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ORIGINAL RESEARCH

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

ADR/Drug Interactions

1. Development of a computerized, mechanism-based drug interaction knowledge base for predicting drug interactions. *John R. Horn, Pharm.D., FCCP*, Richard Boyce, M.S., Carol Collins, M.D., Ira Kalet, Ph.D.; University of Washington, Seattle, WA.

PURPOSE: All available computerized drug interaction (DI) screening programs are based on simple look-up tables of drug pairs. They have been shown to miss up to 30% of interactions and to contain many frivolous or false-positive interactions that lead to alert fatigue. We have developed a pilot Drug Interaction Knowledge base (DIKB) that reasons with information about drugs using a semi-quantitative, rule-based, first-order logic that relies on pharmacokinetic and pharmacodynamic mechanisms to infer potential DIs.
METHODS: DIs can be modeled as a set of rules defining the pharmacokinetics and pharmacodynamics of the drugs. We constructed a curated drug database to support drug-interaction inference based on metabolic mechanisms for the effect of a precipitant drug on an object drug. For each drug (n=267) in the database, we entered assertions of its metabolic properties including pathway(s) of elimination, inhibition, and/or induction. The assertions are assigned levels of evidence (i.e., in vitro or in vivo data), and users can select what assertions will be included based on the level of evidence supporting the assertion. Application of the DIKB produced DI predictions including some that have not been published.
RESULTS: The results of our experiments suggest that a mechanism-based DIKB will require more complex knowledge representation than simply stated drug facts to realize its full potential benefits. We are in the process of building a qualitative model of DIs that will provide an estimate of the DI magnitude.
CONCLUSIONS: Unlike current drug interaction screening systems, our DIKB features an explicit model of the mechanisms by which two or more drugs may interact. A DI resource built with reasoning based on DI mechanisms enables clinicians to make decisions such as the potential for interactions with a newly approved drug or the possible effect of removing a chronically administered drug, without false alerts.

2. Defining rhabdomyolysis as an adverse drug event trigger for medication toxicity. *Joyce A. Jaojoco, Pharm.D.*[1], Paul Phillips, M.D.[2], Harminder Sikand, Pharm.D.[2]; (1)Cardinal Health, Scripps Mercy Hospital, San Diego, CA; (2)Scripps Mercy Hospital, San Diego, CA.

PURPOSE: Rhabdomyolysis is a rare diagnosis and an important adverse drug event. Definition of rhabdomyolysis differs in "metabolic" and "statin literature." This study was done to determine what creatinine kinase (CK) level would trigger an investigation for an adverse drug event.
METHODS: A retrospective analysis of CK and its relationship to rhabdomyolysis was conducted. All patients admitted in a four-hospital system during a 1-month period were evaluated. A data filter was done to include patients with CK > 1,700 IU/L and categorized into 3 groups: CK > 1,700; > 5,000; and > 10,000. Patients were then analyzed to determine whether rhabdomyolysis occurred secondary to an adverse drug event (R-ADE).
RESULTS: Rhabdomyolysis was identified in 61 patients. Mean age was 56 years with 75% (45/61) males. R-ADE occurred in 29.5% (18/61) with an elevated CK > 1,700 IU/L. Most common medications include antidepressants (21%), and lipid lowering agents. R-ADE diagnosis was missed by the physician 50% (9/18) of the time. Decreased creatinine clearance did not correlate with peak CK (r^2=0.07). Rhabdomyolysis was not reported as an adverse drug event (ADE) during this time in the four hospitals. Screening by elevated CK alone increased ADE reporting by 180% during the 1 month investigation.
CONCLUSIONS: Rhabdomyolysis has multiple etiologies. Our data suggest that with the exclusion of diagnosed MI, neuroleptic malignant syndrome, sepsis, or trauma, a CK level > 1,700 IU/L may be indicative of R-ADE. There was no correlation between peak CK and renal dysfunction, suggesting that rhabdomyolysis should not be defined with the association of renal dysfunction. The exact CK to trigger an adverse drug event is still unknown.

3. Adverse effects with long-term clopidogrel use in children. *Amanda M. Howard-Thompson, Pharm.D.*, Kelley Lee, Pharm.D., BCPS, Kelly Bobo, Pharm.D., BCPS, Joel Lutterman, M.D.; LeBonheur Children's Medical Center and University of Tennessee, Memphis, TN.

PURPOSE: Minor bleeds have been reported in approximately 5% of adults receiving concomitant clopidogrel and aspirin therapy. Few reports have been published on safety in children. This retrospective chart review was conducted to assess the safety profile of clopidogrel with and without aspirin. Histamine receptor antagonist and proton pump inhibitor use was also observed.
METHODS: All pediatric inpatients receiving clopidogrel between November 2004 to March 2006 were assessed via a retrospective chart review. Data included: indication, dosing regimen, length of therapy, concomitant aspirin use, aspirin dose, serum creatinine, bleeding episodes (occult blood loss, hemoglobin, hematocrit, and platelets), number of blood transfusions, liver enzymes, age of patient, and weight of patient.
RESULTS: Twenty-five pediatric patients were reviewed. More than half of the patient population was less than 1 year old (mean: 4 years; age range 1 day–20 years) and 44% weighed less than 5 kg (mean: 19.9 kg + 24.1). Sixteen (64%) patients received 1 mg/kg/day (mean: 1.4 mg/kg/day + 1.04), and 20 (80%) received concomitant aspirin therapy. Length of therapy with clopidogrel ranged from 1 day to 1.25 years (mean: 3.8 + 3.6 months). Eight (32%) patients experienced a total of 15 total adverse bleeding events including blood in stool (n=1), hematuria (n=6), bloody emesis (n=2), and general bleeds (n=6). All of these patients were receiving concomitant aspirin therapy. No blood transfusions were associated with adverse bleeding episodes. All eight of these patients received a histamine receptor antagonist or proton pump inhibitor prior to their adverse bleeding event.
CONCLUSIONS: Pediatric patients receiving concomitant clopidogrel and aspirin may be at an increased risk of minor bleeding events compared with adults. Prophylaxis with histamine receptor antagonists and proton pump inhibitors did not appear to prevent adverse events.

Analgesia

4. Intra-articular continuous local anesthetic infusion provides better pain management than femoral block. *Rob W. Hutchison Jr., Pharm.D.*, Mark Raccasi, M.D.; Presbyterian Hospital of Dallas, Dallas, TX.

PURPOSE: To compare pain management outcomes with a continuous infusion of local anesthetic for femoral nerve block, a continuous infusion of local anesthetic for intra-articular infiltration, or no continuous infusion of local anesthetic in acute post-operative orthopedic patients receiving intravenous (IV) opioids.
METHODS: Consecutive case, retrospective study. Setting: Acute surgical, inpatient hospital facility. Patients: Ninety one patients who had a total knee replacement surgical procedure between April 2004 and August 2005 were included. They received intermittent opioids and either continuous infusion of local anesthetic as a femoral nerve block, continuous infusion of local anesthetic by intra-articular continuous infusion, or no continuous local anesthetic (control).
RESULTS: The control group had significantly higher pain scores in the post-anesthesia care unit (PACU) (p=0.002, median pain intensity 8 out of 10, severe pain) than either group receiving a continuous local anesthetic. Over the remainder of the hospital stay, the intra-articular infusion group had significantly better outcomes. They ambulated significantly further (p=0.04 on day 1; p=0.05 for total length of stay), and consumed less opioid on the day of surgery, on day 1, and during the total hospital days (p=0.002). The femoral block group ambulated significantly less distance on days 1 and 2, and had a higher rate of constipation (30%) than either the control or the intra-articular group (13.3% and 17.2% respectively).
CONCLUSIONS: The combination of continuous local infusion of anesthetic (either femoral nerve block or intra-articular) and intermittent opioids in total knee replacement procedures provides better pain management in the PACU than IV opioids alone. Over the remainder of the hospital stay, the intra-articular group had significantly better outcomes (further ambulation with physical therapy and less opioid-induced adverse reactions) than the control group or femoral nerve block group.

5E. Topical Xibrom™ 0.09% significantly reduced ocular pain following cataract surgery. Michael Seward, M.D.[1], David L. Cooke, M.D.[1], *Lisa R. Grillone, Ph.D.*[2], Rachel M. Sachs, B.S.[2]; (1)Great Lakes Eye Care, St. Joseph, MI; (2)ISTA Pharmaceuticals, Inc., Irvine, CA.

Presented at the Annual Meeting of the Association for Research in Vision and Ophthalmology, Fort Lauderdale, FL, April 30–May 4, 2006.

6. Expiration dating of Vitrase® 200 USP units/mL Lidocaine and Bupivacaine admixtures in compliance with USP chapter <797>. George A. Baklayan, M.S., Harold M. Patterson, B.S., Erin S. Collins, B.S., James A. Gow, M.D., Clara K. Song, Pharm.D., *Timothy R. McNamara, Pharm.D.*; ISTA Pharmaceuticals, Inc., Irvine, CA.

PURPOSE: To determine stability of Vitrase® (hyaluronidase injection) ovine 200 USP units/mL when ad-mixed with local anesthetics for ophthalmic surgery. United States Pharmacopeia (USP) Chapter <797>, "Pharmaceutical Compounding – Sterile Preparations," provides requirements for preparing and handling compounded sterile preparations to prevent microbial contamination and establish stability and expiration dating of ad-mixtures.
METHODS: Lidocaine and bupivacaine were tested according to USP. Admixture stability was demonstrated by compounding Vitrase with lidocaine and bupivacaine (1 mL of Vitrase, 2 mL of lidocaine, and 5 mL of bupivacaine) and storing refrigerated for 24 hours. The ad-mixed product was tested for bacteriostasis/fungistasis per the USP method. This test ensured that any sterility test results were valid. The chemical stability of the ad-mixture was evaluated by performing a hyaluronidase activity assay. Microbial risk was assessed by performing a sterility test on the refrigerated, aseptically prepared ad-mixed product.
RESULTS: The ad-mixed product showed no appreciable difference in hyaluronidase activity after 24 hours at refrigerated storage compared with a Vitrase control. There was no appreciable difference in the concentration of either lidocaine or bupivacaine after 24 hours. The sterility of the product that had been stored refrigerated for 24 hours was evaluated with the USP 14-day sterility test and remained sterile.
CONCLUSIONS: There were no appreciable differences in hyaluronidase activity, lidocaine or bupivacaine concentrations, or sterility when ad-mixed. This study provides data required to establish a 24-hour expiration date for Vitrase when ad-mixed with local anesthetics used in ophthalmic surgery and stored at refrigerated temperatures.

Cardiovascular

7E. Influence of NOS3 gene polymorphisms on cytokines and growth factors in the serum of healthy individuals. *Issam Zineh, Pharm.D.*[1], Timothy R. Wessel, M.D.[2], Christopher B. Arant, M.D.[2], Taimour Y. Langaee, Ph.D., MSPH[1], Richard S. Schofield, M.D.[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.

Presented at the XIV International Symposium on Atherosclerosis, Rome, Italy, June 18-22, 2006.

8. Amiodarone toxicity monitoring clinic compared with usual care outcomes. *Oleg Roussanov, M.D.*, Judith Hill, FNP, Katherine Henley, FNP, Nabil Jarmukli, M.D.; Salem VAMC, Salem, VA.

PURPOSE: Amiodarone is an effective Class III antiarrythmic for the treatment of ventricular and supraventricular arrythmias, but it has significant noncardiac side effects.
METHODS: A comparative analysis of amiodarone toxicity detection rates and outcomes was conducted between patients followed up in a specialized amiodarone toxicity monitoring clinic (ATC) in cardiology section and patients followed up in primary care clinics (PCC) at a Veterans Affairs Medical Center. NASPE amiodarone monitoring guidelines were distributed to all providers.
RESULTS: Eighty three and 66 patients receiving amiodarone for atrial (77%) or ventricular (23%) arrhythmias were prospectively followed by the ATC and PCC respectively. Baseline characteristics of age (73 ± 10 vs. 76 ± 8); predominant male gender (99%); and prevalence of coronary artery disease, diabetes, hypertension, hypothyroidism, chronic obstructive lung disease, and smoking were similar between both groups. There were more patients with congestive heart failure in the ATC group than in the PCC group (51% vs. 44%). No significant difference in amiodarone dose 185 ± 46mg vs. 189 ± 34 or duration of therapy was detected. Over the 3 years of follow-up, adverse effects of amiodarone therapy occurred in 50 percent of patients in both groups with similar proportion of hypothyroidism, hyperthyroidism, liver function tests derangement, pulmonary, and eye toxicity. Amiodarone was stopped due to serious adverse effects in 12 (14%) patients in ATC group vs. 4 (6%) in PCC group (p=0.001). Three-year mortality was 22% in ATC group vs. 27% in PCC group (p=0.03).
CONCLUSIONS: Amiodarone toxicity clinic monitoring resulted in higher drug discontinuation rate and improved clinical outcomes compared with usual care in primary care clinics.

9E. Quality of life improvements in patients achieving blood pressure (BP) goal with an olmesartan medoxomil-based treatment algorithm. *David Smith, M.D.*[1], Joel M. Neutel, M.D.[2], Tonous Silfani, Ph.D.[3], Michael Weber, M.D.[4]; (1)Memorial Research Medical Clinic, and Integrium LLC, Long Beach, CA; (2)Orange County Research Center, Tustin, CA; (3)Daiichi Sankyo, Inc., Parsippany, NJ; (4)State University of New York Downstate College of Medicine, Brooklyn, NY.

