numerous when focusing on the continuity of care. Preliminary findings suggest greatest impact in regards to medication selection and dosing. Additional patient enrollment in both inpatient and ambulatory settings, site extension and prolonged study duration is planned.

493. Controlling coronary heart disease risk factors in diabetes: are we successful? *Alan K. Phan, Pharm.D.*[1], LanChi L. Bui, Pharm.D.[2], Jody Jacobson, Pharm.D.[1], Byron Allen, MD[1]; (1)UCI Medical Center, Orange, CA; (2)University of California, Irvine Medical Center, Orange, CA.

PURPOSE: The primary goal of this study is to assess the success rate of controlling risk factors for coronary artery disease in diabetic patients. This will be measured by determining both the percentage of diabetic patients who achieved low density lipoprotein cholesterol (LDL-C) goals as defined by National Cholesterol Education Program (NCEP) guidelines and who reached desired Joint National Committee (JNC-7) blood pressure goals. The data was further analyzed to ascertain whether achievement of NCEP and JNC-7 goals correlates to diabetic control. Prescription quantity per day and BMI were evaluated to determine their correlation to the achievement of these goals.
METHODS: A year-long retrospective chart review of the 61 patients from a diabetes clinic who met inclusion criteria was performed. Inclusion criteria required that patients had a minimum of two clinic visits during the year and that they needed hypoglycemic medication for blood glucose control.
RESULTS: LDL-C goals (<100 mg/dl) were attained by thirty-three of the patients (54%). Number of agents prescribed did not affect LDL-C goal achievement. However, only 10% of our patients were on maximum doses of HMG-CoA Reductase inhibitors. Patients with a HbA1C <7 were 2 times more successful at achieving LDL-C goals than those with a HbA1C>7 (65% to 35% respectively.) Patients with systolic blood pressures less than 140m Hg demonstrated better attainment of LDL-C goals. Overall, 80% of patients were obese, measured by BMIs greater than 26.
CONCLUSION: A large number of patients seen in a diabetes clinic failed to attain national goals defined to reduce cardiac risk indicating that more aggressive therapy is needed to improve outcomes in these patients.

494. Evaluation of a therapeutic statin conversion to a usual care statin conversion. *Amy E. Miller, Pharm.D.*, Joseph J. Saseen, Pharm.D., FCCP, BCPS, Laura B. Hansen, Pharm.D., BCPS; University of Colorado at Denver and Health Sciences Center, Denver, CO.

PURPOSE: This study evaluated the effectiveness of a therapeutic versus an equipotent statin conversion among patients using an indigent-care formulary when atorvastatin was removed in August 2004.
METHODS: This retrospective chart review compared two outpatient populations: 1) University of Colorado Hospital (UCH) family medicine patients converted by a clinical pharmacist from atorvastatin to a formulary product (simvastatin, rosuvastatin, or pravastatin; ± ezetimibe) based on a therapeutic conversion algorithm designed to achieve goal LDL values, and 2) other UCH patients converted from atorvastatin to a formulary product by usual care using an equipotent conversion algorithm designed to provide similar LDL reduction. Patients were identified by refill records and data collected by medical record review. Inclusion criterion was a filled atorvastatin prescription at the UCH pharmacy between May 1, 2004 and July 31, 2004. Exclusion criteria were: concurrent use of amiodarone, verapamil, cyclosporine, or gemfibrozil; history of transplantation or HIV; absence of a fasting lipid panel prior to or after conversion. LDL cholesterol reduction and LDL goal attainment, before and after conversion, were evaluated for both groups.
RESULTS: A total of 334 charts were reviewed; 64 patients currently have complete data (22 therapeutic conversions, 42 usual care conversions). Mean LDL values were 86.1 mg/dL before and 82.8 mg/dL after in the therapeutic conversion group (p=0.66) and 78.6 mg/dL before and 84.0 mg/dL after in the usual care group (p=0.16). LDL goal attainment values were 77.3% before and 95.5% after in the therapeutic conversion group (p=0.1), and 88.1% before and 76.2% after in the usual care group (p=0.2). Patients will continue to be evaluated through August 31, 2005.
CONCLUSIONS: A therapeutic conversion approach using clinical pharmacists may result in better control of dyslipidemia than a usual care approach using an equipotent conversion.

495. Prevalence of complementary and alternative medicine use among healthy women participating in research. *Gregory J. Welder*[1], Christopher B. Arant, MD[2], Timothy R. Wessel, MD[2], Richard S. Schofield, M.D[2], Issam Zineh, Pharm.D[1]; (1)Department of Pharmacy Practice, University of Florida College of Pharmacy, Gainesville, FL; (2)Division of Cardiovascular Medicine, University of Florida College of Medicine, Gainesville, FL.

PURPOSE: Individuals in the United States are increasingly using complementary and alternative medicine (CAM). It is well documented that the majority of these individuals are women. Since biologically-based CAM could confound results of clinical trials, it becomes important to characterize CAM use in research participants. We determined the prevalence and type of CAM use in healthy women participating in a clinical trial of a cholesterol-lowering agent.
METHODS: The records of women participating in an ongoing clinical study were analyzed. CAM use was documented at screening and at each follow-up visit using electronic case report forms. The clinical trial database was then queried to determine the prevalence of CAM use throughout the study period and the type of CAM used.
RESULTS: Of the 30 women enrolled, 57% (N=17) were taking biologically-based CAM at some point during the study. The majority of these women (94%) were taking CAM at study entry. Baseline age, blood pressure, total cholesterol, LDL, HDL, and triglycerides for women on CAM were: 41 ± 16 years, 121/76 ± 12/9 mmHg, 197 ± 40 mg/dl, 100 ± 33 mg/dl, 76 ± 21 mg/dl, and 101 ± 48 mg/dl, respectively. These parameters were not significantly different for women not taking CAM. Sixty-nine percent of women on CAM were taking vitamins; 50% were taking minerals, all of which contained calcium; and 19% were taking a non-vitamin/non-mineral supplement. Non-vitamin/non-mineral supplements included antioxidants (lutein, lecithin, ginkgo, pomegranate, zeazanthin), lipid-modifying agents (red yeast rice, fish oil, garlic, flaxseed oil, linoleic acid), glucosamine/chondroitin, dehydroepiandrosterone, and shark cartilage.
CONCLUSION: Prevalence of biologically-based CAM use in healthy women participating in our trial was greater than 50%. A broad range of CAM modalities were used. The high rate of CAM use among women, particularly at study entry, should be accounted for in clinical trials as results may be confounded via direct CAM use or CAM/treatment interactions.

496. Clinical application of therapeutic drug monitoring (TDM) in HIV/hepatitis C (HCV) patients. *Naomi Boston, Pharm.D.*[1], Judianne Slish, Pharm.D.[1], Linda Catanzaro, Pharm.D.[1], Angela Redlinski, Pharm.D.[1], Chui-Bin Hsiao, M.D.[2], Adel Suliaman, M.D.[2], Gene Morse, Pharm.D.[1]; (1)University at Buffalo School of Pharmacy and Pharmaceutical Sciences, Buffalo, NY; (2)Erie County Medical Center, Buffalo, NY.

PURPOSE: The purpose of this study is to examine TDM of antiretrovirals (ARVs) in patients co-infected with HIV/HCV and identify causes of variability in ARV concentrations.
METHODS: Samples were collected between 12/11/2002 and 3/16/2005, after informed consent was obtained, and assayed by a certified HPLC technique. ARV regimens, demographics, concurrent medications, adherence, toxicity information, concomitant disease states, resistance, and laboratory data were acquired. Expected trough concentrations were defined using product information and primary literature. Concentrations were identified as higher, within or lower than expected ranges.
RESULTS: Thirty-one troughs were obtained from 29 samples. 62% of subjects were male, 41% were black and 52% were white. Mean CD4 count was 379 cells/mm^3, and 83% had undetectable (<50 copies/ml) viral loads. The most common HCV genotype was 1b (41%). Liver biopsy histories were available for 15 patients; grading and staging varied. Fifty-two percent received HCV treatment for six-12 months with recommended standard of care. Eighteen concentrations were within, nine were higher, and four were

lower than the expected range. Factors contributing to unexpected concentrations include drug interactions in four patients, hepatic decompensation in three patients, and malabsorption in one patient. Dose reductions alleviated ARV toxicity in two patients.
CONCLUSIONS: TDM identified extensive pharmacokinetic variability in our HCV co-infected patients. Our findings demonstrate that using TDM in this subset of co-infected patients was useful to adjust doses and resolve symptoms associated with drug toxicity.

497. Empiric use of piperacillin/tazobactam plus ciprofloxacin and subsequent targeting of therapy. *Steven P. Dunn, PharmD*, Ralph H. Raasch, PharmD; University of North Carolina Hospitals, Chapel Hill, NC.

PURPOSE: This study evaluated the rate of appropriate versus inappropriate tailoring of initial, empiric piperacillin/tazobactam plus ciprofloxacin (P/T + C) therapy after the reporting of microbiological results.
METHODS: All adult patients (age > 18 years) who had cultures obtained and who were started on empiric P/T + C within 24 hours of admission during August and September 2004 were evaluated. Patients were excluded if discharged or expired within 72 hours of antibiotic initiation, or if antibiotic therapy would not be influenced by culture results (ie, febrile neutropenia). Patients were then subdivided into those with at least one positive culture from any specimen site, or those whose cultures were all negative. Culture positive patients were judged as having antibiotic therapy appropriately or inappropriately tailored based upon allergies, site of infection and sensitivity results. Day-to-day clinical status of the patient was not evaluated. Other initial empiric antibiotic use (ie, vancomycin) was permitted. Differences between 24-hr antibiotic acquisition costs, frequency of clinical failure, and rates of adverse effects between patients appropriately versus inappropriately tailored were assessed using Fisher's exact test or the Mann-Whitney test.
RESULTS: One hundred twelve patient records were evaluated; 34 patients were excluded. Among the remaining 78 patients, negative cultures were reported in 50 (64%). Among those with positive cultures, 16 (57%) were appropriately, and 12 (43%) were inappropriately tailored. One clinical failure occurred in each group. Patients who were appropriately tailored had lower rates of diarrhea (19% vs. 58%, p=0.039), and lower mean 24-hr antibiotic acquisition costs ($32.26 vs. $56.17, p=0.028).
CONCLUSION: Most patients begun on empiric antibiotics have negative cultures, making tailored therapy impossible. However, when cultures are positive, patients on appropriately tailored therapy have decreased rates of diarrhea and decreased antibiotic drug costs without compromising clinical outcome in comparison to those whose empiric treatment is not changed.

498. Preliminary analysis in vitro susceptibilities of antibiotics and its treatment of adult Acinetobacter meningitis in a medical center in southern *Fangting Chen, master*, ChingLing Tai, master, Wen-Neng Chang, M.D.; Chang Gung Memorial Hospital, Kaohsiung County, Taiwan.

PURPOSE: The strains of *Acinetobacter baumannii* isolated from cerebrospinal fluid (CSF) of adult meningitis patients produced initial multi-resistant to antibiotics rapidly. These characteristics have caused a therapeutic challenge to choose initial empiric antibiotics. The study was designed to find out a better initial empiric antibiotic to choose.
METHODS: We conducted this study from eighteen adult patients with *Acinetobacter* meningitis in 1998 to 2003, twenty-one of the strains isolated from CSF specimens and examined their antibiotics MIC data. The antibiotics were those that physicians usually used to treat adult *Acinetobacter* meningitis, including ceftazidime, ceftriaxone, cefepime, imipenem, meropenem, aztreonam, ciprofloxacin and ampicillin/sulbactam.
RESULTS:These antibiotics MIC90% data (μg/mL): imipenem : 2, meropenem : 4, cefepime >16, ceftriaxone >64, ceftazidime >128. Despite the prognosis of other adult bacterial meningitis can be influenced by underlying diseases or other factors, the *Acinetobacter* meningitis did not have the same condition.
CONCLUSIONS: From this analysis, it was shown that carbapenem was a better choice than the third and fourth cephalosporins. Meropenem as empiric antibiotic to treat *Acinetobacter* meningitis was shown with good results.

499. Treatment efficacy of methicillin-resistant Staphylococcus aureus pneumonia in a university hospital. *Rebecca L. Shaefer, Pharm.D.*, Steve J. Martin, Pharm.D., Diane M. Cappelletty, Pharm.D.; Medical University of Ohio and University of Toledo, Toledo, OH.

PURPOSE: To assess the efficacy of treatment prescribed for patients with MRSA pneumonia and evaluate appropriateness of empiric and definitive therapy for MRSA pneumonia.
METHODS: A retrospective chart review was performed on patients with positive MRSA sputum cultures receiving antibiotic therapy admitted to our institution from January 1 to September 30, 2004. Inclusion criteria for each patient were based on accepted clinical criteria. Patients were excluded based on defined criteria. The primary outcome was treatment efficacy. Clinical parameters were collected daily for 14 days to evaluate treatment efficacy. Each patient was categorized as clinical cure, improvement, or failure.
RESULTS: Seventy-one patients had positive MRSA sputum cultures and received antibiotic therapy (n=56 vancomycin, n=15 linezolid). Forty-six patients were excluded, 4 charts were unavailable, leaving 21 patients for the study (20 vancomycin, 1 linezolid). Fourteen patients achieved clinical cure, 5 clinical improvement, and 2 clinical failure. There were 0 deaths in the cure group, 20% mortality in the improvement group, and 100% mortality in the failure group. Mean hospital LOS (25.5 days cure, 33.8 improvement), mean ICU LOS (13.1 days cure, 19.5 improvement), and mean ventilator time (11.4 days cure, 32.3 improvement) were lower for the cure group versus the improvement group. There were 2 incidences of re-infection in the cure group versus 5 incidences in the improvement group including the 1 patient who received linezolid. The mean trough concentrations for the cure group and the improvement group were 9.6 μg/ml. The mean length of therapy (days) was 12.6 cure versus 12.0 for the improvement group. Ninety percent of the patients were started on appropriate empiric therapy and 100% received appropriate definitive therapy.
SUMMARY: Vancomycin has a 90% clinical cure/improvement rate, linezolid and vancomycin were associated with re-infection, and there appears to be no correlation between vancomycin trough concentrations and treatment efficacy.

500. Predictors of in-hospital mortality for bloodstream infections caused by Enterobacter spp. or *Citrobacter freundii*. *Eli Deal, Pharm.D.*[1], Scott Micek, Pharm.D., BCPS[1], David Ritchie, Pharm.D., FCCP, BCPS[2]; (1)Barnes-Jewish Hospital, St. Louis, MO; (2)Barnes-Jewish Hospital and St. Louis College of Pharmacy, St. Louis, MO.

PURPOSE: Infections caused by bacteria that produce AmpC Beta-lactamases have been associated with high rates of mortality and morbidity. The objective of this study was to determine the impact of multiple factors, including antimicrobial therapy, on the clinical outcome of in-hospital mortality in patients with bacteremia caused by the AmpC Beta-lactamase producers *Enterobacter spp.* and *Citrobacter freundii*.
METHODS: Patients hospitalized at Barnes-Jewish Hospital (St. Louis, MO) with bloodstream infections caused by *Enterobacter spp.* or *Citrobacter freundii* were retrospectively evaluated. Electronic patient medical records and the pharmacy department's database were analyzed. Patients that received antibiotic therapy were segregated according to hospital survival. Univariate analysis and multiple logistic regression were performed to determine independent risk factors associated with in-hospital mortality.
RESULTS: Between 1998-2004, 124 cases of *Enterobacter spp.* or *Citrobacter freundii* bacteremia were identified. In-hospital mortality occurred in 19% of these cases (n=24). Univariate analysis revealed that vasopressor use and mechanical ventilation occurred more frequently in those patients that experienced in-hospital mortality (p<0.005). Factors related to antimicrobial therapy including monotherapy, combination therapy, and choice of agent (imipenem, cefepime, or other agent) were not found to be influential on this outcome (p>0.05). Multiple logistic regression analysis identified resistance to second- and third-generation cephalosporins (adjusted odds ratio [AOR], 3.9; 95% confidence interval [CI], 1.0-14.5; p=0.026) and mechanical ventilation (AOR, 21.6; 95% CI, 5.1-92.1; p<0.001) as independent determinants of mortality.
CONCLUSIONS: Factors related to antimicrobial therapy were not found to be associated with in-hospital mortality among patients with bloodstream infections caused by *Enterobacter spp.* or *Citrobacter freundii*. Patients with cephalosporin-resistant strains or those that required mechanical ventilation had an increased risk of mortality.

501. Risk factors associated with acquisition of vancomycin-resistant Enterococci at a tertiary teaching hospital. *Jenny Y. Chung, Pharm.D.*, Helen S. Lee, Pharm.D., BCPS, Lauri D. Thrupp, M.D.; University of California, Irvine Medical Center, Orange, CA.

PURPOSE: We aimed to identify risk factors associated with the acquisition (colonization and/or infection) of Vancomycin-Resistant Enterococci (VRE) during hospitalization at UCI Medical Center from 6/01/04 to 12/31/04.
METHODS: During the study period, thirty-seven patients were identified to have VRE in any type of culture specimen after 48 hours of admission. Six subjects who reported to have VRE positivity prior to admission were excluded. Review of the medical records of these 31 patients included data collection of VRE culture results, antibiotic exposure, immunosuppressive therapy, surgical history, hospitalization, nursing home residency, ICU admission, and underlying co-morbidities. The review included data collection of 30 days preceding the first VRE culture positivity.
RESULTS: Exposure to select antibiotics during these preceding 30 days was the predominant risk factor for VRE acquisition, followed by ICU admission, history of surgery, recent hospitalization, immunosuppressive therapy, and nursing home residency. 96.7% of the patients were exposed to at least one of the antibiotic agents that have been associated with VRE acquisition in the

literature. The most commonly associated antibiotic was intravenous vancomycin. VRE acquisition took place 17.5 median days after admission. The most common co-morbidities were malignancy and infections with organisms other than VRE.
CONCLUSION: Antibiotic exposure was the number one risk factor for VRE acquisition based on this small retrospective review. In selecting an antimicrobial regimen for patients with certain risk factors, one should be cognizant of this possible association of select antibiotics with VRE acquisition. The findings of this study warrant the need for the further evaluation of indications and appropriateness of select antimicrobial agents these patients received with high frequency during the review period.

502. An evaluation of the initial empiric utilization of piperacillin/tazobactam and subsequent outcomes of switching to narrowed spectrum antibiotics. *Monica Mineo, PharmD.*, Helen Lee, PharmD, Lauri Thrupp, MD, James Joyner, MD, Diana McPherson, RN, Judith Vargo, RN; UC Irvine Medical Center, Orange, CA.

PURPOSE: Initiation of empiric antibiotic therapy, involves the use of very broad spectrum agents, such as piperacillin/tazobactam (pip/tazo), to target the most likely organisms. Current literature supports use of pip/tazo for the treatment of complicated soft-tissue, intra-abdominal, lower respiratory tract infections as well as nosocomial acquired pneumonia. Since the emergence of resistant pathogens with broad spectrum agents is of concern, narrowed antibacterial therapy on the basis of culture and susceptibility results is a logical standard of practice whenever possible. In the recent past, pip/tazo has become a commonly prescribed antibiotic at UC Irvine Medical Center. Therefore, the purpose of this study is to evaluate the empiric utilization and streamlining process of pip/tazo to narrowed spectrum antibiotics.
METHODS: This study is a retrospective chart review (50 medical records) of patients that were initiated on pip/tazo from July 1, 2004 to August 31, 2004. Hospitalized patients over the age of 18 were included. The primary measures included antimicrobial indications and clinical/ microbiological resolution of infection. Secondary measures included, duration of therapy, length of stay, and emergence of resistance.
RESULTS: The most common empiric indication for pip/tazo initiation was nosocomial pneumonia (22%). Of the fifty charts reviewed, seventeen patients had a narrowed antibiotic alternative based on the culture and susceptibility report. Seven of the seventeen patients (41%) were switched to narrowed spectrum antimicrobial therapy based on antimicrobial results. Switched patients had better clinical and microbiological response rates (43% vs. 35% experienced complete clinical resolution; 57% vs 24% microbial eradication). However, this group had fewer initial polymicrobial infections, fewer nosocomial acquired infections and shorter lengths of hospital stay. Only two cases of pip/tazo intermediate resistance were observed.
CONCLUSION: The streamlining of piperacillin/tazobactam therapy, based on culture and susceptibility results, should be considered in patients with single microbial infections that are not nosocomial acquired.

503. Appropriate use of DVT prophylaxis at Audie L. Murphy Veterans Hospital. *Jennifer N. Ashley, Pharm.D.*, Lisa D. Prather, Pharm.D., William D. Linn, Pharm.D.; Audie L. Murphy Memorial Veterans Hospital, San Antonio, TX.