Presented at the Annual Meeting of the American Society of Hypertension, San Francisco, May 14-18, 2005.

10E. Time to achieve blood pressure (BP) goal with an olmesartan medoxomil-based treatment algorithm. *David Smith, M.D.*[1], Joel M. Neutel, M.D.[2], Tonous Silfani, Ph.D.[3], Michael Weber, M.D.[4]; (1)Memorial Research Medical Clinic and Integrium LLC, Long Beach, CA; (2)Orange County Research Center, Tustin, CA; (3)Daiichi Sankyo, Inc., Parsippany, NJ; (4)State University of New York Downstate College of Medicine, Brooklyn, NY.

Presented at the Annual Meeting of the American Society of Hypertension, New York, NY, May 16-19, 2006.

11E. Efficacy of treating stage 2 systolic hypertension with olmesartan medoxomil (OM) and OM/hydrochlorothiazide (HCT) in black and non-black patients. *Steven Chrysant, M.D.*[1], Joel M. Neutel, M.D.[2], Robert Dubiel, R.Ph.[3], Findlay Walker, M.D.[3], Joseph Izzo, M.D.[4]; (1)Oklahoma Cardiovascular and Hypertension Center and University of Oklahoma School of Medicine, Oklahoma City, OK; (2)Orange County Research Center, Tustin, CA; (3)Daiichi Sankyo, Inc., Parsippany, NJ; (4)State University of New York at Buffalo, Buffalo, NY.

Presented at the Annual Meeting of the American Society of Hypertension, San Francisco, CA, May 14-18, 2005.

12. Warfarin and tissue calcification: a new cause for caution? *Jennifer L. Donovan, Pharm.D.*[1], Peter Whittaker, Ph.D.[2]; (1)Massachusetts College of Pharmacy and Health Sciences, Worcester, MA; (2)University of Massachusetts Medical School, Worcester, MA.

PURPOSE: Recent studies suggest that warfarin-based anticoagulation therapy may be linked to cardiac valve calcification. We aimed to establish whether calcification of valves or other tissue occurs with warfarin and to examine whether such calcification was influenced by treatment duration, age, or gender.
METHODS: We performed a retrospective chart review of 100 patients: 50 long-term warfarin recipients and 50 untreated controls, matched for age, gender, and comorbidities. For inclusion, patients required recent echocardiograms, CT-scans, and X-rays. We determined a calcification score (CS) for each patient; 1 point per site was given for calcification reported in the aortic, mitral, or tricuspid valve, aorta, coronary and carotid arteries, peripheral vessels, kidney, lung, or other locations.
RESULTS: The groups were matched for the incidence of hypertension, diabetes, and coronary artery disease (p=NS); however, males were younger (64 ± 3 vs 73 ± 2 years; p=0.03). Most patients received warfarin for valve replacement (42%) or atrial fibrillation (36%), with a mean treatment duration of 99 ± 3 months. Our analysis revealed 5 primary results: (1) Warfarin-associated CS was increased in valves (p=0.01) and at each assessed site except the coronaries. (2) Total CS was higher with warfarin (2.7 ± 0.3) than with controls (1.8 ± 0.2; p=0.02). (3) CS correlated with warfarin treatment duration (p=0.03). (4) When all patients were assessed, CS correlated with age for both groups, but was always higher with warfarin (p=0.02 vs control; ANCOVA). (5) However, this effect was exclusively due to warfarin-induced calcification in males. Total CS was higher for warfarin-treated males (2.4 ± 0.4) versus controls (1.2 ± 0.2; p<0.01), irrespective of age (p<0.01; ANCOVA). In contrast, we found no differences between warfarin-treated and control females.
CONCLUSIONS: Long-term warfarin therapy was associated with significant increases in tissue calcification not only in valves, but also at other sites. For warfarin-treated patients, calcification correlated with treatment duration and age, and was most pronounced in males.

13. The use and outcomes of antifibrinolytic therapy in cardiothoracic surgery patients at 20 U.S. academic medical centers. *Karl A. Matuszewski, MS, Pharm.D.*[1], Robert Schoenhaus, Pharm.D.[2], Mary Ellen Bonk, Pharm.D.[1], James Lane, Pharm.D.[3], Michael Oinonen, Pharm.D., MPH[1]; (1)University HealthSystem Consortium, Oak Brook, IL; (2)UCSD Medical Center, San Diego, DE; (3)UCSD Medical Center, San Diego, CA.

PURPOSE: A recent observational study by Mangano et al found a significant association between the use of aprotinin (AP) in cardiothoracic surgery (CTS) patients and the increased risk of adverse renal, cardiovascular, and cerebrovascular events. Other antifibrinolytics (AF), aminocaproic acid (AA) and tranexamic acid (TA), did not show elevated risks. Our study examined

these findings using a larger, more recent dataset.
METHODS: This observational administrative database study of CTS patients discharged from 20 academic medical centers from October 2002 through September 2005 assessed the use of AA (9751 patients), AP (6855), or no AF agent (46,123) and select patient outcomes. Descriptive and inferential statistics for each comparison group are reported.
RESULTS: Only 17 patients from 4 hospitals received TA; therefore, this agent was excluded from further analysis. Use of AA and AP in CTS patients was 15.5% and 10.9%, respectively. Quarterly use analysis showed a slow decline in the use of AA, with a gradual increase in the use of AP. Variation by hospital using each option was considerable (range: 0% to 50%). Statistically significant differences ($p<0.001$) occurred between AA, AP, and control groups for mortality (2.6%, 5.2%, 3.9%, respectively), prevalence of acute renal failure (6.2%, 10.9%, 6.1%) and hemodialysis (2.8%, 6.4%, 2.6%). No cases of postoperative acute myocardial infarction occurred within the AA or AP groups.
CONCLUSIONS: While the use of AP has been increasing relative to AA, AF use in CTS cases has remained relatively stable over a 3-year period, at under 30%. While significant differences exist between groups for various outcomes, multivariable logistic regression analysis will be necessary to control for the contribution of any confounding variables.

14. Evaluation of the appropriateness of enoxaparin and unfractionated heparin dosing. *James M. Hollands, Pharm.D.*, Chrissi L. Glastetter, Pharm.D., Scott T. Micek, Pharm.D.; Barnes-Jewish Hospital, Saint Louis, MO.

PURPOSE: To evaluate how frequently patients receive appropriate anticoagulation when prescribed enoxaparin or unfractionated heparin (UFH).
METHODS: Medical, surgical, and critically ill patients who received enoxaparin or UFH as therapeutic anticoagulation for treatment of venous thromboembolism, pulmonary embolism, acute coronary syndrome, or atrial fibrillation were identified. Dose of enoxaparin was determined by the treating physician. UFH dosing was determined using the institution's weight-based nomogram. Assessing the appropriateness of the enoxaparin dose was based on actual body weight and renal function. Several assessments were performed for evaluating UFH therapy, including the time to achieve an activated partial thromboplastin time (PTT) in therapeutic range (60–94 seconds) and a PTT above 60 seconds. Percent of PTTs in the subtherapeutic, therapeutic, and supratherapeutic ranges were also assessed.
RESULTS: A total of 109 patients were assessed in this analysis: 56 in the enoxaparin group and 53 in the UFH group. Enoxaparin: Based on renal function and body weight, 86% of the first doses of enoxaparin were dosed appropriately (n=48). 89% of the total days of therapy in the enoxaparin group were dosed appropriately. UFH: 41% of the initial PTTs were therapeutic, and 40% were supratherapeutic. During the first 24 hours, 41% of the PTTs remained therapeutic, and 34% were supratherapeutic. Overall, only 48% of PTTs were therapeutic, and 28% were supratherapeutic.
CONCLUSIONS: Appropriate anticoagulation was achieved with enoxaparin in 89% of the days of therapy. Less than 50% of PTTs fell within the therapeutic range over the course of therapy for UFH. An additional 28% of PTTs were supratherapeutic, suggesting adequate anticoagulation but with a potential for increased adverse events. Patient age, weight, renal function, concomitant disease states, and other characteristics could affect a patient's response to UFH and should be studied. Enoxaparin may provide more consistency in delivering appropriate anticoagulation to a patient.

15. Statin therapy effective and better tolerated when administered every other day among patients with previous adverse effects. *James M. Backes, Pharm.D.*, Cheryl A. Gibson, Ph.D., Nathan E. Hanson, Pharm.D., Andrew D. Gons, Pharm.D., Janelle F. Ruisinger, Pharm.D., Patrick M. Moriarty, M.D.; University of Kansas Lipid, Atherosclerosis, Metabolic and LDL-Apheresis Center, Kansas City, KS.

PURPOSE: Although statins possess an excellent safety profile, approximately 10% of patients discontinue therapy due to an adverse effect. We sought to determine changes in the lipid profile [total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides, TC/HDL ratio and LDL/HDL ratio]; and occurrence of adverse effects when a statin is administered every other day (QODay) among patients with a previous statin intolerance.
METHODS: Medical records in a lipid-specialty clinic were reviewed for patients receiving statin QODay therapy secondary to a previous statin adverse effect. Documentation of medical history, demographic data, concomitant lipid-altering agents, lipid profiles immediately prior to statin QODay use and initial follow up while receiving statin QODay, and duration of QODay therapy, was collected. Patients were excluded if other substantial changes were made in their lipid-altering regimen.
RESULTS: Of 27 patients identified, 16 (59%) (11 female/5 male) tolerated the QODay regimen. The most common previous statin intolerances included myalgias (11; 69%) and increased liver function tests (2; 13%). Twelve (75%) patients received rosuvastatin (mean 4.8 mg QODay), 3 (19%) received atorvastatin (10 mg QODay), and 1 (6%) received pravastatin (10 mg QODay). Overall mean changes were noted for TC (223 vs 163 mg/dL ± 25.45; -27%; $p<0.001$), LDL-C (142 vs 86 mg/dL ± 21; -37%; $p<0.001$), HDL-C (55.75 vs 55.94 mg/dL ± 6.97; +0.3 %; NS), triglycerides (152 vs 129 mg/dL ± 34.65; -15%; $p<0.05$), TC/HDL (4.04 vs 3.01 ± 0.81; -25%; $p<0.001$) and LDL/HDL (2.8 vs 1.6 ± 0.57; -43%; $p<0.001$) from baseline to follow up (mean 3.9 months).
CONCLUSIONS: Statins administered q Day provide significant improvements in TC, LDL-C, triglycerides, and LDL/HDL and TC/HDL ratios and are tolerated in nearly 60% of individuals with a previous statin adverse effect. This dosing regimen provides an important option for statin-intolerant patients requiring substantial LDL-C reductions.

16E. Efficacy of treating stage 2 systolic hypertension with olmesartan medoxomil and olmesartan/hydrochlorothiazide in elderly patients and patients with isolated systolic hypertension. *Joseph Izzo, M.D.*[1], Tonous Silfani, Ph.D.[2], Robert Dubiel, Ph.D.[2], Findlay Walker, M.D.[2]; (1)State University of New York at Buffalo, Buffalo, NY; (2)Daiichi Sankyo, Inc., Parsippany, NJ.

Presented at the Annual Meeting of the American Society of Hypertension, San Francisco, May 14-18, 2005.

17E. Effects of β_2 genetic polymorphisms on β_2-mediated glucose production during beta-blocker titration in heart failure. *Orly Vardeny, Pharm.D.*[1], Kai I. Cheang, Pharm.D.[2], James Zebrack, M.D.[3], Mark A. Munger, Pharm.D., FCCP[4], Edward Michael Gilbert, M.D.[3]; (1)University of Wisconsin School of Pharmacy, Madison, WI; (2)Virginia Commonwealth University, Richmond, VA; (3)University of Utah, Salt Lake City, UT; (4)Department of Pharmacotherapy, University of Utah College of Pharmacy, Salt Lake City, UT.

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18. Evaluation of genetic and nongenetic predictors of MMP-8 serum concentrations in nondiabetic subjects without cardiovascular disease. *Christina L. Aquilante, Pharm.D.*[1], Amber L. Beitelshees, Pharm.D., M.P.H.[2], Issam Zineh, Pharm.D.[3]; (1)Department of Clinical Pharmacy, University of Colorado School of Pharmacy, Denver, CO; (2)Washington University School of Medicine, St. Louis, MO; (3)Department of Pharmacy Practice, University of Florida College of Pharmacy, Gainesville, FL.

PURPOSE: Matrix metalloproteinase-8 (MMP-8) has been implicated in the pathogenesis of cardiovascular disease (CVD). Two common polymorphisms, -799 C/T and -381 A/G, exist in the promoter of the MMP8 gene. We evaluated the relative contribution of genetic and nongenetic variables to serum MMP-8 concentrations in nondiabetic, CVD-free subjects.
METHODS: A blood sample was obtained from nondiabetic subjects ≥ 18 years of age without CVD. MMP8 genotypes were determined by PCR-pyrosequencing. Serum MMP-8 concentrations were assayed in duplicate by ELISA. Mann Whitney U tests were used to compare MMP-8 concentrations between genotype groups (wild-type versus variant carriers) and categorical variables. Spearman's correlations were used to analyze the relationship between MMP-8 concentrations and clinical variables. Stepwise linear regression was used to determine the joint effects of genetic and nongenetic factors on MMP-8 concentrations.
RESULTS: The study consisted of 100 subjects (mean age 37 ± 13 years; 67% women, 96% non-black), 40 of whom had the metabolic syndrome diagnosed by AHA/NHLBI criteria. The overall MMP8 -799T and -381G allele frequencies were 33.5% and 5.5%, respectively. MMP-8 concentrations were not significantly different between MMP8 genotype groups. However, MMP-8 concentrations were significantly higher in subjects with the metabolic syndrome compared with those without the metabolic syndrome (11.71 ng/mL vs. 6.81 ng/mL, $p<0.001$) and in current smokers compared with nonsmokers (13.51 ng/mL vs. 7.53 ng/nL, $p=0.001$). MMP-8 concentrations were significantly correlated with body mass index ($r=0.33$, $p=0.001$); triglyceride/HDL ratio ($r=0.27$, $p=0.006$); triglycerides ($r=0.26$, $p=0.009$); fasting plasma glucose ($r=0.23$, $p=0.02$); and age ($r=0.22$, $p=0.03$). In regression analysis, significant predictors of MMP-8 concentrations were presence of the metabolic syndrome and smoking ($p<0.001$ and $p=0.009$, respectively; $r^2=21.4\%$).
CONCLUSIONS: These data demonstrate that metabolic syndrome and smoking are associated with elevated serum MMP-8 concentrations. The studied MMP8 promoter polymorphisms were not related to MMP-8 concentrations.