PURPOSE: The objective of this study is to determine if patients at high risk for deep vein thrombosis (DVT) receive appropriate prophylaxis when admitted to medicine units of Audie L. Murphy Memorial Veterans Hospital (ALMVH).
METHODS: A retrospective chart review was conducted. One-third of patients hospitalized to medicine units at ALMVH between July 1, 2004 to July 31, 2004 were randomly selected. Patient demographics, age, gender, and ethnicity, were recorded. A DVT risk assessment tool for data collection was developed from available literature and each patient's DVT risk factor(s) were collected. A risk assessment score of 4 or greater was determined to place patients at high risk; therefore, necessitating DVT prophylaxis. Data also included whether a patient received DVT prophylaxis and if it was appropriate. Contraindications to pharmacologic prophylaxis were recorded as well. Exclusion criteria included warfarin therapy prior to admission and continued during hospitalization; admission for DVT/PE; and patients transferred to a medicine unit for census overflow. The final outcome of DVT development within 90 days post-discharge was also recorded.
RESULTS: Data were collected for 202 patients admitted during the specified date range. Twenty-nine patients were excluded from the study because they met criteria stated above, leaving 173 patients eligible for evaluation. Of these, 101 patients had 4 or more risk factors, but only 28 (27.7%) of them received DVT prophylaxis (1 mechanical, 13 UF heparin, 14 LMWH). Furthermore, 10 patients who had less than 4 risk factors indicating low risk received DVT prophylaxis (1 mechanical, 6 UF heparin, 2 LMWH; 1 patient received mechanical and LMWH). Analysis of data is ongoing and should be complete by September 2005.
CONCLUSIONS: Preliminary results indicate that many patients at high risk for DVT/PE are not receiving prophylaxis when admitted to a medicine unit at ALMVH.

504. The role of oral naloxone for opiate-induced constipation. *Kimberly Tallian, Pharm.D.*, Laura Hall, Pharm.D., Lillian Udom, Pharm.D.; University of California San Diego Medical Center, San Diego, CA.

BACKGROUND: Stimulation of opiate receptors in the gastrointestinal (GI) tract by opiates causes constipation by delaying gastric emptying and GI transit time. Intravenous naloxone used orally has been studied for opiate-induced constipation; however, it is not FDA approved for this route of administration or indication for use.
PURPOSE: To develop an algorithm to ensure the safe and rationale use of oral naloxone to manage patients with opioid-induced constipation.
METHODS: This was a retrospective review of all inpatients who received oral naloxone between July 2004 and April 2005. Patients were compared for differences in indication, concomitant laxatives, efficacy, pain control influence, dosage regimens, therapy duration and prescribing errors.
RESULTS: Thirty-one patients used oral naloxone for the management of constipation in combination (first-line n=8 or refractory n=17) or alone (n=2). Other or unknown indications for use (n=5) were found. No patients demonstrated definite improvement in their bowel frequency related to oral naloxone use. The remaining patients showed an unclear (n=17) or unknown (n=14) improvement in constipation. Patients received various dosage regimens with doses ranging from 2.4 mg to 48 mg/day (average dose = 10.4 mg/day) over 1 to 30 days (average duration =3D 6.5 days). No correlation was seen between naloxone dosage and reversal of pain based on pain scores or opioid requirements. One prescribing error related to the wrong route of administration was identified but was intercepted prior to administration.
CONCLUSIONS: More cost-effective, established laxatives should be administered as first-line therapy for opiate-induced constipation at optimal doses. Oral naloxone should be reserved for patients with refractory constipation who have failed other treatment options. Institution-wide safety measures including sound-alike and look-alike alerts to distinguish between routes of administration as well as awareness regarding its potential impact on pain control are also needed.

505. Evaluating the appropriate usage of epoetin alfa in an acute care setting within a teaching institution. *Elizabeth Chiu, Pharm.D.*, Rehana Jamali, Pharm.D., William Steier, M.D., Warren Shapiro, M.D.; Brookdale University Hospital and Medical Center, Brooklyn, NY.

PURPOSE: Lack of established guidelines for epoetin alfa use and significant monetary expenditure led to the development of a new dosing protocol to improve efficacy while reducing improper prescribing and cost.
METHODS: The initial dosing protocol was derived from medical literature. A three-times-a-week dosing regimen was projected to be more economical than the equally efficacious once-weekly regimen. Education was provided on proper anemia management. A prospective chart review (n=53) was performed by a pharmacist from December 2004 to February 2005 to assess adherence and evaluate the efficacy of the protocol. Data collection included: patient's demographics, diagnoses, indications, dosage and schedule, iron therapy, blood transfusions, laboratory monitoring, and the medication administration record (MAR).
RESULTS: Ninety-one percent (48/53) of dosing schedules evaluated were compliant with the protocol; however, patients had an indeterminable hemoglobin response due to multiple transfusions or brief length of stay. Fifty-one percent (27/53) had FDA-approved indications for anemia treatment. Inappropriate laboratory monitoring was found in 30% (16/53) of patients due to lack of iron studies. Comparison of epoetin alfa usage under protocol with a theoretical once-weekly dosing regimen revealed a cost savings of 35% with protocol use.
CONCLUSIONS: Implementation of a pharmacy-managed epoetin alfa protocol has improved drug utilization and cost efficacy. Based upon the initial drug use evaluation (DUE), the protocol was revised and guidelines were developed to include a uniform dosing schedule, appropriate usage, laboratory monitoring, and iron therapy. A follow up DUE is being performed to evaluate the results of these changes.

506. Achieving therapeutic valproic acid levels in patients receiving combination therapy with phenytoin versus valproic acid monotherapy. *Erin M. Megerle, Pharm.D.*, Shiv K. Seth, Ph.D.; The Ohio State University Medical Center, Columbus, OH.

PURPOSE: Phenytoin (PHT) and valproic acid (VPA) are commonly used in combination for seizure treatment and prevention. This combination therapy often achieves subtherapeutic VPA levels, due to enzyme inducing properties of PHT. The recommended VPA starting dose for the indication of seizures is 15 milligrams/kilogram/day. However, the literature provides little information regarding the appropriate VPA starting dose when combined with PHT. The purpose of this study is to determine an appropriate VPA starting

dose to achieve therapeutic levels in patients receiving PHT concomitantly for an indication of seizures and to compare the newly identified dose to the dose needed to achieve therapeutic levels in patients receiving VPA monotherapy.
METHODS: A retrospective chart review is being conducted including patient admissions between January 1, 2000 and June 1, 2004 at The Ohio State University Medical Center. The study will review patients who received PHT and VPA simultaneously and patients who received VPA monotherapy during admission for an indication of seizures. Inclusion criteria are documented diagnosis of seizures and therapeutic PHT and VPA levels during admission. Patients are excluded if drug levels are unavailable or subtherapeutic. Data collected include dosing and time of administration, drug levels and time of blood draw, albumin, serum creatinine, liver function tests, concurrent drugs, and if seizures occurred during admission. The primary outcome is to determine the VPA dose needed to achieve therapeutic VPA levels as monotherapy versus in combination with PHT.
RESULTS: To date, 210 admissions have been reviewed for potential inclusion into the combination therapy group. Thirty-three admissions met the inclusion criteria. Therapeutic VPA levels were achieved with a mean dose of 39 milligrams/kilogram/day. The mean VPA level achieved was 67.6 mg/L.
CONCLUSION: Preliminary results show that patients receiving concomitant PHT and VPA therapy require over two times the recommended VPA starting dose of 15 milligrams/kilogram/day.

507. Effect of HMG-CoA reductase inhibitors on outcomes in patients with subarachnoid hemorrhage. *Khushali Patel, PharmD*, Eljim P. Tesoro, PharmD, Jeffrey Mucksavage, PharmD; University of Illinois Medical Center at Chicago, Chicago, IL.

PURPOSE: This study evaluates the effects of statins in subarachnoid hemorrhage (SAH) patients admitted to the Neurosurgical Intensive Care Unit (NSICU) at the University of Illinois Medical Center at Chicago. The endpoints measured are the incidence of vasospasm and clinical outcomes across the Fisher and Hunt and Hess grading scales.
METHODS: This is a retrospective matched controlled analysis of SAH patients admitted to the NSICU from January 2000 to October 2004. Patient demographics, past medical history, cerebral angiogram reports, transcranial Doppler reports, Fisher, Hunt and Hess, and Glasgow coma scale (GCS) scores on admission, aneurysm type and treatment, incidence of vasospasm and treatment, length of hospital stay, and Glasgow outcomes scales (GOS) on discharge were documented and compared.
RESULTS: Forty-one patients were identified as taking a statin prior to admission: 63% female, 73% Caucasian, 23% with Hunt and Hess grade 4 and 32% Fisher grade 4 (25% vs. 33% respectively in the control group). Twenty-nine percent of patients in the statin group had a GCS < 9 vs. 40% in the control group. A greater proportion of eligible patients in the statin group had CAD. Angiographically documented vasospasm was observed in 36% of patients on statins vs. 60% in the control group. Of the 36% in the statin group, 29% received vasospasm treatment (12% angioplasty; 22% triple-H therapy) versus 47% in the control group (53% angioplasty and 53% triple-H therapy). GOS evaluations are still pending and will be completed before presentation.
CONCLUSION: Statins appear to have a protective effect in patients with SAH as seen by the decreased incidence of vasospasm. The relationship between the timing of initiation and observed benefit is unclear, and would be better assessed in larger prospective trials.

508. Nutritional support in the acute care patient post-ventricular assist device placement. *Abby Re, PharmD*[1], Jane M. Gervasio, PharmD, BCNSP[1], Robert D. Warhurst, PharmD[2], Gary P. Zaloga, MD[2]; (1)Butler University, Indianapolis, IN; (2)Clarian Health Partners, Indianapolis, IN.

PURPOSE: There is little information addressing the appropriate route of nutrition support post- ventricular assist device (VAD) placement. Concerns for using enteral nutrition secondary to poor gastrointestinal perfusion exist. The objective of this study was to 1) assess nutrition support given to critical patients post-VAD placement, and 2) evaluate tolerability and outcomes in patients who received oral, enteral, or parenteral nutrition.
METHODS: A retrospective chart review assessed nutrition support given in the acute phase defined as post-operative days 1-8 following VAD placement. A VAD registry was used to identify patients who received a VAD between 1992 and 2004. Data collection included: type of nutrition support, ventilator days, days with renal failure, days with hyperglycemia, hospital length of stay (LOS), and intensive care unit (ICU) LOS.
RESULTS: Thirty-seven patients receiving a VAD were identified; 21 patients received an oral diet, 9 patients received enteral nutrition (EN), and 7 received parenteral nutrition (PN). No statistical differences in patient demographics were observed. Outcome data are reported in Table 1. The average ICU LOS and hospital LOS was shorter in the enteral group than the parenteral group; however, this was not statistically significant.

Days	Oral (N =21)	EN (N = 9)	PN (N= 7)	p value
Ventilator support	2.2 (±1.2)	6.0 (±2.1)	4.1 (±2.4)	<0.05
Hyperglycemia (BG > 120mg/dL)	3.9 (±2.5)	4.7 (±2.7)	3.4 (±2.2)	0.21
Renal failure (Scr > 2mg/dL)	0.8 (±2.0)	0.2 (±0.7)	1.1 (±3.0)	0.51
Elevated total bilirubin (TB > 2mg/dL)	2.6 (±3.4)	3.9 (±3.6)	6.6 (±3.0)	<0.01
Hospital LOS	103.5 (±63)	87.3 (±44)	123.6 (±53)	0.06I
CU LOS	24.2 (±23)	39.8 (±26)	41.0 (±16)	0.23

CONCLUSION: Patients post-VAD placement were able to tolerate enteral nutrition either orally or via tube feedings. VAD patients are critically ill patients post placement; however, parenteral nutrition is not warranted due to poor gastrointestinal perfusion.

509. Evaluation of methods to lower aluminum loads in neonatal parenteral nutrition solutions. *Chris Amaya, Pharm.D.*, Luvy Amaya, Pharm.D., Brent Fox, Pharm.D.; Texas Health Resources, Fort Worth, TX.

Aluminum, a contaminant from the manufacturing process in intravenous parenteral solutions, is known to accumulate in adults and neonates who have received parenteral nutrition, particularly in those who have impaired renal function or exposed to large aluminum loads. Therefore, we looked at different methods to lower the aluminum content in neonatal TPNs. This was a retrospective, randomized, single-center study. Ninety patients were randomized to each group, and categorized according to weight (≤1 kg, >1 kg–<2 kg, ≥2 kg; mean ± SD, 0.66 ± 0.13, 1.39 ± 0.21, 2.55 ± 0.48). Within these categories, patient's baseline TPN aluminum load, TPN aluminum load calculated after changing manufacturers, and TPN aluminum load calculated after changing manufacturers and revising the compounding process were recorded and reviewed. There was a significant decrease in baseline aluminum loads (µg/kg/24 hrs) per group (baseline mean ± SD, 101.09 ± 12.6, 101.56 ± 9.32, 100.97 ± 20.47) compared to aluminum loads after changing manufacturers (mean ± SD, 43.17 ± 4.04, p<0.001, 43.36 ± 2.91, p<0.001, 43.13 ± 7.19, p<0.001). A significant decrease was also seen between baseline aluminum loads and after changing manufacturers and prioritizing salts in µg/kg/24 hrs (mean ± SD, 21.89 ± 3.10, p<0.001, 39.36 ± 1.92, p<0.001, 38.36 ± 5.87, p<0.001). The TPN aluminum concentrations were decreased by an average of 79% for patients ≤1 kg; 61% for patients >1-<2 kg; and 62% for patients ≥2 kg.

510. Pharmacokinetic assessment of "dose-banded" cancer chemotherapy. *Sabine A. Kaestner, M.Med.*[1], Valerie A. Walker, M.Sc.[2], Tim J. Perren, M.D.[2], Graham J. Sewell, Ph.D.[3]; (1)University of Bath, Bath, United Kingdom; (2)Medical Oncology Unit, St. James's University Hospital, Leeds, United Kingdom; (3)Kingston University, Kingston-upon-Thames, United Kingdom.

PURPOSE: In "dose-banding" (DB), individually calculated cancer chemotherapy doses, based on body surface area (BSA), are fitted to dose-ranges or "bands," and the mid-point of each band is a pre-determined standard dose provided by one or more pre-filled syringes. Although DB facilitates improved quality control of infusions, and reduced out-patient waiting times, it must be justified in terms of efficacy and safety. This study compares pharmacokinetic (PK) measures obtained with DB and individualised doses of 5-fluorouracil (5-FU) as surrogates of normal- and tumour-tissue drug exposure.
METHODS: PK-variability (AUC, C_{max}) and dose-deviations for 5-FU were studied following DB and individualised dosing of 5-FU in breast cancer patients (n=13) receiving adjuvant chemotherapy in a prospective, open-label, cross-over study (patient consent and ethics approval obtained). 5-FU was presented in alternate cycles as either banded or individualised doses, matching clock-time of 5-FU-administration to avoid circadian-dependent PK. Plasma 5-FU-concentrations, from blood-samples withdrawn pre-dosing and at six time-points over 90 minutes post-dosing, were obtained with a validated HPLC-assay, and PK-modelling was performed using WinNonlin.
RESULTS: Inter-individual variability in 5-FU AUC-values, as evaluated by the coefficient of variation (standard deviation (SD)/mean), was 33% following individualised dosing and 29% following DB. The deviation (mean ± SD) from the BSA-calculated dose introduced by DB was 1.2 ± 1.3%, which compared favourably to the 1.1 ± 1.4% deviation resulting from the conventional practice of rounding individualised doses to a convenient dose volume.
CONCLUSION: This study indicates that DB does not increase variability in 5-FU tissue exposure, as represented by PK-measures. Additionally, DB did not introduce deviations from BSA-calculated doses that were any greater than those caused by arbitrary dose-rounding in current clinical practice. Data-sets from a statistically significant sample size will be presented to inform the practice of DB, which is widely used for out-patient chemotherapy in the UK.

511. Determination of in vitro growth inhibition by novel farnesyl diphosphate analogues. *Rebecca R. Gallt, Student*, Cynthia A. Mattingly, B.S.,

David L. DeRemer, Pharm.D., Val R. Adams, Pharm.D. BCOP FCCP; University of Kentucky College of Pharmacy, Lexington, KY.

BACKGROUND: Mutation of the ras gene is found in approximately 30% of human cancers and is associated with disregulated tumor growth. Ras is a monomeric GTPase associated with the plasma membrane and cycles between an inactive GDP and active GTP bound state which can initiate various cell signaling pathways. In order for ras to become functional, posttranslational modification must occur by farnesyltransferase or geranylgeranyltransferase (GGTase I or II). Currently, farnesyltransferase inhibitors (FTIs) are being evaluated in clinical trials with limited efficacy. Investigators at our institution have created novel farnesyl analogues that are incorporated into ras, and presumably prevent it from being active. We hypothesize that these novel compounds are active against lung cancer and breast cancer.
PURPOSE: To determine the in vitro drug sensitivity of two NSCLC cell lines and one breast cancer cell line to treatment with novel farnesyl diphosphate analogues and to determine phosphorylation of mitogen-activated protein kinase (MAPK).
METHODS: NCI H460, MCF-7, and A549 cells were exposed to novel farnesyl diphosphate analogues. Cellular effects were determined via SRB assay and the T/C%, GI50, TGI, and LC50 were calculated. All cell lines were treated for various times with an active compound to determine the phosphorylation of MAP kinase via Western blot analysis.
RESULTS: According to criteria established by the NCI-Developmental Therapeutics Program, 11/38 compounds screened are active. MAPK phosphorylation was inhibited in A549 cells, but appeared to be upregulated in MCF-7 and H460 cells. Complete data to be presented at meeting.

512. A pharmacokinetic (PK) study of oral CC-5013, a novel thalidomide analogue, in patients with refractory metastatic cancer. *Tanyifor Tohnya, PharmD*[1], Alex Sparreboom, PhD[1], Jurgen Venitz, MD, PhD[2], Catherine Parker, BSN[1], William L Dahut, MD[1], William D. Figg, PharmD[1]; (1)National Cancer Intitute/National Institutes of Health, Bethesda, MD; (2)VCU Medical College of Virginia, Richmond, VA.

PURPOSE: The clinical activity of thalidomide in malignant tumors is due, at least in part, to its antiangiogenic and immunomodulatory properties. CC-5013, a more potent and less toxic analogue of thalidomide is investigated in this clinical trial. This is a phase I study, which seeks to characterize safety, pharmacokinetics and anticancer activity of CC-5013.
METHODS: Eligible patients diagnosed with refractory solid tumors received escalating doses (5-20 mg) of CC-5013 according to a modified Fibonacci scheme. CC-5013 is administered as oral capsules once daily at least 2 hrs prior to or 2 hrs after any meals and patients are treated for 28 days per cycle. In the absence of dose limiting toxicities (DLTs) or significant clinical deterioration patients were treated for another 28 days.
RESULTS: PK profiles are available for 13 patients. Maximum tolerated dose (MTD) was determined to be 10 mg per day. DLTs were observed in 2 patients at the 20 mg dose level. The DLTs included grade 3 non-hematological toxicities i.e. deep vein thromboses and hypotension. A sensitive and selective LC/MS method with limit of quantitation (LOQ) of 5 ng/mL was used for analysis. There was considerable PK inter-patient variability. In the dose range studied there were no statistical differences observed between the different dose levels for either apparent clearance values (P = 0.47) or the apparent volume of distribution (Vz) values (P = 0.23). Dose-normalized AUC(0-inf), dose-normalized peak concentrations (C_{max}), or half-life (t1/2) did not vary between the different dose levels (P > 0.12).
CONCLUSIONS: CC-5013 exhibits rapid oral absorption, the data suggest CC-5013 is not highly bound to plasma proteins. A change from daily dosing for 28 days per cycle, to daily dosing for 21 days then 7 days off drug improved patients' tolerance to CC-5013 hence further study of CC-5013 is warranted.

513. A clinical pathway to monitor and treat dyslipidemia in the allogeneic stem cell transplant setting. *Anne McDonnell, Pharm.D.*, Kristi Lenz, Pharm.D; Medical University of South Carolina, Charleston, SC.

PURPOSE: Dyslipidemias can be an adverse effect of certain immunosuppressants. The purpose of this project is to design and assess the efficacy of a clinical pathway for the management of dyslipidemias in the allogeneic stem cell transplant (allo-SCT) setting in patients on immune suppression with cyclosporine.
METHODS: A retrospective analysis was performed of allo-SCT patients over a three-month period at our institution to determine monitoring practices. It was determined that only one of five living allo-SCT patients over a 3-month period had baseline monitoring for dyslipidemias. Next, UHC hospitals with SCT programs were polled regarding their practices in monitoring and managing lipids and triglycerides in their allo-SCT patients. Of the responders, no program had a standardized method to monitor and to treat dyslipidemias. Using the ATP III guidelines, we developed a guideline to monitor fasting lipid panels in allo-SCT patients. A clinical pathway was developed to help guide clinicians in monitoring and treating dyslipidemias in this setting. Transplant coordinators and clinicians were educated about the clinical pathway. Data collection occurred in all allo-SCT patients over a period of three months to assess if the clinical pathway was useful.
RESULTS: Since implementation in the allo-SCT transplant setting, monitoring has been compliant with pre-transplant and week-one lipid panels. Of these patients, two of three patients required medication for elevated triglycerides at baseline and were treated. Data collection is ongoing.
CONCLUSION: A clinical pathway for the monitoring and treatment of triglycerides and cholesterol maybe an effective tool for clinicians in the management of patients. To date, our program has been successful in maintaining compliance and monitoring patients. The efficacy and statistical significance will be further elucidated as more patients are accrued.

514. The correlation between newborn with respiratory distress syndrome and patent ductus arteriosus with indomethacin therapy thereafter. *Fangting Chen, master*, Chingling Tai, master, Zon-Min Lee, master, Ping-Yu Lee, master; Chang Gung Memorial Hospital, Kaohsiung County, Taiwan.