19. Crossover comparison of fenofibrate 160 mg and fenofibrate 145 mg in dyslipidemic patients with cardiovascular disease. *Daniel Hilleman, Pharm.D.*[1], Stephanie Maciejewski, Pharm.D.[2]; (1)Creighton University Medical Center, Omaha, NE; (2)Creighton Cardiac Center, Omaha, NE.

PURPOSE: To compare lipid parameters during treatment with fenofibrate (FFB) 160 mg and 145 mg in a population of dyslipidemic patients with cardiovascular disease.
METHODS: A retrospective chart review was conducted in patients taking FFB 160 mg/day for a minimum of 6 months who were switched to FFB 145 mg/day for a minimum of 3 months. LDL, HDL, and TG levels determined prior to and after the switch were compared.
RESULTS: 130 patients were included in analyses. 68 (52%) patients were on FFB alone and 62 (48%) were on FFB plus a statin (FFB + ST). LDL on FFB 145 mg/day and FFB 145 mg/day + ST was significantly lower compared with LDL on FFB 160 mg/day (p=0.009) and FFB 160 mg/day + ST (p=0.002). TG on FFB 145 mg/day and FFB 145 mg/day + ST was significantly lower compared with TG on FFB 160 mg/day (p=0.001) and FFB 160 mg/day + ST (p<0.0001). HDL was not significantly different between the formulations with or without statin therapy. The percentage of patients with a > 5% improvement in LDL, HDL, and TG following the switch to FFB 145 mg/day was 39%, 12%, and 39%, respectively. The percentage of patients with a > 5% worsening in LDL, HDL, and TG was 12%, 12%, and 12%, respectively. The percentage of patients with a > 10% improvement in LDL, HDL, and TG following the switch to FFB 145 mg/day was 12%, 2%, and 25%, respectively. The percentage of patients with a > 10% worsening in LDL, HDL, and TG was 3%, 4%, and 6%, respectively.
CONCLUSIONS: FFB 145 mg/day formulation is associated with significant improvements in LDL and TG compared with 160 mg/day formulation. The mechanism of this improvement could not be determined from this study, but may be related to improved bioavailability.

20. Improved cardiovascular goal attainment following erectile dysfunction therapy — a retrospective review. *Alicia B. Forinash, Pharm.D., BCPS*[1], Mounir Shenouda, M.D.[2], Todd A. Armstrong, Pharm.D., BCPS[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: Erectile dysfunction (ED) is prevalent among men with hypertension, diabetes, and dyslipidemia. A recent study demonstrated improved adherence to antihypertensive and antidiabetic medication after initiating ED therapy. The purpose of this retrospective chart review was to determine whether cardiovascular (CV) goal attainment improved after starting phosphodiesterase-5 (PDE5) inhibitor therapy.
METHODS: Patients receiving ED therapy were identified using the medical group's electronic medical record (EMR). A two-sided HIPAA compliant data collection form was developed using TELEforms scan technology. Blood pressure (BP) and cholesterol values pre- and post-ED therapy were recorded from the patients' EMRs. In addition, CV risk factors and other demographic information were collected. Medication adherence data were not available. Following chart abstraction, forms were scanned into Microsoft Excel and then imported into SPSS (version 14) for analysis. NCEP ATP III LDL and JNC 7 BP targets were used to determine percent goal attainment. A 2-tailed paired t-test and a McNemar test were used for continuous and categorical data, respectively.
RESULTS: We evaluated 82 patients who had BP and cholesterol values pre- and post-ED therapy. The mean age of these men was 58.1 ± 10.1 years (range: 31–83 years). Mean LDL, systolic, and diastolic BP values significantly decreased from pre- to post-ED therapy (p<0.05), 107.9 to 97.9 mg/dL, 132.8 to 127.4 mm Hg, and 82.7 to 76.4 mm Hg, respectively. Likewise, there was a significant improvement (p<0.03) in LDL and BP goal attainment from pre- to post-ED therapy, 65% to 78% and 45% to 62%, respectively.
CONCLUSIONS: In this retrospective chart review, mean LDL and BP values, as well as CV goal attainment, were significantly improved following ED therapy. Further studies are needed to determine the impact of PDE5 inhibitor therapy on CV medication adherence and subsequent goal attainment.

21. Female sex, but not history of myocardial infarction, is associated with aspirin resistance in patients with stable coronary artery disease. *Steven P. Dunn, Pharm.D.*[1], Mike Dorsch, Pharm.D.[2], Jin Sun Lee, B.S.[3], Donald Lynch, B.S.[3], Jo E. Rodgers, Pharm.D.[4], Debbie Montague, Pharm.D.[5], Susan A. Smyth, M.D., Ph.D.[1]; (1)University of Kentucky Chandler Medical Center, Lexington, KY; (2) University of Michigan Hospitals and Health Centers, Ann Arbor, MI; (3)University of North Carolina School of Medicine, Chapel Hill, NC; (4)University of North Carolina School of Pharmacy, Chapel Hill, NC; (5)University of North Carolina Hospitals, Chapel Hill, NC.

PURPOSE: The purpose of this study was to evaluate whether biologic aspirin resistance would be more prevalent in patients with a history of acute myocardial infarction (AMI) while taking aspirin compared with patients with stable coronary artery disease (CAD).
METHODS: A case-control study was performed in adult patients with a history of CAD currently on daily aspirin taken within 48 hours of enrollment. Subjects were divided into case and control groups based on history of documented AMI on aspirin therapy. Patients were excluded if they had renal dysfunction (CrCl < 20 mL/min), had symptoms of AMI, or had received additional anti-platelet agents prior to enrollment. Aspirin resistance was assessed using the VerifyNow® Aspirin Assay. In addition, multivariate analyses were performed to assess independent predictors of aspirin resistance in this population.
RESULTS: Ninety-eight consecutive patients were enrolled. Baseline characteristics were similar between case and control groups, with the exception of age (p=0.0137). Eight of the 49 case patients (16.3%) and 6 of the 49 control patients (12.2%) were aspirin resistant (OR=1.397, 95% CI=0.447, 4.367, p=0.5655). Using multivariate analyses, female sex was the only independent predictor of aspirin resistance (OR=3.922, 95% CI=1.095, 14.044, p=0.0357) in the overall population. Six of the 14 aspirin-resistant patients receiving 81 mg daily of aspirin were placed on higher doses (325 mg daily) for 3 days, and all 6 were found to be aspirin responsive when re-tested.
CONCLUSIONS: Past history of AMI does not appear to be associated with biologic aspirin resistance. Females with coronary artery disease were more likely to be aspirin resistant than males. Additionally, biologic aspirin sensitivity may be improved by increased doses of aspirin.

22E. Longer duration of nesiritide infusion may be associated with worsening renal function. *Sheryl L. Chow, Pharm.D., BCPS*[1], Jessica T. Peng, Pharm.D.[1], Mark P. Okamoto, Pharm.D.[2], J. Thomas Heywood, M.D.[3]; (1)Western University of Health Sciences, College of Pharmacy and Centinela Freeman Regional Medical Center, Pomona, CA, Inglewood, CA; (2)Western University of Health Sciences, Pomona, CA; (3)Scripps Clinic, La Jolla, CA.

Presented at the Heart Failure Society of America, Seattle, WA, September 10-13, 2006.

23. Frequency and manifestations of drug interactions with amiodarone, dofetilide, or sotalol at academic heath centers. *Beatrice B. Wong, Pharm.D.*[1], Michael A. Crouch, Pharm.D.[1], Spencer E. Harpe, Pharm.D., Ph.D., M.P.H.[1], Michael J. Oinonen, Pharm.D., M.P.H.[2]; (1)Virginia Commonwealth University, Richmond, VA; (2)University HealthSystem Consortium, Oak Brook, IL.

PURPOSE: Drug-drug interactions (DDIs) can amplify the risk of adverse events with antiarrhythmic agents. This study documents the in-hospital frequency and manifestations of potential DDIs with amiodarone, dofetilide, or sotalol.
METHODS: This was a retrospective cohort analysis of the University HealthSystem Consortium Clinical Resource Manager (32 academic health centers). We included patients treated with amiodarone, dofetilide, or sotalol discharged between January 1, 2004, and March 30, 2005; patients at increased risk of sudden death were excluded. A potential DDI was defined as the concurrent administration of predetermined agents with amiodarone, dofetilide, or sotalol for greater than 24 hours. The frequency of potential DDIs was determined in the entire sample and then categorized by type of provider (cardiology vs. non-cardiology). The primary end point of the study was the incidence of in-hospital death or cardiac arrest among patients with and without a potential DDI.
RESULTS: We identified 31,314 patients receiving amiodarone (n=26,995), dofetilide (n=812) or sotalol (n=3,507). The frequency of potential DDIs with these agents was 18.3%, 2.2%, and 6.6%, respectively. In the entire sample, a higher frequency of potential DDIs occurred in those managed by non-cardiology providers (p<0.001). In the amiodarone group, the incidence of in-hospital death or cardiac arrest was higher in those with a potential DDI than in those without (17.6% vs. 14.4%; p<0.001). Length of hospital stay and total cost of care were also higher if a potential DDI was present with amiodarone. The sample sizes in the dofetilide and sotalol groups were insufficient to perform primary outcome analyses.
CONCLUSIONS: Potential DDIs were common in hospitalized patients treated with amiodarone, and their occurrence may increase in-hospital mortality or cardiac arrest. Ongoing analysis is examining whether specific factors or types of DDIs with amiodarone predispose patients to an adverse event.

24. Sequential use of aprotinin and epsilon-aminocaproic acid in patients undergoing cardiac surgery: prescribing frequency and impact on renal outcomes. *Brian J. Barnes, Pharm.D.*, Patricia A. Howard, Pharm.D., FCCP, BCPS (AQ CV), Dennis W. Grauer, Ph.D., Gregory F. Muehlebach, M.D., Jeffrey B. Kramer, M.D., Micheal E. Gorton, M.D., William A. Reed, M.D.; University of Kansas Medical Center, Kansas City, KS.

PURPOSE: A recent study (NEJM 2006;354:353-65) raised concerns about the safety of antifibrinolytic agents (AAs) following cardiothoracic surgery (CTS). Although the study identified 4.5% (226/5065) of patients who received more than one AA, these patients were excluded. Our objective was

to determine the frequency of sequential AA use and its impact on acute renal failure (ARF).
METHODS: We conducted a retrospective analysis of institution-specific data (2002-2005) obtained from the Society of Thoracic Surgeons national database and medication administration records. Use of epsilon-aminocaproic acid (EACA) or aprotinin in patients undergoing CTS was determined. Patients who received one agent as prophylaxis in the operating room (OR), but a different agent as treatment for postoperative bleeding, were considered to have received sequential AAs. A validated risk-index to predict post-CTS ARF was calculated for all patients. Categorical and continuous variables were compared using chi-squared tests and ANOVA, respectively.
RESULTS: Among 1700 patients, 1513 (89%) received only EACA and 41 (2.4%) received only aprotinin. However, 146 (8.6%) received sequential AAs. Preoperative risk for developing ARF was similar in patients receiving aprotinin or sequential AAs, but lower in the EACA group. ARF alone, and ARF requiring dialysis, occurred significantly ($p<0.001$) more often in the sequential AA group (15%/8%) compared with either the aprotinin (7%/2%) or EACA (5%/1%) groups.
CONCLUSIONS: Sequential use of EACA and aprotinin was associated with an increased risk of ARF. Establishing a system process to identify which AA was used intraoperatively will prevent sequential AA use in the ICU.

25E. On-treatment levels of HDL-C and the ratio of LDL-C/HDL-C as predictors of cardiovascular events in the Treating to New Targets (TNT) Study. *Philip Barter, M.D.*[1], Antonio Gotto, M.D., DPhil[2], John LaRosa, M.D.[3], Scott Grundy, M.D., Ph.D.[4], John J. Kastelein, M.D.[5], Vera Bittner, M.D.[6], Jean-Charles Fruchart, Pharm.D.[7]; (1)The Heart Institute, Camperdown, Australia; (2)Weill Medical College of Cornell University, New York, NY; (3)State University of New York Health Science Center, New York, NY; (4)University of Texas Southwestern Medical Center, Dallas, TX; (5)University of Amsterdam, Amsterdam, Netherlands; (6)University of Alabama, Birmingham, AL; (7)Institut Pasteur, Lille, France.

Presented at the Scientific Session of the American College of Cardiology, Atlanta, GA, March 11-14, 2006.

26. Aprotinin is not effective in cardiac surgery patients at low risk for blood transfusion. *Judith L. Kristeller, Pharm.D., BCPS*[1], Brian Roslund, Pharm.D., Candidate[1], Russell F. Stahl, M.D., FACS[2]; (1)Wilkes University, Wilkes-Barre, PA; (2)Community Medical Center, Scranton, PA.

PURPOSE: Aprotinin is commonly used to decrease transfusions in primary and repeat cardiac surgery patients. The purpose of this study is to determine if aprotinin reduces postoperative blood transfusions in cardiac surgery patients considered low risk for requiring blood transfusions.
METHODS: Using an electronic database of all cardiac surgery patients, we retrospectively identified a group of low-risk patients over 2 years from 1/04–12/06. Inclusion criteria used to classify patients as low risk were those undergoing non-emergent, primary CABG only, having a hemoglobin > 12 gm/dL, and not receiving clopidogrel or warfarin within 5 days preoperatively. Low-risk patients were divided into two groups, those who received aprotinin, and those who did not. During 2004, aprotinin was used only in patients considered high-risk for bleeding, but in 2005 use expanded to all patients. Statistical analysis includes the chi-square test for nominal variables and Student's T-test for continuous variables.
RESULTS: A total of 147 patients received aprotinin, and 142 patients served as the control group. Baseline characteristics were similar in the two groups. There was no difference in transfusion requirements between patients who received aprotinin and those who did not. The average donor exposure to any blood product in the aprotinin group was 1.3 units/patient compared with 1.2 units/patient in the non-aprotinin group ($p=0.77$). Postoperative infusion of PRBC was 0.86 units in the aprotinin patients compared with 0.8 units in the non-aprotinin patients ($p=0.8$). There was no difference in other outcomes, including renal insufficiency, MI, stroke, LOS, and mortality.
CONCLUSIONS: Although there is a significant amount of evidence that aprotinin decreases transfusions in primary and repeat cardiac surgery patients, we were not able to demonstrate that effect in this low-risk population. To our knowledge there are no studies evaluating the efficacy of aprotinin in the low-risk population described here.

27E. Combinations of torcetrapib with atorvastatin raise HDL-C, lower LDL-C, and are well tolerated: results from a phase 2 clinical trial. *Thomas Thuren, M.D., Ph.D.*[1], Amy Longcore, Ph.D.[2], Coralie Powell, Ph.D.[1], James Strand, Ph.D.[2], Kathryn Durham, Ph.D.[1], Charles Shear, Ph.D.[1]; (1)Pfizer Global Research and Development, New London, CT; (2)Pfizer Global Research and Development, Ann Arbor, MI.

Presented at the 78th Scientific Session of the American Heart Association, Dallas, TX, November 13-16, 2005.

28E. The benefits of intensive lipid lowering in patients with stable coronary heart disease and systolic blood pressure above or below 140 mm Hg: a post hoc analysis of the Treating to New Targets (TNT) study. *John B. Kostis, M.D.*[1], Andrei Breazna, Ph.D.[2], John LaRosa, M.D.[3]; (1)Robert Wood Johnson Medical School, New Brunswick, NJ; (2)Pfizer Inc, New York, NY; (3)State University of New York Health Science Center, New York, NY.

Published in J Clin Hypertens 2006;8(6):455.

29E. Effect of differential treatment adherence on outcome in the IDEAL trial. *Ingar Holme, Ph.D.*[1], Michael Szarek, M.S.[2], Terje Pedersen, M.D., Ph.D.[1]; (1)Ulleval University Hospital, Oslo, Norway; (2)Pfizer Human Health, New York.

Presented at the International Symposium on Atherosclerosis, Rome, Italy, June 18-22, 2006.

30E. Comparison of the efficacy of intensive atorvastatin versus standard simvastatin therapy in patients with acute coronary syndrome: the IDEAL Trial. *Terje Pedersen, M.D., Ph.D.*[1], Anders G. Olsson, M.D., Ph.D.[2], Nilo B. Cater, M.D.[3], Michael Szarek, M.S.[3], Mogens Lytken Larsen, M.D., D.M.Sc.[4], Matti J. Tikkanen, M.D., Ph.D.[5]; (1)Ulleval University Hospital, Oslo, Norway; (2)University Hospital Linkoping,, Linkoping, Sweden; (3)Pfizer Inc, New York, NY; (4)Arhus University Hospital, Arhus, Denmark; (5)Helsinki University Hospital, Helsinki, Finland.

Presented at the World Congress of Cardiology, Barcelona, Spain, September 2-6, 2006.

31. Impact of Omega-3 fatty acid (OFA-3) treatment on the arachidonic acid (AA)/eicosapentaenoic acid (EPA) Ratio in Healthy Volunteers and Patients with Coronary Artery Disease. *Stephanie Maciejewski, Pharm.D.*, Tammy Burns, Pharm.D., Katie M Speidel, Pharm.D., William R Hamiliton, Pharm.D., Daniel E Hilleman, Pharm.D.; Creighton Cardiac Center, Omaha, NE.

PURPOSE: To determine the AA/EPA ratio in healthy volunteers and patients with coronary artery disease (CAD) prior to and after treatment with 1.5 g/day and 3.0 g/day of OFA-3.
METHODS: Diet in volunteers and CAD was low in OFA-3 (< 2 serving/wk). Treatment included 1.5 g/day OFA-3 (OmegaPlex®, Advocare Inc) for 4 weeks followed by 3 g/day OFA-3 for an additional 4 weeks. Laboratory analysis included AA/EPA ratio, hs-CRP, and a lipid profile, at baseline and after treatment with each dose level of OFA-3.
RESULTS: 28 volunteers and 30 CAD completed the trial. Concomitant drug therapy in the patients with CAD included lipid lowering drugs in 27, antiplatelet agents in 27, and folic acid in 4. Baseline AA/EPA ratio in volunteers and CAD was 23.7 ± 12.5 and 39.6 ± 19.0, respectively. The AA/EPA ratio was significantly decreased with 1.5 g/day OFA-3 to 9.0 ± 4.2 and 10.3 ± 8.8, respectively. The AA/EPA ratio was further reduced with 3.0 g/day OFA-3 to 5.1 ± 3.2 and 4.9 ± 2.6, respectively. The hs-CRP, HDL, and LDL were not substantially affected with OFA-3 treatment. TGs were not reduced in CAD, but were significantly decreased in volunteers (baseline 137 mg/dl; 1.5 g/day 110 mg/dL; 3.0 g/day 93 mg/dL). Lack of effect in CAD may have been due to concomitant use of other lipid lowering drugs.
CONCLUSIONS: Baseline AA/EPA ratio in both volunteers and CAD were extremely elevated. OFA-3 treatment significantly reduced the AA/EPA ratio in both volunteers and CAD. OFA-3 had no effect on hs-CRP in either group. OFA-3 reduced TGs in volunteers but not CAD.

32. Carvedilol or metoprolol to prevent atrial fibrillation following cardiac surgery. *Gregory V. Abbott, Pharm.D.*, Jackie M. Roh, Pharm.D., BCPS, Edward B. Gerhardt, M.D., Bridget Harding, R.N.; Moses Cone Memorial Hospital, Greensboro, NC.
PURPOSE: The efficacy of beta-blockers in decreasing atrial fibrillation following cardiac surgery has been demonstrated in randomized trials. It is unknown, however, whether any one beta-blocker is more effective than another beta-blocker at preventing this arrhythmia. A retrospective study has suggested that carvedilol may be more effective than either metoprolol or atenolol. The purpose of this study was to compare the incidence of atrial fibrillation following cardiac surgery in patients receiving carvedilol versus those receiving metoprolol.
METHODS: Patients were randomized to receive open-label carvedilol 6.25 mg by mouth 2 times/day or metoprolol 12.5 mg by mouth 2 times/day beginning the morning of surgery. Dose titration was at the discretion of the cardiothoracic surgeon. The primary end point was the incidence of atrial fibrillation until hospital discharge. Secondary end points included hospital and intensive care unit length of stay, percentage of study drug given, and an evaluation of a recently published risk index.
RESULTS: Fifty-four patients completed the study. Postoperative atrial fibrillation occurred in 22.2% of patients in the carvedilol group and 29.6% of

patients in the metoprolol group (p=0.53). There was no difference in either hospital or intensive care unit lengths of stay, in rates of study drug administered, or in risk indices between the two groups. Risk index did correlate well to overall incidence of atrial fibrillation.
CONCLUSIONS: In this small study group of open-heart surgery patients, carvedilol was as safe and effective as metoprolol for the prevention of atrial fibrillation following cardiac surgery. Larger studies may need to be conducted to more clearly elucidate the role of carvedilol in the prevention of atrial fibrillation following cardiac surgery.

33E. Intensive lipid lowering with atorvastatin is associated with a significant improvement in renal function: the Treating to New Targets (TNT) Study. *James Shepherd, M.D.*[1], Nanette Wenger, M.D.[2]; (1)Royal Infirmary, Glasgow, United Kingdom; (2)Emory University School of Medicine, Atlanta, GA.

Presented at the Scientific Session of the American College of Cardiology, Atlanta, GA, March 11-14, 2006.

34. Can statin use impact atrial fibrillation occurrence and recurrence? A meta-analysis. *Aarti A. Patel, M.B.A., Pharm.D.*[1], C. Michael White, Pharm.D.[2], Jeffrey Kluger, M.D.[3], Craig I. Coleman, Pharm.D.[2]; (1)University of Connecticut School of Pharmacy, Storrs, CT and Hartford Hospital, Hartford CT, Hartford, CT; (2)University of Connecticut, Hartford, CT; (3)Hartford Hospital, Division of Cardiology, Hartford, CT.

PURPOSE: In addition to lowering cholesterol, statins reduce inflammation, which could invoke an anti-fibrillatory effect. Although several controlled and observational trials have suggested an association between statin use and a reduction in the incidence of onset, recurrent, paroxysmal and postoperative atrial fibrillation (AF), other studies have not shown an antifibrillatory effect. Because this is the case, we conducted a meta-analysis of existing relevant studies to determine the impact of statins on AF.
METHODS: Three investigators systematically searched databases (MEDLINE, Embase, Web of Science, Cochrane Database of Systematic Reviews) from 1966 to May 2006 and reviewed citations in relevant articles to identify studies that met the following inclusion criteria: randomized or adjusted observational trials, comparison of patients receiving or not receiving a statin, and reported data on the incidence of AF. A random-effects model was used.
RESULTS: Eleven trials reporting the results of 12 analyses were identified for inclusion into this meta-analysis. In total, 2,489 and 2,697 patients were included in the statin and control groups, respectively. Statin use significantly reduced the odds of developing [odds ratio; 0.56 (95% CI=0.44–0.72); Q statistic p=0.002]. Neither assessment of the funnel plot nor Egger's weighted regression statistic (p=0.02) could rule out the possibility of publication bias. In subgroup and sensitivity analyses, limiting studies to postoperative AF (n=3), recurrent AF (n=5), new-onset AF (n=4), published studies (n=6), and randomized control trials (n=5) did not affect overall conclusions nor did the use of a fixed-effects model (p<0.046 for all comparisons).
CONCLUSIONS: Use of statin therapy was associated with reduced odds of experiencing AF, thus providing additional evidence of a statin's benefit beyond its lipid-lowering activity.

35E. Vascular responses to hypercapnia in patients with obstructive sleep apnea. *John M. Dopp, Pharm.D.*, Kevin J. Reichmuth, M.D., Dominic S. Puleo, B.S., Don Hayes, M.D., James B. Skatrud, M.D., Barbara J. Morgan, Ph.D., PT; University of Wisconsin, Madison, WI.

Presented at the International Conference of the American Thoracic Society, San Diego, CA, May 19-24, 2006.

36. Lipid goal achievement in a private practice setting. *Terri W. Jerkins, M.D.*, Randy K Jerkins, Pharm.D.; Mid-State Endocrine Associate, Nashville, TN.

PURPOSE: HMG CoA reductase inhibitors ("statins") are often used at higher doses to achieve LDL goals in patients with diabetes. Simvastatin is one statin with evidence showing efficacy in lowering cardiovascular risk in diabetics, but can be associated with dose-related side effects at higher doses. New evidence supports the use of atorvastatin in the treatment of diabetic patients to reduce cardiovascular events, including stroke and myocardial infarction. We examined the efficacy of switching diabetic patients not at goal on standard dose simvastatin to atorvastatin.
METHODS: Diabetic or pre-diabetic patients with hyperlipidemia that had not reached goal (LDL < 100 mg/dL or < 70 mg/dL in patients with stroke, myocardial infarction, or stent placement) on their current simvastatin medication were switched to atorvastatin on a mg-to-mg dose exchange. Patients had random blood draws (not fasting) 1 month after the switch, and then 3–4 months after the change.
RESULTS: 67 patients on simvastatin (mean dose 40.5 mg) were switched to atorvastatin (mean dose 36.5 mg). Switching from simvastatin to atorvastatin resulted in a reduction of total cholesterol from a mean of 187.7 mg/dL to 163.5 mg/dL; triglycerides from a mean of 199.5 mg/dL to 155.4 mg/dL; LDL from a mean 95 mg/dL to 78.7 mg/dL. Switching from simvastatin to atorvastatin had no significant effect on HDL levels (mean 53.3 mg/dL on simvastatin to 52 mg/dL on atorvastatin). Overall, 82% of the patients that switched to atorvastatin reached the LDL goal. There were no adverse effects or abnormal laboratory values in any of the switched patients.
CONCLUSIONS: Many patients with diabetes treated with statins do not reach recommended LDL goal. Switching patients on chronic simvastatin therapy to atorvastatin therapy in a community-based setting resulted in significantly increased LDL goal attainment in this difficult to treat population.