PURPOSES: Patent ductus arteriosus (PDA) is a common problem in very premature neonates, resulting in a significant left-to-right shunt and an increase in left ventricular output.1,2 PDA is also a common complication in neonates ventilated for respiratory distress syndrome (RDS), 3; however, there was little published literature describing the correlation between Chinese neonates born with or without RDS and PDA with indomethacin theapy thereafter.
METHODS: In total 540 neonates admitted to our neonatal intensive care unit (NICU) from Jul. 1, 2002 through Mar. 31, 2004 have been enrolled in this study. The gestational age (GA) ranges from 23 to 42 weeks. Birth date, gestational age, RDS or not, X ray image, finding of cardiac sonography, indomethacin use or not, and the starting day of using indomethacin were all recorded.
RESULTS: Twenty-nine (5.37%) of 540 included neonates received indomethacin. Eight (12.31%) of the 65 neonates with RDS received indomethacin, and 21 (4.42%) of the 475 neonates without RDS received indomethacin thereafter. Neonates born with RDS seemed to have higher probability of developing PDA, which prompts the use of indomethacin. However, in the group of 252 prematures with GA≤34 weeks, 7 (11.67%) of the 60 neonates with RDS received indomethacin, and 21 (10.94%) of the 192 neonates without RDS received indomethacin therafter. The difference (p=0.875) was not significant.
CONCLUSION: The occurrence rate of PDA with indomethacin therapy in prematurity with GA≤34 weeks (11.11%) was higher than that (0.35%) of neonates with GA>34 weeks. However, there was no correlation between RDS and PDA with indomethacin therapy thereafter in the prematurity with GA≤34 weeks.

515. Incidence and prevalence of Redman's syndrome in pediatric patients receiving vancomycin. *Elizabeth A. Farrington, Pharm.D.*, Sara J.D. Bork, Pharm.D.; University of North Carolina, Durham, NC.

PURPOSE: Pediatric drug reference texts recommend that vancomycin be administered over one hour. These administration guidelines for pediatric patients are extrapolated from administration guidelines for adult patients. In adults, the rate of infusion is slowed with increased dose, (i.e. 1 gm administered over one hour, 1.5 gm over one and a half hours). In pediatrics, there is no known dose/kg identified at which the rate of infusion should be slowed. There is limited published information on the recommended rate of infusion of vancomycin, as well as limited data on the incidence and prevalence of redman's syndrome in pediatric patients. The primary goal of the pilot study was to establish incidence and prevalence of redman's syndrome in pediatric patients receiving intravenous vancomycin. In addition, this study evaluated weight-based rates of infusion in the pediatric population and their correlation, if any, to the presentation of redman's syndrome.
METHODS: A six-month, retrospective pilot study was conducted to determine incidence and prevalence of redman's syndrome in pediatric patients, age 0-18 years old, who received intravenous vancomycin while inpatient at North Carolina Children's Hospital. The study population was divided into three groups, those with redman's syndrome, those with a history of redman's syndrome and those without.
RESULTS: The incidence and prevalence of redman's syndrome were 8.6% and 26.9% respectively. The Pierson correlation coefficient between weight-based rate of infusion and the presentation of redman's syndrome was 0.29. There was a trend towards a significant increase in the incidence of redman's syndrome in patients who received infusion rates greater than 20 mg/kg/hr, however the number of patients was small (n=3).
CONCLUSIONS: A prospective study will be conducted in all patients receiving infusion rates > 20 mg/kg/hr to evaluate the relationship between infusion rate in mg/kg/hr and the development of redman's syndrome in a larger number of patients.

516. Comparison of intervention strategies in promoting parenteral-oral drug switching for hospitalized patients. *Roungtiva Muenpa, Graduate, student*[1], Chulaporn Limwattananon, Ph., D[1], Supon Limwattananon, Ph., D[1], Viroj Tangcharoensathien, Ph.D[2], Panpit Suwangool, MD.[3], Jon C. Schommer, Ph.D[4]; (1)Faculty of Pharmaceutical Sciences, Khon Kaen University, Khon Kaen, Thailand; (2)International Health Policy Program, Nonthaburi, Thailand; (3)Department of internal medicine, Bangkok, Thailand; (4)Department of Pharmaceutical Care and Health Systems, Minneapolis, MN.

PURPOSE: A quasi experiment was conducted at Lampang Hospital, Thailand during May 2003 to January 2005 to compare the effectiveness of the pharmacist interventions between using the problematic case-based reminders and multifaceted group interventions in promoting parenteral-oral (IV-PO) drug switching for hospitalized patients.
METHODS: Medical charts were reviewed prospectively by a clinical pharmacist for two consecutive weeks in three phases for each intervention; phase I as a baseline period, phase II as short term effect period, and phase III as four months post intervention or long term effect period. Candidates for the switching were identified according to the guideline approved by experts and the P&T committee. Excess days and potentially avoidable costs were compared using generalized linear model.
RESULTS: The problematic case-based reminders were more effective than the multifaceted group interventions. The problematic case-based reminders could reduce (1) the incidence of switching candidates from 29.2% to 15.2% ($p<0.001$), (2) excess days by 41.8% ($p<0.001$) and (3) potentially avoidable costs by 31.9% ($p=0.021$) whereas the multifaceted group interventions could reduce only the incidence of switching candidates from 25.7% to 19.7% ($p=0.001$). No statistically significant reducing of the studied outcomes was found in long-term effect of both interventions. Compared with the problematic case-based reminders, excess days and potentially avoidable costs of the multifaceted group interventions were higher by 81.5% ($p<0.001$) and 92.3% ($p<0.001$), respectively.
CONCLUSIONS: The problematic case-based reminders were the effective strategy in promoting IV-PO switching. It was a cost-saving program and should be applied in order to reduce health care costs.

517. Therapeutic and financial impact associated with the use of tiotropium in a Veterans Affairs medical center. *David A. Davis, PharmD*, E. M. Hampton, PharmD; Oklahoma City Veterans Affairs Medical Center, Oklahoma City, OK.

PURPOSE: This study was undertaken to determine the therapeutic and fiscal impact of adding tiotropium to the formulary for treatment of chronic obstructive pulmonary disease.
METHODS: The electronic medical records of all patients prescribed tiotropium who would complete 6 months of therapy prior to June 30, 2005 were evaluated. Respiratory medication use, admissions to the hospital, duration of stay, and emergency room visits for 6 month periods before and after the initiation of tiotropium were documented for all patients.
RESULTS: A total of 40 patients have met the inclusion criteria to date. Drug product costs rose slightly less (8%) than anticipated (15%) based on 100% compliance dispensing. Tiotropium use was associated with fewer hospital admissions (16 vs. 6, $p=0.02$) and respiratory related admissions (9 vs. 2, $p=0.03$). There was also a trend toward fewer hospital days (79 vs. 24, $p=0.05$). Based on institutional data, the estimated resulting cost avoidance exceeded $44,000. Rescue medication use, long acting fl-agonist use, and inhaled corticosteroid use were similar for both the pre- and post-tiotropium periods. The use of ipratropium, however was decreased due per protocol calling for its discontinuation. The net estimated cost avoidance to the system per patient was $2,000 per year.
CONCLUSION: The use of tiotropium in the Oklahoma City VA appeared to slightly increase drug costs. Patterns of other COPD medication use did not appear to change significantly. While drug costs increased in this patient population, those costs were offset by decreased hospital admissions and emergency room visits. It appears that use of tiotopium could decrease overall costs in our medical center. A future direction of this study would be inclusion of larger numbers of patients and lengthening of the pre- and post-tiotropium time periods to corroborate our preliminary findings.

518. The -344C/T promoter polymorphism of the aldosterone synthase gene (CYP11B2) is not associated with increased risk for morbidity and mortality in heart failure patients. *Mariellen J. Moore,* Maximilian T Lobmeyer, BS Pharm, Jaekyu Shin, PharmD, Yan Gong, PhD, Issam Zineh, PharmD, Taimour Y Langaee, PhD, Daniel F Pauly, MD; University of Florida, Gainesville, FL.

PURPOSE: The -344C/T promoter polymorphism (rs1799998) in the aldosterone synthase gene (CYP11B2) has been associated with hypertension and cardiac hypertrophy, but data are conflicting. Given the role of aldosterone in heart failure (HF), we tested, whether the CYP11B2 -344C/T variant is associated with risk for adverse outcomes (heart transplantation, death, or hospitalization due to HF exacerbation) in HF patients.
METHODS: HF patients from an outpatient clinic were enrolled and followed for adverse event (death, heart transplant, heart failure hospitalization) every 6 months for up to 4 years. Drug therapy was consistent with contemporary practice guidelines. Genotyping for the -344C/T variant was accomplished using polymerase chain reaction followed by Pyrosequencing. After adjustment for non-genetic predictors of HF adverse events, we used COX proportional hazard regression to model time to first adverse outcome with the -344C/T variant. Patients without adverse outcomes were censored at the last visit. The statistical analyses were performed using SAS (SAS Institute Inc, Cary, NC).
RESULTS: During a median 2.5 year follow-up period, 233 patients had complete clinical and genetic data. One hundred thirteen patients had a first adverse outcome. The frequencies of the -344C and -344T alleles were 39% and 61%, respectively. Higher New York Heart Association functional class was significantly associated with increased risk for the adverse outcomes (hazard ratio (HR) 1.83, 95% confidence interval (CI) 1.42–2.36), while higher left ventricular ejection fraction (HR 0.98, CI 0.96–0.99), and higher serum sodium level (HR 0.94, CI 0.88–0.99) at baseline significantly decreased the risk. The -344C/T variant was not associated with adverse outcomes (HR 1.166, CI 0.705–1.927, p-value = 0.55).
CONCLUSIONS: While we showed traditional predictors to be associated with outcomes in our HF population, we were unable to demonstrate any association of the aldosterone synthase (CYP11B2) -344C/T polymorphism with increased risk for adverse outcomes in HF.

519. Development of a predictive model for non-small cell lung cancer risk. *Kristine Hahn, PharmD*[1], Stevens Smith, PhD[2], Timothy Baker, PhD[3], Marilyn Larson, BA, CCRP[4], Anne Traynor, MD[4], Joan Schiller, MD[4], Jill M. Kolesar, PharmD[5]; (1)University of Wisconsin Comprehensive Cancer Center, Madison, WI; (2)University of Wisconsin Department of Medicine & Center for Tobacco Research and Intervention, Madison, WI; (3)University of Wisconsin Department of Psychology & Center for Tobacco Research and Intervention, Madison, WI; (4)University of Wisconsin Department of Medicine, Madison, WI; (5)University of Wisconsin School of Pharmacy, Madison, WI.

PURPOSE: We hypothesize that a collection of polymorphisms, currently known and unknown, predict genetic susceptibility to non-small cell lung cancer (NSCLC) development. This pilot study is designed to use 1) whole genome mapping to identify new polymorphisms associated with non-small cell lung cancer risk, and 2) genotype polymorphisms currently known to be associated with non-small cell lung cancer risk. These two components are necessary to develop a comprehensive NSCLC predictive model.
METHODS: This pilot case-control study involves obtaining a single blood sample from 24 former or current smokers with NSCLC, 24 former or current smokers, and 24 non-smoking volunteers for genotyping and gene mapping. Former or current smokers as well as non-smoking volunteers are matched to NSCLC subjects with respect to age, gender, ethnicity and smoking history. Affymetrix GeneChip Mapping Assay is used to genotype 10,204 single nucleotide polymorphisms (SNPs). An evaluation of known polymorphisms associated with NSCLC risk including CYP1A1, CYP2A6, CYP2A13, CYP3A4/5 and NQO1 will also be evaluated by pyrosequencing. Patterns of polymorphism from the three cohorts will be compared between the groups.
RESULTS: A total of 24 subjects with NSCLC, 1 subject who is a former or current smoker and 8 normal volunteers have been recruited. The Affymetrix assay has been used to successfully analyze two patient samples. The SNP call rate is 93.67% and signal detection average is 99.68%. Additional results are expected to be completed by October 2005 and will be described in the poster presentation.
CONCLUSION: Whole genome mapping is feasible in blood samples obtained from subjects with NSCLC by the Affymetrix GeneChip Mapping Assay.

520. Comparison of cyclosporine monitoring between two-hour (C2) levels and trough (C0) levels in pediatric liver transplant patients. *ChingLing Tai, master*, Fangting Chen, master, HsiuJung Hu, master, YawSen Chen, M.D., ChaoLong Chen, M.D.; Chang Gung Memorial Hospital, Kaohsiung County, Taiwan.

PURPOSE: To determine whether adoption of C2 or C0 monitoring in pediatric liver transplant patients would cause significant differences in renal, liver function, acute rejection, infection rate, adverse effects and drug dose achieving therapeutic level on post operation day (POD) 7, POD30 and POD 90.
METHODS: From January 2001 to December 2002, a total of 30 consecutive pediatric liver transplant recipients, who took Neoral®-base immuno-suppression with azathioprine or/Mycophenolate mofetil and steroid were evaluated. According to the timing of cyclosporine monitoring, patients were divided into C0 or C2 group. There were 15 patients in each group

respectively.
RESULTS: Baseline characteristics were similar, except the mean age at operation. Acute rejection rate was not significantly different between the two groups (C0: 3/15; C2: 2/15; P > 0.05). However, the incidence of moderate acute rejection was lower in C2 group (moderate in one, mild in the other) than in C0 group (moderate in all 3 patients). The renal function, liver function and adverse effects were not different between the two groups. The dose of cyclosporine achieving therapeutic level was significantly different in both groups on POD7 and POD 30. On POD 7, the mean dose of C2 group (39.55 mg/ kg/day) was significantly higher than C0 group (29.39 mg/kg/day) (P<0.05). However, on POD 30, the average dose of C2 group (12.9 mg/kg/day) was significantly lower in C0 group (17.38 mg/kg/day) (P<0.05). On POD 90, the mean dose of C0 (10.87mg/kg/day) and C2 (10.44 mg/kg/day) were not different (P>0.05).
CONCLUSIONS: There was no significant difference between C2 and C0 group in the acute rejection rate, renal function, liver function and incidence of adverse effects. On POD 7 the cyclosporine dosage was lower in C0 group. However, on POD 30, the dosage was lower in C2 group.

521. The population pharmacokinetics of digoxin in Taiwan study. *ChingLing Tai, master*[1], YingPing Hsing, master[1], PingYu Lee, master[1], HsiunLin Wen, master[1], Yung-Jin Lee, doctor[2], Yi-Hung Tsai, doctor[2]; (1)Chang Gung Memorial Hospital, Kaohsiung County, Taiwan; (2)Kaohsiung Medical University, Kaohsiung, Taiwan.

PURPOSE: The purpose of this study was to explore the relative and clinical factors by Data Mining that influenced digoxin therapeutic levels in Taiwanese. After these factors were identified, they would be used as covariates in digoxin population pharmacokinetic study and estimated the equation with retrospective cases. The risk factors will be an implement as the alarm system to assist physician for digoxin therapy.
METHODS: In this study, 181 single sampling data were collected retrospectively to be the data mining background. Patients' demographic data were recorded as well as digoxin serum levels, disease factors (such as congestive heart failure, arterial fibrillation, and sinus tachycardia), physiological status (renal and liver function), drug-drug interactions (calcium channel blocker, angiotensin conversing enzyme inhibitors, antacid, and diuretics), and other possible factors would also be included (such as sex, age, body weight, blood pressure, and electrolyte).
RESULTS: The final population pharmacokinetic equation for Digoxin clearance was CL=(0.111×CLcr+1.72×CHF+3.44×SEX)×(1.306), and the minimum value of objective function was 40.552.
CONCLUSION: The estimated values of population parameters may assist clinicians in the individualization of digoxin dosage regimens. The relationships among the pharmacokinetic parameters, the demographic data, and the patient-specific covariates were established in this study.

522. Validation of microdialysis and ultrafiltration sampling techniques for the pharmacokinetic study of phenytoin in man. *Curtis E. Haas, Pharm.D., FCCP, BCPS*[1], Jamie L. Nelsen, Pharm.D.[1], David C. Kaufman, MD[2], Alan Forrest, Pharm.D.[1]; (1)University at Buffalo, Buffalo, NY; (2)School of Medicine and Dentistry, University of Rochester Medical Center, Rochester, NY.

PURPOSE: To validate microdialysis (MD) and ultrafiltration (UF) as alternative, minimally invasive sampling techniques to characterize the pharmacokinetic (PK) parameters of phenytoin in man.
METHODS: This is a single-phase PK study with parallel sampling from the plasma, saliva and extracellular fluid of subcutaneous (SC) tissue of the anterior thigh using a MD probe (MD-2000, LM-10 Probe, BAS). We will enroll as many healthy volunteers as necessary to provide eight evaluable data sets. On day-1, Phenytoin MD drug recovery (DR) experiments using the delivery method were performed. On day-2, a 24-hour PK study was performed following an oral dose of phenytoin 500 mg. All MD experiments were run at a flow rate of 1 µL/min. Plasma and saliva ultrafiltrate were generated (Centrifree UF Device) for measurement of free drug. Phenytoin concentrations were assayed using an HPLC method. A complete compartmental PK analysis will be performed using weighted nonlinear regression analysis upon completed enrollment. Results presented here have been generated using non-compartmental analysis (WinNonlin, v. 4.1). Potential relationships between $AUC_{0\text{-last}}$ and % AUC between collection intervals for the MD and plasma samples are compared.
RESULTS: Eight subjects have been enrolled; six providing evaluable MD data sets, three providing evaluable saliva ultrafiltrate data sets. Mean dialysate DR was 54.0 + 7.6 % of plasma free drug concentration as determined by AUC0-last. This was consistent with % DR observed in the delivery experiments, 50.1 + 3.2 %. DR as measured by % AUC between collection intervals was consistent between all three matrices.
CONCLUSION: MD is a minimally invasive drug sampling strategy that appears to provide dialysate drug concentration data that correlates reasonably well with plasma free drug data. Saliva ultrafiltration appears promising and may be a simple and useful tool for certain drugs. Alternative sampling techniques may expand drug research in the ICU.

523. A pharmacokinetic (PK) model for nitroglycerin (GTN) in the presence of sumatriptan (SMT). *E. Shang, Ph.D.*, O. Okasanya, Pharm.D., A. Forrest, Pharm.D., Q. Ma, Ph.D., E Bednarczyk, Pharm.D.; University at Buffalo, University at Buffalo, Buffalo, NY.

BACKGROUND: The GTN headache model has been used for testing the effectiveness of anti-migraine therapy medications including the triptans. The PK of GTN in the presence of abortive or prophylactic anti-migraine therapies has never been reported. In this study, we measured serial GTN concentration before and after sumatriptan administration in Iverson's headache model.
METHODS: Seven healthy non-migaineur subjects received intravenous GTN at 0.125, 0.25 and 0.5 µg/kg/min in a stepped infusion at 15-minute intervals. Six mg of SQ SMT was administered while the GTN infusion rate was kept at 0.5µg/kg/min for additional 60 minutes. Arterial GTN concentrations were assayed by GC-EC. SMT concentrations were measured by reverse phase HPLC with fluorescence detection. PK parameters and a Hill-type biophase model of SMT interaction with steady state GTN clearance (CLss,gtn) were fit using maximum likelihood followed by MAP-Bayesian analysis (ADAPT II).
RESULTS: A two-compartment model with first-order absorption with a lag time was well fit for the PK of SMT. Estimated parameters values are within the range of published values (Fullerton et al. 1999). The mean (± SD) values of CLss, gtn prior to SMT was 40.3 ± 3.6 L/min. The maximum fractional increase (Emax) in CLss,gtn by SMT administration was 5.30 ± 2.86. The average concentration of SMT associated with 50% increase of Emax (EC_{50}) was 41.6 ± 7.20 µg/L. Estimated Hill's constant was 5.05 ± 1.68. The clearance of SMT between central compartment and the effect compartment was 0.00154 ± 0.00003 L/min.
CONCLUSIONS: Our findings suggest a significant PK interaction between SMT and GTN. Although the mechanism of such interaction is not clear, this finding strongly suggests that the pharmacodynamic effect of SMT upon GTN-induced headache may be the result of changes in GTN CLss,gtn by SMT rather than a direct effect. Further confirmation of these findings is underway.

524. Efficiency evaluation of hospital pharmacy services using data envelopment analysis. *Tananan Ratanachodpanich, MSC*[1], Supon Limwattananon, Ph.D.[1], Chulaporn Limwattananon, Ph.D.[1], Kitti Pitaknitinan, MSc[2]; (1)Faculty of Pharmaceutical Sciences, Khon Kaen University, Khon Kaen, Thailand; (2)Bureau of Health Service System Department, Ministry of Public Health, Nontaburi, Thailand.

PURPOSE: This study aimed to measure efficiency of hospital pharmacy services using Data Envelopment Analysis (DEA). Evaluation efficiency of pharmacy service will help to identify the inefficient unit and how to improve them to become an efficient unit.
METHODS: Technical efficiency evaluation of 155 district hospitals in Thailand was performed using DEA. Input orientation and variable return to scale (VRS) were assumed. Input variables were full-time equivalent (FTE) pharmacists, pharmacy technicians and supportive personnel. Output variables were number of prescriptions, expense of purchased drugs, inventory stock value, value of drugs supplied, number of patients receiving the pharmaceutical care, frequency of providing pharmacy education and surveillance on food safety.
RESULTS: Of 155 hospitals, 9.68%, 55.48%, 22.58%, 8.39% and 3.87% were 10, 30, 60, 90 and 120 bed-size hospital. Drug dispensing was the principal service (52% of FTE pharmacist) and approximately 9% to 15% of FTE pharmacist provided each other services; purchasing and inventory control, pharmaceutical care, health consumer protection, and others. There were 42 pharmacy services that were identified as efficient units across four specifications which consider all services (4, 22, 6, 6, and 4 units in 10, 30, 60, 90 and 120 bed-size hospital, respectively). Among four specifications, the number of efficient units ranged from 48 (30.97%) to 64 (40.65%) units. The average efficiency scores ranged from 0.80 to 0.86. There were 52% to 68% of pharmacy services that were identified as high efficient units (efficiency score 0.75-1.00). When measuring only the efficiency of drug dispensing service and pharmaceutical care, there were 21 pharmacy services that were identified as efficient units which 17 units were the efficient pharmacy services in overall efficiency dimension.
CONCLUSION: Approximately one third of pharmacy services were efficient units. Among the inefficient units, input reduction or increasing output should be concerned to become the efficient unit.