37. Clinical outcomes in heart failure patients receiving continuous intravenous inotropic therapy. *LouAnn C. Branch, Pharm.D.*[1], Paul E. Nolan, Pharm.D.[1], Michael S. McCarthy, B.S.[2], Jack G. Copeland III, M.D.[3]; (1)University of Arizona College of Pharmacy, Department of Pharmacy Practice and Science, Tucson, AZ; (2)Transplant Services, University Medical Center, Tucson, AZ; (3)University of Arizona College of Medicine, Section of Cardiothoracic Surgery, Tucson, AZ.

PURPOSE: The purpose of this single-center study was to compare selected clinical outcomes of patients with advanced congestive heart failure (CHF) on a heart transplantation waiting list who were receiving continuous intravenous inotropic therapy (IVIT) to those not receiving IVIT.
METHODS: The complete study population consisted of 224 patients at least 18 years of age, who were entered into a cardiac transplant waiting list between January, 2000, and December, 2005. The patients were divided into 3 groups: Group 1 consisted of 42 patients initially listed as United Organ Network Sharing (UNOS) Class IA/IB, and who were receiving continuous IVIT. Group 2 consisted of 167 patients initially listed as UNOS Class 2 and not receiving IVIT at the time of listing. Group 3 consisted of 15 patients implanted with a mechanical circulatory assist device (MCAD) at the time of listing. All-cause mortality was the primary end point. The need for heart transplantation or MCAD served as secondary end points. Clinical data were entered prospectively and analyzed retrospectively by intention-to-treat using Kaplan-Meier survival analysis.
RESULTS: The 1-year actuarial survival rate was 86.6% in Group 1; 92.3% in Group 2; and 100% in Group 3 (p=0.642). Regarding heart transplantation, 45.8% of Group 1 patients were transplanted versus 63.4% of Group 2 patients and 92.3% of Group 3 patients (p<0.001). Regarding the need for hemodynamic support with a MCAD, 21.4% of Group 1 patients versus 4.7% of Group 2 patients required a MCAD as a bridge to heart transplantation (p<0.001).
CONCLUSIONS: There are no significant differences in survival between patients on a cardiac transplant waiting list receiving continuous IVIT and patients awaiting cardiac transplantation and not receiving continuous IVIT. However, patients receiving continuous IVIT are more likely to require hemodynamic support with a MCAD.

38E. Effect of perioperative nesiritide administration on postoperative renal function and clinical outcomes in patients undergoing cardiac surgery. *Nader Moazami, M.D.*[1], Jenny Smith, Pharm.D., BCPS[2]; (1)Washington University of St. Louis (NAPA Primary Investigator), One Barnes Jewish Hospital, St. Louis, MO; (2)Washington University of St. Louis, One Barnes Jewish Hospital, St. Louis, MO.

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39E. Perioperative nesiritide use is associated with decreased 180-day mortality in heart failure patients undergoing cardiac surgery. *Nader Moazami, M.D.*[1], Jenny Smith, Pharm.D., BCPS[2]; (1)Washington University of St. Louis (NAPA Primary Investigator), One Barnes Jewish Hospital, St. Louis, MO; (2)Washington University of St. Louis, One Barnes Jewish Hospital, St. Louis, MO.

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40. Beta-blocker dose influences cardiac response to spironolactone in heart failure. *Kathryn Momary, Pharm.D.*[1], Joseph R. Camp, B.S.[1], Vicki L. Groo, Pharm.D.[1], Thomas Stamos, M.D.[2], Larisa H. Cavallari, Pharm.D.[1]; (1)University of Illinois at Chicago, College of Pharmacy, Chicago, IL; (2)University of Illinois at Chicago, College of Medicine, Chicago, IL .

PURPOSE: The Randomized Aldactone Evaluation Study demonstrated survival benefits with spironolactone in heart failure; however, only about 10% of participants were taking a beta-blocker at baseline. Thus, it is unclear whether spironolactone provides additional benefits to beta-blocker therapy.

We sought to determine whether beta-blocker dose influences cardiac response to spironolactone in heart failure.
METHODS: Blood samples were collected from 29 patients with chronic stable HF before and 6 months after spironolactone initiation. Serum markers of cardiac fibrosis, including procollagen type I amio-terminal peptide (PINP) and procollagen type III amino-terminal peptide (PIIINP), were determined by radioimmunoassay at both time points and compared between patients on low and high beta-blocker doses. Low and high beta-blocker doses were defined as <50% and ≥50%, respectively, of the target beta-blocker dose; target dose was defined as carvedilol 25 mg bid (or 50 mg bid for weight > 85 kg) or metoprolol 200 mg/day.
RESULTS: Baseline characteristics, vasodilator therapy, and procollagen concentrations were similar between patients on low (n=9) and high (n=20) beta-blocker doses. The median spironolactone dose was 25 mg/day in each group. The low-dose group had greater reductions in PINP [median (interquartile range) change of -14.3 (-19.3 to -9.8) versus -2.5 (-9.8 to 8.2), p=0.01] and PIIINP [-1.4 (-2.4 to -0.9) versus 0.1 (-1.3 to 0.9), p=0.01] compared with the high-dose group. Both PINP and PIIINP decreased in 100% of those in the low-dose group, but only 35% of those in the high dose group, p=0.03.
CONCLUSIONS: We observed greater reductions in markers of cardiac fibrosis among patients taking low versus high doses of beta-blocker. Our data suggests that spironolactone may be of particular benefit in patients with heart failure who can not tolerate beta-blocker up-titration, at least in terms of effects on cardiac remodeling.

41. A retrospective analysis of nesiritide use in patients with acute decompensated heart failure. *Jessica A. Starr, Pharm.D.*, Jean M. Nappi, Pharm.D.; Medical University of South Carolina, Charleston, SC.

PURPOSE: Nesiritide has FDA labeling approval for the treatment of patients with acute decompensated heart failure (ADHF) due its ability to rapidly reduce cardiac filling pressures and improve dyspnea. Recently, there have been reports indicating that nesiritide may adversely affect renal function and mortality. Numerous studies have shown that renal dysfunction is associated with unfavorable outcomes in patients with heart failure. The purpose of this retrospective analysis is to assess the effects of nesiritide on renal function.
METHODS: Medical records of patients hospitalized between January 2004 and July 2005 treated with nesiritide for ADHF for at least 12 hours were reviewed. Specific parameters evaluated include an increase in serum creatinine (SCr) > 0.5 mg/dL, systolic blood pressure, length of hospital stay, in hospital mortality, duration of nesiritide infusion, and intravenous (IV) diuretic use.
RESULTS: Seventy-five patients were analyzed. Twenty-six patients experienced an increase in SCr > 0.5 mg/dL. Treatment dose and duration did not differ between those patients who had an increase in SCr > 0.5 mg/dL and those who did not. Concomitant intravenous diuretics were used in 85% of patients who experienced this increase versus 90% of patients who did not. The average systolic blood pressure was 94 mm Hg in both groups. The mean length of hospital stay was longer in those patients with an increase in SCr > 0.5 mg/dL averaging 18 days versus 13 days. The in-hospital mortality rate was higher at 35% in patients who experienced this increase compared with 10% of patients who did not.
CONCLUSIONS: Nesiritide increases SCr > 0.5 mg/dL independent of dose, duration of therapy, blood pressure changes, and concomitant IV diuretic use. This increase in SCr is associated with an increase in hospital stay and in-hospital mortality.

42. Adverse events with high-dose statin therapy: a meta-analysis. *Matthew A. Silva, Pharm.D., R.Ph.*, Paul Belliveau, Pharm.D., RPh, Nicole Nolan, Pharm.D., R.Ph., Michele Matthews, Pharm.D., R.Ph., Courtney Jarvis, Pharm.D., R.Ph.; Massachusetts College of Pharmacy and Health Sciences, Worcester, MA.

PURPOSE: The value of intensive LDL-C lowering with high-dose statins in patients with stable coronary heart disease (CHD) and acute coronary syndrome (ACS) is under debate. We performed a meta-analysis to quantify the incremental benefit and harm of high-dose versus moderate-dose statin therapy in patients with CHD and ACS.
METHODS: MEDLINE, EMBASE, and the Cochrane Register of Controlled Trials were searched for prospective, randomized trials comparing high and moderate-dose statins for secondary prevention of cardiovascular events in patients with stable coronary artery disease or ACS. Studies were excluded if data on cardiovascular death (CVD), myocardial infarction (MI), all-cause mortality (ACM), stroke, and liver and muscle toxicity were excluded. The Mantel-Haenszel method was used to calculate odds-ratios, 95% confidence intervals, and p-values; simple numbers-needed to-treat/harm were subsequently calculated.
RESULTS: Pooling of four trials meeting inclusion criteria suggests that high-dose statin therapy reduced CVD (OR=0.86; 95% CI [0.75-0.99]; p=0.031), fatal/non-fatal MI (OR=0.84; 95% CI [0.76-0.93]; p=0.001) and fatal/non-fatal stroke (OR=0.82; 95% CI [0.72-0.94]; p=0.004) compared with moderate-dose statin therapy. High-dose therapy was associated with more serious adverse drug events requiring discontinuation (OR=1.28; 95% CI [1.18-1.39]; p≤0.001), LFT abnormalities (OR=4.84; 95% CI [3.27-6.16]; p≤0.001), CPK elevations (OR=9.97; 95% CI [1.28-77.9]; p=0.028) or any serious adverse event (OR=1.44; 95% CI [1.33-1.55]; p≤0.001) compared with moderate-dose statin therapy. Treating 1000 patients with high-dose statins instead of moderate-dose statin therapy will prevent an additional 4 CVDs, 10 MIs and 6 strokes while causing 33 serious adverse events, 21 adverse events requiring discontinuation and 12 instances of elevated LFTs.
CONCLUSIONS: This analysis reemphasizes the importance of assessing individual patient characteristics before the initiation of high-dose statin therapy. High-dose statin therapy provides additional efficacy beyond moderate-dose statin therapy in patients at high risk for CV events, but it has a higher additional risk of adverse events.

43. Risk-adjusted outcomes of patients receiving either e-aminocaproic acid or Aprotinin for antifibrinolytic prophylaxis during on-pump cardiac surgery. *Jeremy D. Flynn, Pharm.D.*, E. Zachary Ramsey, Pharm.D., W. Scott Akers, Ph.D., Pharm.D., Doug Steinke, Ph.D., R.Ph., Kelly Smith, Pharm.D., Phillip Camp, M.D., Chand Ramaiah, M.D., Victor Ferraris, M.D., Ph.D; University of Kentucky Chandler Medical Center, Lexington, KY.

PURPOSE: Cardiac surgery is often accompanied by substantial coagulopathies secondary to the use of cardiopulmonary bypass (CPB) which can result in significant blood loss. Antifibrinolytic agents, like aprotinin and ϵ-aminocaproic acid, have been shown to decrease blood loss and transfusion requirements. The purpose of this study was to compare the outcomes associated with the use of aprotinin and ϵ-aminocaproic acid in on-pump cardiac surgeries.
METHODS: This study was a single-center, retrospective, chart review. Each patient's medical record (n=350) was reviewed to ascertain demographic data, antifibrinolytic prophylaxis used, and outcomes. Two common risk stratification tools for cardiac surgery (EURO-SCORE and STS Risk calculator) were used. The primary end point was perioperative blood product transfusions. Secondary end points included 24-hour chest tube drainage, length of stay (LOS), mortality, total cost and adverse events. A regression analysis was conducted to adjust for differences in preoperative risk between groups.
RESULTS: There were several differences in baseline characteristics between groups which resulted in significantly higher risk scores for the aprotinin group (p<0.05) as calculated by EURO-SCORE and STS Risk. There were no significant differences between groups for blood product transfusions or 24-hour chest tube drainage. The aprotinin group was found to have longer ICU and hospital LOS, hospital mortality, and 30-day mortality. The total cost was also significantly higher in the aprotinin group. There were no differences between groups in adverse events observed. Following a regression analysis to adjust for differences in preoperative risk, the LOS end points and total cost remained significant, but mortality was no longer significantly different between groups.
CONCLUSIONS: Aprotinin and ϵ-aminocaproic acid resulted in no differences in blood product transfusion or chest tube drainage. However, the aprotinin group had a significantly longer ICU and hospital length of stay and total cost, which remained significantly different after being adjusted for risk.

44. Enoxaparin dosing in obese patients with non-ST-segment elevation acute coronary syndrone (NSTE ACS): results from CRUSADE. *Sarah A. Spinler, Pharm.D.*[1], Fang-Shu Ou, Ph.D.[2], Matthew T. Roe, M.D.[3], W. Brian Gibler, M.D.[4], E. Magnus Ohman, M.D.[2], Eric D. Peterson, M.D.[3]; (1)Philadelphia College of Pharmacy, University of the Sciences in Philadelphia, Philadelphia, PA; (2)Duke Clinical Research Center, Durham, NC; (3)Duke Clinical Research Institute, Durham, NC; (4)University of Cincinnati, Cincinnati, OH.

PURPOSE: The purpose of this study was to compare enoxaparin dosing and bleeding outcomes in different strata of total body weight (TBW) in patients enrolled in CRUSADE, a national registry and quality improvement initiative of patients with NSTE ACS.
METHODS: A final study population of 19,061 patients enrolled in CRUSADE between 01/01/04 and 03/31/06 who received at least one dose of enoxaparin were included. Patients were excluded if they were transferred to another institution, had an estimated creatinine clearance < 30 mL/min, underwent CABG, or were missing dosing information. Major bleeding was defined as an absolute HCT drop of ≥ 12%, intracranial hemorrhage, retroperitoneal bleed, baseline HCT ≥ 28% with red blood cell (RBC) transfusion or baseline HCT ≤ 28% with a RBC transfusion and a witnessed bleeding event. A generalized estimating equations method that produces estimates similar to those from ordinary logistic regression was used to explore the association between enoxaparin dose (mg/kg TBW) and major bleeding.
RESULTS:

TBW	≤100 kg>	101-150 kg	> 150 kg	P-value (Trend test)
N	15,162	3,724	175	
TBW kg*	78 (68-88)	111 (105-121)	164 (157-180)	<.0001
Enoxaparin Initial Dose*	1.00 (0.94-1.03)	0.95 (0.83-0.99)	0.65 (0.47-0.94)	<.0001
Non-CABG major bleeding (%)	7.8	5.9	8.0	0.0015
Adjusted OR (95% CI) Enoxaparin Initial Dose (mg/kg)	0.98 (0.70-1.38)	0.73 (0.34-1.58)	17.0 (1.34-215.1)	

*Values are median and 25th-75th percentile.

After adjustment for demographic and clinical variables, in general, enoxaparin dose (mg/kg TBW) was not significantly associated statistically with major bleeding. However, for patients weighing more than 150 kg, the odd ratio is marginally significant (p=0.029).

CONCLUSIONS: A lower dose of enoxaparin (mg/kg TBW) was administered to obese patients with NSTE ACS enrolled in CRUSADE. Major bleeding increases slightly in this patient group. When sufficient amount of data are available, a separate analysis targeting patients' weighing more than 150 kg should be conducted.

Critical Care

45. Duration of stress ulcer prophylactic therapy in critically ill patients. Paul D. Wohlt, Pharm.D., *Jeffrey T. Fish*, *Pharm.D.*; University of Wisconsin Hospital and Clinics, Madison, WI.

PURPOSE: This study assessed the appropriateness of continuing stress ulcer prophylactic (SUP) therapy in critically ill patients at the University of Wisconsin Hospital and Clinics transferred from a medical/surgical intensive care unit (MICU/SICU) to a hospital ward and then again at hospital discharge.

METHODS: Medical records of 523 patients admitted between July 1 and September 31, 2005, were evaluated for appropriateness of SUP continuation during hospitalization and at hospital discharge. Eligible subjects were considered to be appropriately discharged from the hospital-prescribed SUP therapy if they met the following criteria: mechanically ventilated, coagulopathic, diagnosed with gastroesophogeal reflux disease, peptic ulcer disease, history of gastrointestinal (GI) ulceration or bleeding within the past year, prescribed a proton pump inhibitor (PPI) or histamine-2 receptor antagonist (H_2RA) prior to admission, or developed a GI bleed during hospitalization.

RESULTS: Stress ulcer prophylactic therapy was prescribed for 90.6% of 394 hospitalized, study eligible patients. On day of MICU/SICU discharge, 88.5% of patients were continued on SUP. Based on study criteria, 59.8% of patients discharged from the MICU/SICU did not have an indication for SUP use. On day of hospital discharge 56.6% of patients were continued on SUP. Based on study criteria, 24.4% of MICU/SICU patients were prescribed agents used for SUP without a clear indication on day of hospital discharge (55.2% on PPI; 44.8% on H_2RA).

CONCLUSIONS: The results of this study demonstrate that 24.4% of patients admitted to the MICU/SICU inappropriately remain on agents used for SUP on day of hospital discharge. This practice of over-prescribing SUP needlessly places patients at risk for developing adverse events secondary to increased gastric pH and developing toxicities associated with the medications themselves, and also places a financial burden on both individual patients and the health care system.

46E. A model-based estimate of transfusion risk and utilization in United States intensive care units. *Marya D. Zilberberg, M.D., FCCP*[1], Patrick Lefebvre, M.A.[2], Chureen Carter, Pharm.D., M.S.[1], Monika Raut, Ph.D.[1], Francis Vekeman, M.A.[3], Mei-Sheng Duh, M.P.H., Sc.D.[4], Andrew F. Shorr, M.D., M.P.H., FCCP[5]; (1)Ortho Biotech Clinical Affairs, LLC, Bridgewater, NJ; (2)Groupe d'Analyse, Ltée., Montreal, QC, Canada; (3)Analysis Group, Inc., Montreal, QC, Canada; (4)Analysis Group, Inc, Boston, MA; (5)Washington Hospital Center, Washington, DC.

Presented at the Annual Meeting of the American College of Chest Physicians, Salt Lake City, UT, October 21-16, 2006.

47E. Anemia and transfusions among critically ill patients on prolonged mechanical ventilation. *Andrew F. Shorr, M.D., M.P.H., FCCP*[1], Lee Stern, M.S.[2], Monika Raut, Ph.D.[3], Lisa R. Rosenblatt, M.D.[2], Samir H. Mody, Pharm.D., M.B.A.[3], Sarah Hendlish, M.P.H.[2], John J. Doyle, Dr.P.H.[2], Marya D. Zilberberg, M.D., FCCP[3]; (1)Washington Hospital Center, Washington, DC; (2)Analytica International, New York, NY; (3)Ortho Biotech Clinical Affairs, LLC, Bridgewater, NJ.

Presented at the Annual Meeting of the American College of Chest Physicians, Salt Lake City, UT, October 21-16, 2006.

48E. The effect of nebulized epoprostenol on mortality in patients with acute respiratory distress syndrome. *A. Joshua Roberts, Pharm.D.*, A. Shaun Rowe, Pharm.D., BCPS; University of Tennessee Medical Center, Knoxville, TN.

Presented at the 37th Annual Southeastern Residency Conference, Athens, GA, April 27-28, 2006.

49E. Factors predicting the receipt of packed red blood cell (pRBC) transfusions among critically ill patients. *Joseph F. Dasta, M.Sc.*[1], Samir H. Mody, Pharm.D., M.B.A.[2], Trent McLaughlin, Ph.D.[3], Jaclyn M. LeBlanc, Pharm.D.[1], Yingjia Shen, M.S.[4], Marsie Genetti, M.S.[4], Monika Raut, Ph.D.[2], Catherine Tak Piech, M.B.A.[2]; (1)College of Pharmacy, The Ohio State University, Columbus, OH; (2)Ortho Biotech Clinical Affairs, LLC, Bridgewater, NJ; (3)Stanford University Medical Center, Stanford, CA; (4)Wolters Kluwers Health, Yardley, PA.

Presented at the Annual Meeting of the American College of Chest Physicians, Salt Lake City, UT, October 22, 2006.

50E. Predictors of mortality for methicillin-resistant *Staphylococcus aureus* healthcare-associated pneumonia: lack of a treatment effect related to vancomycin pharmacokinetic indices. *Meghan N. Jeffres, Pharm.D.*[1], Warren Isakow, M.D.[2], Scott T. Micek, Pharm.D., BCPS[1], Josh A. Doherty, B.S.[3], David J. Ritchie, Pharm.D., BCPS, FCCP[1], Peggy S. McKinnon, Pharm.D.[1], Marin H. Kollef, M.D., FCCP[2]; (1)Barnes-Jewish Hospital, St. Louis, MO; (2)Washington University School of Medicine, St. Louis, MO; (3)BJC Healthcare, Saint Louis, MO.

Presented at the International Conference of the American Thoracic Society, San Diego, CA, May 19-24, 2006.

51E. Cost-effectiveness of intensive insulin therapy in critically ill patients: a meta-analysis. *Mark A. Malesker, Pharm.D.*, Lee E Morrow, M.D., Tammy L Burns, Pharm.D., Daniel E Hilleman, Pharm.D.; Creighton University Medical Center, Omaha, NE.

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52. Impact of erythropoietic use on receipt of packed red blood transfusions from a multicenter database of critically ill patients. *Joseph F. Dasta, M.Sc.*[1], Samir H. Mody, Pharm.D., M.B.A.[2], Trent McLaughlin, Ph.D.[3], Jaclyn M. LeBlanc, Pharm.D.[1], Yingjia Shen, M.S.[4], Marsie Genetti, M.S.[4], Monika Raut, Ph.D.[2], Catherine T. Piech, M.B.A.[2]; (1)College of Pharmacy, The Ohio State University, Columbus, OH; (2)Ortho Biotech Clinical Affairs, LLC, Bridgewater, NJ; (3)Stanford University Medical Center, Stanford, CA; (4)Wolters Kluwers Health, Yardley, PA.

PURPOSE: The standard treatment for acute anemia among critically ill patients is packed red blood cell(pRBCs) transfusions, despite well-published risks and complications. This study evaluated the impact of erythropoietic stimulating protein(ESPs) use on the receipt of transfusions among patients admitted to the intensive care unit (ICU), coronary care unit (CCU), and intermediate care unit.

METHODS: A retrospective cohort analyses of patients ≥ 18 years admitted to the ICU, CCU, and/or intermediate care unit from 139 hospitals was conducted for the period Jan 2004–May 2005. pRBC and ESP use were identified using revenue codes and HCPCS codes. A multivariate logistic regression model was used to evaluate the association between ESP use and pRBC transfusions, controlling for demographics, clinical variables, comorbid conditions, and ICU patient diagnosis. Logistic regression models were also run for subsets of patients with similar ICU lengths of stay (three subsets: ICU LOS 3,5,7 days) to control for exposure opportunity.

RESULTS: 29,331 patients received ≥ pRBC transfusion during his or her ICU/CCU/intermediate care unit stay compared with 150,890 patients not receiving pRBC transfusion. 11,394 patients received at least one dose of an ESP. Patients receiving ESPs had a lower likelihood of receiving pRBCs than those not receiving an ESP (OR:0.256,95%CI:0.237–0.277). The odds of receiving pRBC remained significantly lower among ESP patients with ICU LOS 3 days (OR:0.242,95%CI:0.182–0.321). This trend held for patients with ICU LOS 5 days (OR:0.285,95%CI:0.216–0.376) and 7 days (OR:0.208,95%CI:0.149–0.289).

CONCLUSIONS: The use of ESPs among critically ill patients was associated with a nearly 4-fold decreased risk of receiving pRBC transfusions after stratifying patients by their ICU LOS and controlling for various confounders. This naturalistic study of > 11,000 patients who received ESPs supports the findings from previous randomized controlled trials that ESPs decrease the need of pRBC transfusions in critically ill patients.

53. A time-motion analysis of tight glycemic control protocols in the intensive care unit. *Pamela A. Foral, Pharm.D., BCPS*[1], Mark A. Malesker, Pharm.D.[1], Ann C. McPhillips, R.N.[2], Keith Christensen, Pharm.D.[1], Daniel E. Hilleman, Pharm.D., FCCP[1]; (1)Creighton University Medical Center, Omaha, NE; (2)Alegent Health Immanuel Medical Center, Omaha, NE.

PURPOSE: Tight glycemic control protocols (TGCP) in the intensive care unit (ICU) are associated with improved clinical outcomes. The potential disadvantage of TGCP is increased nursing workload. This study determined the time spent by nurses implementing the TGCP.
METHODS: A time-motion analysis of nurses implementing TGCP was performed at three metropolitan hospitals. The cumulative time (CT) required by nurses to manage a TGCP was defined as meter start to result chart. The CT included: determining blood glucose (BG) levels via handheld POC glucose meter; taking appropriate therapeutic action; and documenting the BG result. The process was assessed by a third-party observer using a stopwatch.
RESULTS: Forty-five patients treated with a TGCP were observed with 454 BG levels evaluated. The CT involved to manage a normal BG (n=188) was 14.1 minutes. The CT to manage a hypoglycemic result (n=8) was 32.7 minutes. During a hypoglycemic episode, other activities included glucose administration, contacting the physician, checking the patient's vitals, and rechecking BG. The CT to manage a hyperglycemic result when an insulin drip needed to be initiated (n=18) was 51.6 minutes. This time included a 32.6-minute period between obtaining an elevated BG, contacting the physician, and receiving the insulin drip from the pharmacy. The CT to manage a hyperglycemic result when an insulin drip dosage adjustment (n=240) was required was 29.7 minutes.
CONCLUSIONS: A hyperglycemic BG while receiving the TGCP was the most common event observed, with a CT from meter start up to the adjustment of the infusion being 15.8 minutes and total CT to charting the result of 29.7 minutes. These data will serve as a benchmark for future studies evaluating the efficiency of implementing TGCP in the ICU. Future research is needed in the area of nursing resources and TGCP.

54. A prospective evaluation of propylene glycol clearance and potential toxicities during continuous infusion lorazepam in critically ill patients. *Jamie L. Nelsen, Pharm.D.*[1], Curtis E. Haas, Pharm.D.[2], Bahru Habtemariam, Pharm.D.[3], Amy Partridge, Pharm.D.[2], David C. Kaufman, M.D.[4], Steven L. Welle, Ph.D.[4], Alan Forrest, Pharm.D.[2]; (1)SUNY Upstate Medical University, Syracuse, NY; (2)University at Buffalo, School of Pharmacy and Pharmaceutical Sciences, Buffalo, NY; (3)Cognigen Corporation, Williamsville, NY; (4)University of Rochester, School of Medicine and Dentistry, Rochester, NY.