525. Results of a therapeutic interchange across the continuum of care. *Jeanna A. Miller, Pharm.D.*[1], Dianne B. Williams, Pharm.D., BCPS[1], J. Russell May, Pharm.D., FASHP[2]; (1)Medical College of Georgia Health System, Augusta, GA; (2)University of Georgia, Augusta, GA.

PURPOSE: A therapeutic interchange program across the continuum of care is

evaluated. The study is focused on the safety and efficacy of a therapeutic interchange program on hospitalized patients and attempts to determine if the interchanged medications are continued once the patient is discharged. The study also analyzes the financial impact to the institution as well as to the patient after discharge.
METHODS: A convenience sample of 100 newly admitted inpatients who received an interchange medication(s) was reviewed to evaluate the safety and efficacy of the interchange medication, and to determine if the therapeutic equivalent was continued or if the admission medication was resumed at discharge. The patient's community pharmacy was contacted to assess the financial impact to the patient by determining a change in their prescription price.
RESULTS: No adverse drug reactions, safety concerns and/or therapy failures were documented. Upon discharge, 61 patients were restarted on their home medications, 19 patients were not continued on either medication, 16 patients were continued on the therapeutic interchange medication and 4 patients were not applicable. Four patients continued on the interchange medication purchased the medication, but no additional expense was incurred. The cost savings for the institution for the first 3 months of the program is $25,410. A full analysis of the financial impact to the patient and the institution is in progress.
CONCLUSIONS: The therapeutic interchange program has shown a financial benefit to the institution while providing a safe and efficacious alternative medication to the patient. The majority of patients were restarted on their home medication at discharge.

526. Prazosin Therapy Safety Data (PTSD) trial: hemodynamic evaluation of prazosin in veterans with posttraumatic stress disorder nightmares–a retrospective chart review. *Mercedes Dombi, Pharm.D.*; Department of Veterans Affairs Medical Center, Portland, OR.

PURPOSE: The purpose of this retrospective electronic chart analysis was to determine whether veterans tolerated doses of prazosin needed to ameliorate posttraumatic stress disorder (PTSD) related nightmares determined by a mean change in blood pressure.
METHODS: Electronic medical records of 67 patients using prazosin for PTSD-related nightmares at the Portland Veteran Affairs Medical Center between January 2003 and December 2004 were reviewed. Patient demographics, hemodynamic parameters, and subjective evidence of improvement in nightmares were documented. Nearly half (45%) of the 122 possible patients were excluded due to a lack of documentation of hemodynamic parameters.
RESULTS: The mean change in systolic blood pressure was 12.92 mmHg ± 20.11 ($p<0.001$) and 5.29mmHg ± 15.60 ($p=0.007$) in diastolic blood pressure. This change was statistically significant in patients prescribed a mean dose of 4mg of prazosin. Main side effects experienced were dizziness (12%), syncope (9%), and hypotension (4%). Of the 39% of patients that experienced an adverse drug reaction only 20% discontinued prazosin due to an adverse reaction. Hypotension was not well reported as evidenced by a discontinuation due to greater than 20mmHg decrease in blood pressure of 60%. Overall 62% of patients had improvement in nightmare symptoms rated by the Clinical Global Impression of Change (CGI-C) scale. Prazosin was continued by 42% of patients one year after initiation of therapy.
CONCLUSION: Prazosin is tolerated by PTSD patients for the relief of nightmare symptoms. To support use of prazosin, qualitative/quantitative documentation of efficacy in nightmares is essential. In addition, improved documentation of hemodynamic parameters for evaluation of safety and tolerability is important when used in PTSD-related nightmares.

527. Drug-related admissions in renal transplant recipients. *Stefanie Harris, PharmD, Candidate*, Agnes Lo, PharmD, A Osama Gaber, MD; University of Tennessee, Memphis, TN.

PURPOSE: Renal transplant recipients may be at an increased risk of drug-related hospitalizations due to the complexity and toxicities of immuno-suppressive drug regimens, the need for numerous concurrent medications, and altered renal function. This study examines the incidence and reasons for readmissions in renal transplant recipients within 90 days after renal transplantation.
METHODS: The study population (n=66) consisted of all renal transplants performed between January 1, 2004 and December 31, 2004. Reasons for readmissions were classified by admission diagnosis as: drug-related, rejection, infection, surgical complications, and others. The relationship between drug-related toxicity and readmission was determined using the Naranjo algorithm. Risk factors associated with readmission were examined.
RESULTS: During the study period, 28/66 (42%) renal transplant recipients were readmitted within the first 90 days after initial discharge. A total of 42 readmissions occurred during this time period. The median time to readmission was 8 days (range 1 to 80 days) after initial discharge from the hospital. The admission diagnoses were: direct drug toxicity (19%), rejection (10%), surgical complications (29%), infection (13%), and others (29%). Using the Naranjo algorithm, 23/42 (54%) readmissions were possibly related and 7/42 (17%) were probably related to drug therapy. There were no differences in demographics, etiology of end stage renal disease, incidence of delayed graft function, and re-transplantation between renal transplant recipients who were readmitted and those who were not readmitted. The initial length of hospitalization was also similar between the groups.
CONCLUSIONS: Readmission following renal transplantation is common. Majority of these readmissions are related to drug therapy. Thus, future research is needed to determine if these drug-related readmissions can be prevented.

528. What's the plan B: patient and prescriber perceptions of emergency contraception. Lynn McCann, Pharm.D.Candidate, *Patricia Wigle, Pharm.D.*; University of Cincinnati College of Pharmacy, Cincinnati, OH.

PURPOSE: In April 2003, Barr Pharmaceuticals attempted to gain over-the-counter (OTC) approval for Plan B. The FDA ruled against the switch, claiming additional safety data in female patients < 16 years of age was required. No decision has been made regarding Barr Pharmaceuticals most recent submission. This study will determine what female patients > 16 years of age know and believe about emergency contraception. This data will help pharmacists better understand what some of the perceptions and misconceptions of this population may be if Plan B does gain OTC status. The knowledge of physicians will also be evaluated. Due to the current prescription status of the medication, it is important to understand how prescribers feel about emergency contraception and how their opinions may impact the patients under their care.
METHODS: Forty patients were approached for survey interviews. Patients who were > 18 years of age, pre-menopausal and female were included. Patients who did not fit the inclusion criteria, declined interview or presented with acute pain or psychiatric disorders were excluded. If a patient did not complete the interview for any reason, the survey was not counted in the final analysis. Eleven medical residents were given written surveys for completion.
RESULTS: The patients and prescribers evaluated whether they felt 8 different patient populations were appropriate candidates for emergency contraception. The percent deemed appropriate ranged from 64-93%. Notably, the range was 69-75% for the surveyed women who had children. The patient responses were consistent for the remainder of the questions. The prescriber responses varied depending on year in residency.
CONCLUSIONS: The patients and prescribers were similar in their views of who is an appropriate candidate for emergency contraception. As expected, prescribers were more knowledgeable of the potential failure rates for available contraceptives, as well as the administration and use of emergency contraceptives.

529. First year pharmacy student perception of emergency contraception. *Patricia Wigle, Pharm.D.*, Ray Jang, Ph.D., Lynn McCann, Pharm.D.; University of Cincinnati College of Pharmacy, Cincinnati, OH.

PURPOSE: Given the current ethical and moral controversy surrounding dispensing prescriptions for emergency contraception and the potential for these products to go over-the-counter, pharmacy students were surveyed about their opinions regarding Plan B.
METHODS: Eighty-one first year pharmacy students were given written surveys for completion during their Communications course. A one page description of emergency contraception was provided because the students had not had therapeutics courses at the time of the survey. Incomplete surveys were not included in the analysis.
RESULTS: Sixty-eight students were pharmacy interns. Thirty-three percent of the pharmacists they worked with, and 50% of the students, would dispense Plan B only under certain circumstances or would refuse to dispense it. Twelve percent believe Plan B should be available over-the-counter. Thirty-five percent of the students stated they would refuse to fill a prescription for Plan B even if it was in stock. Sixty-eight percent of the students believed patients < 18 years of age were not appropriate candidates for Plan B. Seven other patient populations were also evaluated by the students as appropriate or inappropriate candidates.
CONCLUSIONS: Opinions about emergency contraception varied among the first year pharmacy students. Male students and students with children tended to answer more conservatively.

RESEARCH INSTITUTE

The following papers, based on Fellowships and Research Awards provided by the ACCP Research Institute, will be presented. Full titles and authors are listed, although a complete abstract may not be available for all papers at the time of this printing.

532. ACCP Frontiers Research Award: Methodologic Lessons Learned in a Pilot Program to Improve Hypertension Control. Sean Hennessy, Pharm.D., Ph.D., *Charles E. Leonard, Pharm.D.*, Wei Yang, MS, Stephen E. Kimmel, MD,

MSCE, Raymond R. Townsend, MD, Alan. G. Wasserstein, MD, Thomas R. Ten Have, PhD, MPH, Warren B. Bilker, PhD; University of Pennsylvania, Philadelphia, PA.

PURPOSE: To measure the effectiveness of a multifaceted intervention in improving hypertension control.
METHODS: We performed a randomized trial in an academic health system using an ambulatory electronic medical record. We randomized physicians seeing at least 10 hypertensive patients to no intervention (N=54) or to a multifaceted, provider- and patient-directed intervention (N=39) consisting of academic detailing and mailing of educational materials to patients. The primary outcome was BP <140/90 mm Hg at the last visit during the six-month follow-up period, as recorded by medical staff in the course of clinical care.
RESULTS: Treated (N=5401) and untreated (N=5295) patients differed with respect to sex (54% vs. 60% female), percent black (40% vs. 48%), past diabetes (30% vs. 21%), and past kidney disease (11% vs. 8%). The p-values for these comparisons were <0.001. In the treated group, the proportion of patients with a BP <140/90 increased from 54% to 66%, and mean BP declined from 134/79 to 131/77. However, in the control group, the proportion of patients with a BP <140/90 also increased, from 53% to 62%, and mean BP declined from 136/80 to 133/77. The odds ratio for the association between treatment and achievement of a follow-up BP of <140/90, adjusting for baseline differences, was 1.13 (95% confidence interval [CI] not accounting for clustering: 1.02 to 1.26; accounting for clustering: 0.87 to 1.47).
CONCLUSIONS: At best, this intervention had a modest effect. Whether an effect of this magnitude would be worth the cost of an academic detailing program is unknown. In contrast, a pre-post comparison of the treated group provides a misleading picture of the intervention's effectiveness, underscoring the importance of including a concurrent control group and accounting for clustering by physician in such studies.