PURPOSE: To characterize the clearance of propylene glycol (PG) in critically ill patients receiving continuous infusion (CI) lorazepam and evaluate the occurrence of potential toxicities.
METHODS: ICU patients receiving CI lorazepam for > 48 hours were enrolled with no exclusion criteria. Blood samples were obtained daily while receiving lorazepam for up to 5 days. Demographic, clinical, laboratory data and details regarding all PG sources were recorded. Several pharmacokinetic models were evaluated using NONMEM® to characterize the disposition of PG. Covariate analyses were performed using forward addition and backward elimination processes. Linear regression analysis was used to evaluate the relationship between PG concentrations and osmolality, osmol gap (OG), and lactate. Significant PG accumulation was defined as > 25 mg/dL. Appropriate nonparametric statistical methods were used for comparisons.
RESULTS: A total of 203 PG concentrations (n=50) were obtained. Median lorazepam infusion rate was 2.1 mg/hour (0.5–18). Median duration of lorazepam prior to the first sample was 54 hour (40–380). The median time between sample collections was 24 hour (12–35). A linear, one-compartment model with inter-occasion variability (IOV) on clearance best described the data. Population mean PG clearance was 14.6 L/hour (inter-individual variability CV: 20.5%). Significant covariates on clearance were TBW and APACHE-II score. PG concentration correlated poorly with osmolality, OG and lactate. Eight patients had 21 PG concentrations > 25mg/dL. When PG concentrations were significantly elevated, the median lorazepam infusion rate prior to sample collection was higher; 6.4 (1.9–11.3) versus 2.0 (0.5–7.4) mg/hour (p=0.0003). Hyperosmolality was common (47%), although not clearly related to PG concentration. No convincing evidence of PG toxicity was observed.
CONCLUSIONS: A linear first-order model with IOV on clearance adjusted for TBW and APACHE-II score predicted PG concentration in a heterogeneous cohort of ICU patients. Significant PG accumulation occurred in 8 patients (16%) despite relatively low doses of lorazepam.

55. Evaluation of Direct Thrombin Inhibitor Dosing and Safety in the Management of Heparin-Induced Thrombocytopenia. *Lee P. Skrupky, Pharm.D.*, Jennifer R. Smith, Pharm.D.; Barnes-Jewish Hospital, Saint Louis, MO.

PURPOSE: Currently there are three direct thrombin inhibitors (DTIs) available for use including lepirudin, argatroban and bivalirudin. DTIs are commonly used in the management of heparin-induced thrombocytopenia (HIT), and yet no standard recommendations for dosage adjustment exist for argatroban or bivalirudin. This observational study evaluated the dosing, monitoring, and safety of DTI therapy for HIT.
METHODS: All inpatients who received treatment with lepirudin, argatroban, or bivalirudin for either highly suspected or confirmed HIT between November 27, 2005, and March 7, 2006, were evaluated. Initial dosage, dosage adjustments, time to therapeutic aPTT, aPTT monitoring, and bleeding events were recorded.
RESULTS: There were 7, 12, and 9 courses of therapy with lepirudin, argatroban, and bivalirudin, respectively, for a total of 28 unique courses of DTI therapy. The mean initial doses used for lepirudin, argatroban, and bivalirudin were 0.12 ± 0.04 mg/kg/hr, 0.84 ± 0.48 µg/kg/min, and 0.05 ± 0.04 mg/kg/hr, respectively. Twenty-three (82%) required dosage adjustment to either reach or maintain a therapeutic aPTT. Dosage adjustment was required to reach a therapeutic aPTT in 43%, 33%, and 44% of the patients receiving lepirudin, argatroban, and bivalirudin, respectively. The mean times to first therapeutic aPTT were 16.3 ± 14.2, 9.3 ± 9.1, and 15.8 ± 12.3 hours, respectively. The mean doses at the time of the first therapeutic aPTT were 0.09 ± 0.05 mg/kg/hour, 0.90 ± 0.52 µg/kg/min, and 0.08 ± 0.06 mg/kg/hour, respectively. Five patients (21%) had bleeding events while on DTI therapy. Three patients had gastrointestinal bleeding, and the remaining events were bleeding from a tracheostomy site and hematuria.
CONCLUSIONS: Direct thrombin inhibitors rapidly achieved therapeutic aPTTs in the management of patients with HIT. However, dosage adjustments were frequently required and a high rate of bleeding was observed. Guidelines for dosage adjustment of argatroban and bivalirudin are needed.

56. Pharmacokinetic (PK) and pharmacodynamic (PD) properties of heparin following subcutaneous administration in critically ill surgical patients. *Curtis E. Haas, Pharm.D.*[1], Jamie L. Nelsen, Pharm.D.[2], David C. Kaufman, M.D.[3], Jenny C. Yang, Pharm.D.[1], Qing Ma, Ph.D.[1], Alan Forrest, Pharm.D.[1], Charles W. Francis, M.D.[3]; (1)University at Buffalo, School of Pharmacy and Pharmaceutical Sciences, Buffalo, NY; (2)SUNY Upstate Medical University, Syracuse, NY; (3)University of Rochester, School of Medicine and Dentistry, Rochester, NY.

PURPOSE: Characterize and compare steady-state PK and PD properties of SC low-dose unfractionated heparin (LDUFH) in ICU and non-ICU surgery patients.
METHODS: Single-center, prospective study of 20 ICU and 10 non-ICU surgery patients receiving LDUFH 5000U SC Q8H for venous thromboembolism prevention. Blood was obtained at 0, 1, 2, 3, 4, 6, and 8 hours following a steady-state dose. Plasma was analyzed for heparin activity (anti-Xa and HEPTEST), tissue factor pathway inhibitor (TFPI), and antithrombin (AT). The primary end point was area under the curve ($AUC_{0\text{-}8h}$) for anti-Xa. Secondary end points were $AUC_{0\text{-}8h}$ for TFPI and HEPTEST, and AT activity at 0 hours.
RESULTS: ICU patients were more likely to be male, and have a lower estimated Clcr, higher APACHE II score, and greater positive fluid balance than non-ICU patients. Anti-Xa $AUC_{0\text{-}8h}$ were consistently low with no significant difference between study groups (Median: 0.718 vs. 0.715 IU/mL*h; p=0.83). HEPTEST $AUC_{0\text{-}8h}$ results were similar (Median 0.275 vs. 0.222 IU/mL*h; p=0.53). TFPI $AUC_{0\text{-}8h}$ was greater in ICU patients (Median: 548 vs. 323 IU/mL*h; p=0.009); however, activities for all patients were low and within the normal range. Median AT activity was decreased in both groups (Median: 52.5 vs. 58.4%; p=0.18). Maximal anti-Xa activity was low in both groups (Median: 0.13 vs. 0.11 IU/mL), with very flat activity vs. time curves. Peak anti-Xa activity was ≤ 0.2 IU/mL for 18 of 20 ICU and 10 of 10 non-ICU patients, and ≤ 0.1 IU/mL for 8 of 20 ICU and 3 of 10 non-ICU patients.
CONCLUSIONS: There were no clinically significant differences in PK/PD parameters between the two study groups. Anti-Xa, HEPTEST, and TFPI results were consistently low across both groups, questioning the adequacy of the current dose of LDUFH in surgical patients.

57E. Erythropoiesis-stimulating protein utilization and clinical outcomes in anemic, critically ill patients admitted to the intensive care unit (ICU): results from the ASSESS study. *Gretchen M. Brophy, Pharm.D.*[1], Valerie C. Sheehan, Pharm.D.[2], Thomas Rowe, Pharm.D., M.B.A.[3], Glenn Voss, Pharm.D.[4], Lynnae S. Jackson, M.B.A.[5], Debra Scarlata, Ph.D.[5], Paul Audhya, M.D.[5]; (1)VCU Medical College of Virginia, Richmond, VA; (2)Baylor University Medical Center, Dallas, TX; (3)Multicare Health System, Tacoma, WA; (4)Avera McKennan Hospital and University Health Center, Sioux Falls, SD; (5)Amgen, Inc, Thousand Oaks, CA.

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58E. Utilization patterns of erythropoiesis-stimulating proteins (ESPs) and

associated clinical outcomes in anemic, critically ill patients with renal impairment admitted to the intensive care unit (ICU): results from the ASSESS study. *Gretchen M. Brophy, Pharm.D.*[1], Mark J. Shapiro, M.D.[2], Katherine R. Tuttle, M.D.[3], Debra Scarlata, Ph.D.[4], Paul Audhya, M.D.[4]; (1)VCU Medical College of Virginia, Richmond, VA; (2)State University New York, Stony Brook, NY; (3)Sacred Heart Medical Center, Spokane, WA; (4)Amgen, Inc, Thousand Oaks, CA.

Presented at the Summer Meeting of the American Society of Health-System Pharmacists, Orlando, FL, June 28, 2006.

59E. Biomarker kinetics in cerebrospinal fluid of traumatic brain injury patients. *Gretchen M. Brophy, Pharm.D.*[1], Jose A. Pineda, MD[2], Linda Papa, M.D., M.Sc.[3], Stephen B. Lewis, M.D.[3], Alex B. Valadka, M.D.[4], H. Julia Hannay, Ph.D.[5], Shelley C. Heaton, Ph.D.[3], Ming C. Liu, Ph.D.[4], Jada M. Aikman, Research Assistant[4], Veronica Akle, Research Assistant[4], Joseph J. Tepas III, MD[6], Kevin W. Wang, Ph.D.[4], Claudia S. Robertson, MD[4], Ronald L. Hayes, Ph.D.[4]; (1)VCU Medical College of Virginia, Richmond, VA; (2)Washington University, St. Louis, MO; (3)University of Florida, Gainesville, FL; (4)Baylor College of Medicine, Houston, TX; (5)University of Houston, Houston, TX; (6)University of Florida, Jacksonville, FL.

Presented at the 24th Annual National Neurotrauma Society Symposium, St. Louis, Missouri, July 7-9, 2006.

60. Incidence of and adverse sequelae associated with propofol infusion syndrome in a neurosciences critical care unit. *Stacey Folse, Pharm.D., M.P.H.*, John J. Lewin III, Pharm.D., BCPS, Kenneth Shermock, Pharm.D., Tamer Abdelhak, M.D., Paul Nyquist, M.D.; The Johns Hopkins Hospital, Baltimore, M.D.

PURPOSE: The primary objective of this study was to characterize the incidence of propofol infusion syndrome (PRIS) in Neurosciences Critical Care Unit (NCCU) patients.
METHODS: Charts were reviewed for patients admitted to the NCCU from January 1, 2001, to September 30, 2005, who received propofol. Patients were included if they met the following criteria: 1) continuous propofol infusion greater than 12 hours, 2) development of hypotension, bradycardia, or hemodynamic instability requiring vasopressors at any time during infusion. Patients who received one-time doses of propofol were excluded. Two neurointensivists reviewed charts for patients meeting the inclusion criteria to determine if PRIS was present. A kappa statistic was calculated to quantify agreement between reviewers. Discrepancies between reviewers were resolved by a third reviewer.
RESULTS: Forty-nine patients with 53 courses of propofol therapy met the inclusion criteria. There were 0 confirmed cases of PRIS and 2 possible cases. A kappa statistic of 0.22 was calculated, which indicates fair agreement. The most common reason for propofol infusion initiation was sedation (70%). The majority of patients (68%) received maximum infusion rates of greater than 80 µg/kg/min. Sixty-eight percent of patients required hemodynamic support. The majority of courses of therapy did not have lactic acid (73.6%), triglyceride (77.4%), and creatine kinase (62.2%) levels monitored. However of those patients who were monitored, more than half (57.1%) developed lactic acidosis while 20% had elevated creatine kinase levels.
CONCLUSIONS: Despite the use of large doses of propofol, there were no confirmed cases of PRIS. Two possible cases of PRIS were identified, but could not be confirmed due to lack of supporting laboratory data. The small kappa statistic is consistent with the ill-defined nature of PRIS in the literature. Based on our results, we recommend that patients receiving greater than 80 µg/kg/min have appropriate labs and vital signs monitored.

61. Prevalence of anemia and erythropoiesis-stimulating protein use among patients with reduced kidney function admitted to the intensive care unit. *Gretchen M. Brophy, Pharm.D.*[1], Spencer E. Harpe, Pharm.D., Ph.D.[1], Michael A. Pyles, Ph.D.[1], David A. Holdford, Ph.D.[1], Thomas Comstock, Pharm.D.[2], Paul Audhya, M.D.[2], Donald F. Brophy, Pharm.D., M.S.[1]; (1)VCU Medical College of Virginia, Richmond, VA; (2)Amgen, Inc, Thousand Oaks, CA.

PURPOSE: Reduced kidney function and anemia are common comorbidities in critically ill patients admitted to the intensive care unit (ICU). This study was conducted to determine 1) the prevalence of reduced kidney function and anemia on hospital admission in patients requiring an ICU stay, and 2) the utilization of erythropoiesis-stimulating proteins (ESPs) in this patient cohort.
METHODS: This is a retrospective review of data from 42,398 ICU patients admitted to 34 U.S. hospitals (January 2001 to June 2005). Laboratory and drug utilization data were provided through the Solucient® ACTracker® database. Inclusion criteria were ICU stay > 24 hours, age ≥ 18 years, and no acute renal failure diagnosis code. Reduced kidney function was conservatively defined as hospital admission serum creatinine > 1.6 mg/dL for men and > 1.4 mg/dL for women; anemia was defined as hemoglobin < 11 g/dL.
RESULTS: Of the total ICU population, 9018 (21.3%) patients had reduced kidney function on hospital admission. The mean (SD) age of this cohort was 70.3 (14.9) years; 53.4% were female; 13.4% required dialysis. The prevalence of anemia in patients without reduced kidney function was 20.0% vs. 36.8% in patients with reduced kidney function (OR 2.33; 95% CI 2.21, 2.45). An ESP was prescribed for 23.7% of ICU patients with reduced kidney function and anemia.
CONCLUSIONS: In this study, more than 20% of ICU patients had reduced kidney function on hospital admission, and more than one-third of these were anemic. Patients with reduced kidney function on hospital admission were 2.3 times more likely to have anemia than patients without reduced kidney function. The majority of ICU patients with reduced kidney function on hospital admission and anemia did not receive ESP therapy. Further studies are needed to assess ESP utilization patterns in the ICU and to evaluate their potential role in improving patient outcomes.