536. Kos Dyslipidemia Research Award: Impact of high-dose atorvastatin on C-reactive protein and IL-1 receptor antagonist concentrations in normocholesterolemic women. *Issam Zineh, PharmD*[1], Gregory J. Welder, .[1], Timothy R. Wessel, MD[2], Christopher B. Arant, MD[2], Richard S. Schofield, MD[2]; (1)Department of Pharmacy Practice, University of Florida College of Pharmacy, Gainesville, FL; (2)Division of Cardiovascular Medicine, University of Florida College of Medicine, Gainesville, FL.

PURPOSE: Cardiovascular disease (CVD) is the leading cause of death among women in the United States, yet women are under-represented in statin clinical trials. Furthermore, atherosclerosis can begin in the absence of overt dyslipidemia. Cytokines and other inflammatory molecules likely play a role. We investigated whether high-dose atorvastatin favorably shifts immune balance in women without dyslipidemia.
METHODS: Healthy women ≥ 18 years old with normal cholesterol and no CVD or risk equivalents were eligible. Use of lipid-lowering agents or regular anti-inflammatory drugs was not permitted. Eligible women received atorvastatin 80 mg daily. Baseline and 8 week fasting lipids, high sensitivity serum C-reactive protein (CRP, a marker/mediator of inflammation), and IL-1 receptor antagonist (IL-1ra, an inhibitor of the inflammatory effects of IL-1) concentrations were assessed. Analyses were by paired *t*-test with significance set at p<0.05.
RESULTS: Average age, BMI, total cholesterol, LDL, HDL, triglycerides, and blood pressure for the 10 women studied were 31 ± 12 years, 23 ± 4 kg/m^2, 186 ± 40 mg/dl, 93 ± 33 mg/dl, 74 ± 17 mg/dl, 99 ± 54 mg/dl, and 118/74 ± 10/14 mmHg, respectively. Median CRP concentrations decreased from 1.3 mg/L at baseline to 0.6 mg/L after 8 weeks of atorvastatin (p=0.067). IL-1ra concentrations increased from 456 pg/ml to 612 pg/ml (p=0.019).
CONCLUSIONS: High-dose atorvastatin significantly increased serum IL-1ra while decreasing CRP in normocholesterolemic women, thereby improving the balance of anti-inflammatory versus inflammatory mediators in the circulation. Our data offer insights into the immunomodulatory effects of statins. Furthermore, these data suggest statin treatment might benefit women even prior to development of overt CVD risk conditions such as dyslipidemia or hypertension.

537. TAP Pharmaceuticals Gastrointestinal Investigator Development Research Award: The effects of cephalexin on N-formulated peptide transport and intestinal hyperpermeability Caco-2 cells. *David R. Foster, Pharm.D.*, Xiaomei Zheng, M.S.; Purdue University, Department of Pharmacy Practice, Indianapolis, IN

531. ACCP Career Development Research Award: P-glycoprotein (pgp) and Renal Clearance (CLr) of Antibiotics in Cystic Fibrosis (CF). *Paul Beringer, Pharm.D.*, J. Krienghauykiat, Pharm.D., X. Zhang, M.S., L. Bi, M.D., S. Louie, Pharm.D., T. Synold, Pharm.D., M. Gill, Pharm.D., G. Burckart, Pharm.D., A. Rao, M.D., B. Shapiro, M.D.; University of Southern California (USC), Los Angeles, CA.

BACKGROUND: The pharmacokinetics of a number of antibiotics is altered in CF. Animal studies demonstrate that Pgp is upregulated in CFTR knockout mice. Dicloxacillin (DC) is a substrate for Pgp and the organic anion transporter (OAT). We hypothesize that renal tubular Pgp is upregulated in CF resulting in increased CLr of compounds which are Pgp substrates.
METHODS: 24 (n=12 CF, 12 healthy volunteers [HV]) subjects underwent a randomized crossover study of DC, DC+PB, and DC+CsA. CsA and PB are known inhibitors of Pgp and OAT transporters respectively. Iothalamate was given each day to measure glomerular filtration rate (GFR). Noncompartmental pharmacokinetic analysis was performed with blood and urine data obtained at specified times each study day. MDR1 genotype and mRNA expression in peripheral blood lymphocytes were also obtained.
RESULTS: Data on subjects: n=20 (9 CF, 11 HV). DC CLr (9.8 vs 6.9 L/h, p>0.05), GFR (6.9 vs 7.3 L/h, p>0.05), and MDR1 mRNA expression (8.4 vs 9.9, p>0.05) did not differ between CF and HV. However, intrasubject DC CLr was reduced in the presence of PB or CsA resulting in higher plasma levels of DC. The mean magnitude of decrease in DC CLr with PB was 76% (p <0.01) for both CF and HV, whereas with CsA there was a 9% decrease (p>0.05).
CONCLUSIONS: DC CLr appears to be more dependent upon glomerular filtration and tubular secretion mediated by OAT than on Pgp. A tend towards a higher CLr was noted in CF.

538. Watson Anemia Investigator Development Research Award: Comparison of oxidative stress markers in hemodialysis (HD) patients receiving iron dextran (ID), sodium ferric gluconate (SFG) and iron sucrose (IS). *Amy B. Pai, Pharm.D.*, Antonia Harford, M.D., Alex Boyd, B.S., Charles McQuade, Philip Zager, M.D.; University of New Mexico, Albuquerque, NM.

Intravenous iron supplementation in HD patients may enhance free iron and oxidative stress. This prospective, crossover study compared the appearance of non-transferrin bound iron (NTBI) and markers of oxidative stress after single IV doses of ID, SFG and IS.
METHODS: Twelve subjects were assigned to receive each intravenous iron product in random sequence with a 2 week washout between products. Serum samples for transferrin saturation (TSAT), NTBI, malondialdehyde (MDA) were obtained at baseline, 30, 60, 120,and 360 minutes after iron infusion. A serum sample for heme-oxygenase-1 (HO-1) RNA was obtained baseline and 360 minutes.
RESULTS: Mean ± SD NTBI values were significantly higher at 30 minutes after SFG and IS compared to ID (10.1 ± 7.6, 3.8 ± 3.0 and .23 ± 0.4 μM, respectively. p<0.001 SFG vs ID, p=0.002 IS vs ID) There was a significant positive correlation between TSAT and the presence of NTBI for SFG and IS (r^2=0.37 and 0.45, respectively p<0.001) but not for ID (r^2= 0.09 p=NS). After SFG administration, significantly more samples had increases in MDA from baseline (p=0.006). There was no apparent relationship between HO-1 RNA and NTBI. Increased MDA levels from baseline were associated with the presence of NTBI, baseline TSAT > 30%, transferrin < 180 mg/dL and ferritin > 500 ng/mL (P<0.05); however, only transferrin < 180 mg/dL was independently associated (OR 4.8 95% CI 1.2–15.3).
CONCLUSIONS: SFG and IS administration were associated with greater NTBI appearance compared to ID; however, only SFG had significant increases in markers of oxidative stress. The relationship between NTBI from IV iron and oxidative stress warrants further exploration.

530. ACCP-Ortho McNeil Infectious Diseases Fellowship: The effects of lopinavir/ritonavir on the renal clearance of tenofovir. *Jennifer J. Kiser, Pharm.D.*, Monica L. Carten, M.D., Peter L. Anderson, Pharm.D., Courtney V. Fletcher, Pharm.D., FCCP; University of Colorado Health Science Center, Denver, CO.

533. Amgen Biotechnology Investigator Development Research Award: T-cell responses to hepatitis B surface antigen in vaccinated lung transplant patients. *Mary S. Hayney, PharmD*[1], Frances L. Pelsue, B.S.[2], Renee M. Fohl, B.S.[1], Nicholas A. Wiegert, B.S.[1]; (1)University of Wisconsin, Madison, WI; (2)University of Minnesota, Minneapolis, MN.

PURPOSE: Patients with end-stage lung disease awaiting lung transplantation are candidates for hepatitis B vaccination, but they have low antibody responses to the vaccine series which wane quickly after transplant. The objective of this study was to compare the hepatitis B vaccine-induced T cell immune response to hepatitis B surface antigen (HBsAg) among patients awaiting lung transplantation, post-lung transplant patients, and healthy controls. We hypothesized that T cell immunity would be similar among the groups.
METHODS: Fifteen vaccinated healthy controls, 11 patients awaiting lung transplantation, and 11 post-transplant patients were enrolled. Human peripheral blood mononuclear cells (PBMC) were isolated for use in the trans vivo delayed type hypersensitivity (DTH) assay. PBMC alone and with antigen were injected into the footpads of immunodeficient mice causing swelling that is an index of T cell sensitization. We estimated that a difference of $7x10^{-4}$ inches would be a clinically significant difference, and the power to detect

this difference is greater than 90%.
RESULTS: The healthy control group is younger than the lung transplant patients. However, we found no difference in DTH swelling elicited by HBsAg or with tetanus toxoid used as a positive control.

	Healthy controls	Pre-transplant	Post-transplant	p-value
Age (years)	33.5 ± 2.4	50.9 ± 3.8	46.6 ± 3.6	0.001
HBsAg (x10^{-4} inches)	34.7 ± 4.3	31.9 ± 3.4	34.3 ± 4.3	0.878
TT (x10^{-4} inches)	15.7 ± 2.8	22.8 ± 6.5	23.1 ± 3.8	0.342

CONCLUSIONS: Patients awaiting lung transplantation and patients after lung transplant mount DTH responses to HBsAg that are similar to healthy controls. The role of T cell responses in protection from infection requires further study.

535. Bristol-Myers Squibb Central Nervous System Research Award: Evaluation of the cerebral hemodynamic effects of remifentanil in patients at risk for increased intracranial pressure. *Denise Rhoney, Pharm.D.*[1], Jeffrey Fong, Pharm.D.[2], Xi Liu, Pharm.D.[1], Dennis Parker, Jr., Pharm.D.[1], William M. Coplin, M.D.[1]; (1)Wayne State University, Detroit, MI; (2)Detroit Receiving Hospital, Detroit, MI.

534. AstraZeneca Psychiatry Investigator Development Research Award: 5HT2CR-759C/T Polymorphism and glucose control in the elderly receiving antipsychotics. *Vicki L. Ellingrod, Pharm.D.*, Jeffrey R. Bishop, Pharm.D., Jessica Moline, B.S., Susan K. Schultz, M.D.; University of Iowa College of Pharmacy, Iowa City, IA.