Drug Information

62E. Onset of antidepressant action and acute efficacy and safety of duloxetine versus escitalopram and placebo in the treatment of major depressive disorder. Andrew Nierenberg, M.D.[1], John Greist, M.D.[2], Craig Mallinckrodt, Ph.D.[3], Apurva Prakash, B.A.[3], John Watkin, D.Phil.[3], Angelo Sambunaris, M.D.[4], *Jeffrey Hille, M.P.H.*[3], Madelaine Wohlreich, M.D.[3]; (1)Massachusetts General Hospital, Boston, MA; (2)Healthcare Technology Systems, Madison, WI; (3)Eli Lilly and Company, Indianapolis, IN; (4)Atlanta Institute of Medicine & Research, Marietta, GA.

Presented at the Annual Meeting of the American Psychiatric Association, Toronto, ON, Canada, May 20, 2006.

63E. Sexual functioning in long-term treatment of MDD: duloxetine, escitalopram, and placebo. Anita Clayton, M.D.[1], Craig Mallinckrodt, Ph.D.[2], Madelaine Wohlreich, M.D.[2], Michael Robinson, M.D.[2], Megan Jones, Pharm.D.[2], Apurva Prakash, B.A.[2]; and *Shilpa S. Ekbote, Pharm.D.*[2] (1)University of Virginia Health System, Charlottesville, VA; (2)Eli Lilly and Company, Indianapolis, IN.

Presented at the Annual Meeting of the American Psychiatric Association, Toronto, ON, Canada, May 20, 2006.

64E. Efficacy of duloxetine in the treatment of generalized anxiety disorder in patients with clinically significant painful physical symptoms. Risa Weisberg, Ph.D.[1], Mauricio Fava, M.D.[2], James Hartford, M.D.[3], Janelle Erickson, Ph.D.[4], Deborah D'Souza, Ph.D.[4], *Shilpla Ekbote, Pharm.D.*[5], James Russell, M.D.[4]; (1)Brown University, Providence, RI; (2)Massachusetts General Hospital, Boston, MA; (3)Hartford Research Group, Florence, KY; (4)Eli Lilly and Company, Indianapolis, IN; (5)Eli Lilly and Company, Ann Arbor, MI.

Presented at the Annual Meeting of the College of Psychiatric and Neurologic Pharmacists, Baltimore, MD, April 25, 2006.

65. Evaluation of dietary supplement advertisements in print media. *Amy S. Peak, Pharm.D.*, Annie Schluge, Pharm.D.; Butler University, Indianapolis, IN.

PURPOSE: The purpose of this study is to analyze direct-to-consumer advertising in print media for compliance with Federal Trade Commission rules and regulations regarding the promotion of dietary supplements.
METHODS: Dietary supplement advertisements from 20 laymen's magazines were evaluated. Individual advertisements were evaluated for identification of product ingredients, direct or implied claims, scientific support provided for claims made, presence of qualifying safety or efficacy information, participation in any verification program, a statement regarding lack of Food and Drug Administration (FDA) evaluation, and manufacturer contact information.
RESULTS: Approximately 62% of the 204 advertisements evaluated did not disclose product ingredients. Product claims were made in 96% of the advertisements, including 1,079 direct and 63 implied claims regarding effects on body structure or function. More than 78% did not refer to any type of study supporting product use. Of the 49 advertisements referring to a study, 5 studies had been published, 1 of which was in a peer-reviewed journal. Only 3 advertisements provided clear and noticeable safety information. More than 83% of the advertisements did not provide any safety information. Although qualifying efficacy information was present in 26% of the advertisements, it usually was not provided in a clear and noticeable manner. No advertisements indicated participation in a verification program. Fewer than half of the advertisements included a disclaimer regarding lack of FDA evaluation. Manufacturer contact information was commonly provided (> 80%).
CONCLUSIONS: Many dietary supplement advertisements do not comply with the Federal Trade Commission's guidelines. Several dietary supplement

advertisements contain unsubstantiated claims. More than 95% of dietary supplement advertisements make claims while only 2% appear to be supported by readily available scientific data. Many advertisements do not include qualifying safety or efficacy information, and when included it is unlikely to be in a clear and noticeable manner as directed by the Federal Trade Commission.

66. Lack of physician knowledge regarding actual costs of commonly prescribed medications. *Amy S. Peak, Pharm.D.*, Steffany Wright, Pharm.D.; Butler University, Indianapolis, IN.

PURPOSE: Previous studies have suggested that physicians are unaware of actual costs of commonly prescribed medications. The primary objectives of this study are to determine whether physicians can identify the least expensive medication within common drug classes and accurately predict true drug prices.
METHODS: Prescribers affiliated with internal medicine and family practice teaching programs in Indianapolis, Indiana, were invited to complete an electronic survey in which they were asked to identify the least expensive medication in five common drug classes, and to distinguish the correct price range for the least expensive medication in the class. All prices were based on what an uninsured customer would pay for a 1 month supply of the given medication at local pharmacies. Participants were also asked to indicate where they typically obtain prescription pricing information.
RESULTS: Approximately 35% of the 328 prescribers responded to the survey. Most physicians (79%) were able to identify the least expensive Selective Serotonin Reuptake Inhibitor, but only 10% could correctly identify the actual price range. Approximately 58% correctly identified the least expensive Proton Pump Inhibitor, but only 6% indicated the correct price range. Nearly 20% of respondents correctly identified the least expensive HMG CoA Reductase Inhibitor, with 19% correctly indicating the price range. Approximately 14% of physicians correctly identified the least expensive intranasal steroid; 22% indicated the appropriate price range. Less than 10% of physicians were able to correctly identify the least expensive ACE Inhibitor, while 21% indicated the true price range. Programs on personal digital assistants are the most common source of prescription pricing information.
CONCLUSIONS: Physicians' abilities to identify the least expensive medication within a drug class are highly variable and dependent upon drug class. Regardless of drug class, most physicians are unable to correctly identify the actual price range of commonly prescribed medications.

67E. Evidence-based medicine skills taught at U.S. pharmacy schools. *Patrick J. Bryant, Pharm.D., FSCIP*[1], Isaac Butler, Pharm.D.[1], Karen P. Norris, Pharm.D.[1], Jacqueline S. Marinac, Pharm.D.[2]; (1)University of Missouri - Kansas City School of Pharmacy Drug Information Center, Kansas City, MO; (2)Pfizer, Inc, Shawnee, KS.

Presented at the Annual Meeting of the American Association of Colleges of Pharmacy, San Diego, CA, July 8-12, 2006.

68. Characterization of the discontinuation rate of angiotensin-converting enzyme inhibitors subsequent to post-initiation elevation in serum creatinine. *Joyce Wong, Pharm.D.*[1], Cynthia Jackevicius, B.Sc.Phm., M.Sc., Pharm.D., FCSHP, BC[1], Shelly DePeralta, NP[2], Freny Vaghaiwalla Mody, M.D.[2]; (1)Western University of Health Science, Pomona, CA; (2)Veteran Affairs Greater Los Angeles Healthcare System (VAGLAHS), Los Angeles, CA.

PURPOSE: Angiotensin-converting enzymes inhibitors (ACEI) are underutilized despite benefits in cardiovascular diseases, in part due to concerns of a rise in serum creatinine (SCr). The objectives of this study were to assess: 1) the prevalence of SCr increase post-ACEI initiation, 2) the discontinuation rate subsequent to this increase, 3) the threshold at which ACEI discontinuation occurs, and 4) for patients with baseline SCr > 2 mg/dL the change in SCr associated with chronic ACEI use.
METHODS: All outpatients initiating ACEI 1/1/02–12/31/04 within the healthcare system were included. Patients were divided by baseline SCr: ≤ 1.5, 1.5–2.0, and > 2.0 and patients with SCr available were followed up at 1 and 3 months. A multiple logistic regression model was constructed with the discontinuation rate subsequent to an increase in SCr post-ACEI initiation as the outcome. Patients with baseline SCr>2.0mg/dL were followed up in 1 year to detect changes in SCr with chronic ACEI use.
RESULTS: The mean increase in SCr prior to ACEI discontinuation was 26%, and discontinuation rates were 5.1%, 10.8%, and 11.8% respectively by groups ($p<0.0001$). The regression model found that a change in SCr was not associated with ACEI discontinuation but was associated with gender, congestive heart failure, systolic blood pressure < 100 mm Hg, use of NSAIDs, diuretics and beta-blockers. Patients with a baseline SCr > 2.0 mg/dL who used ACEI for 1 year had a median change of -0.01mg/dL.
CONCLUSIONS: The magnitude of increase in SCr post-ACEI initiation was similar to prior studies. ACEI discontinuation was associated with the co-morbidities and concomitant medication use. The discontinuation of ACEI was not related to the subsequent rise in SCr. ACEI use at 1 year in patients with SCr > 2 mg/dL was associated with a decrease in SCr. This decrease in SCr is important to note because patients with SCr > 2 mg/dL still benefited from ACEI and should not be discontinued as seen in common practice.

Education/Training

69E. Board certification of pharmacy residency program directors. *Noelle E. Daugherty, Pharm.D.*, Melody Ryan, Pharm.D., BCPS, Frank Romanelli, Pharm.D., BCPS, Kelly M. Smith, Pharm.D.; University of Kentucky Medical Center, Lexington, KY.

Presented at the Southeastern Residency Conference, Athens, GA, April 27, 2006.

70. Argatroban therapy for heparin-induced thrombocytopenia in acutely ill patients. *Anthony Gray, M.D.*[1], Diane E. Wallis, M.D.[2], Marcie J. Hursting, Ph.D.[3], Eliezer Katz, M.D., FACS[4], Bruce E. Lewis, M.D.[5]; (1)Lahey Clinic, Burlington, MA; (2)Midwest Heart Specialists, Downer's Grove, IL; (3)Clinical Science Consulting, Austin, TX; (4)CTI Clinical Trial and Consulting Services, Blue Ash, OH; (5)Loyola University Medical Center, Maywood, IL.

PURPOSE: To evaluate dosing, clinical outcomes, and effects of argatroban therapy in acutely ill patients with heparin-induced thrombocytopenia (HIT), a prothrombotic, immune-mediated adverse reaction to heparin therapy.
METHODS: From a registry of previous multicenter, historically-controlled studies of argatroban therapy in HIT, we retrospectively identified all patients with HIT who had at least one prespecified medical condition (acute respiratory distress syndrome, trauma) or indication for heparin therapy (cardiac surgery, ventricular assist device, acute myocardial infarction, acute coronary syndrome, pulmonary embolism) consistent with acute illness. Patients received either argatroban, adjusted to maintain activated partial thromboplastin times (aPTTs) 1.5–3 times baseline, or historical control therapy.
RESULTS: We identified 488 patients: 390 received argatroban (mean ± SD dose of 1.9 ± 1.2 µg/kg/min for 6.0 ± 5.2 days; mean aPTT during therapy, 63 ± 15 seconds), and 98 received no direct thrombin inhibition. An all-cause, 37-day composite end point of death, amputation, or new thrombosis occurred in 133 (34.1%) argatroban-treated patients versus 38 (38.8%) controls ($p=0.41$). Argatroban, versus control, however, significantly reduced a thrombosis-related composite end point of death due to thrombosis, amputation secondary to ischemic complications of HIT, or new thrombosis (17.7% versus 30.6%, $p=0.007$), and also new thrombosis (11.5% versus 26.5%, $p<0.001$); and death due to thrombosis (1.3% versus 7.1%, $p=0.004$). Major bleeding was similar (7.7% versus 8.2%; $p=0.84$). From regression analysis, adverse outcomes were more likely to occur in patients who were initially diagnosed with HIT and thrombosis, had undergone cardiac surgery, were not Caucasian, or had more severe thrombocytopenia.
CONCLUSIONS: In acutely ill HIT patients, argatroban 1.9 ± 1.2 µg/kg/min, versus historical control, provides effective antithrombotic therapy without increasing major bleeding. Patients with more severe thrombocytopenia or HIT-related thrombosis upon HIT diagnosis have a poorer prognosis, emphasizing the importance of prompt recognition/treatment of HIT in acutely ill patients.

71. Integration of cases from the IowaTeach database into a clinical practice skills course. *Michael E. Ernst, Pharm.D.*[1], John M. Swegle, Pharm.D.[2], Christine M. Catney, M.A., Pharm.D.[2], Hazel H. Seaba, M.S.[2], Jay D. Currie, Pharm.D.[2]; (1)College of Pharmacy, and Dept of Family Medicine, College of Medicine. The University of Iowa, Iowa City, IA; (2)College of Pharmacy, The University of Iowa, Iowa City, IA.

PURPOSE: Cases incorporated into teaching facilitate active learning of students and help them develop problem-solving/critical thinking skills. Standard casebooks quickly become outdated or too well-known to students. IowaTeach is a novel online database of authentic pharmacy practice cases developed to provide renewable, up-to-date cases to faculty. We report students' perceptions of IowaTeach cases used in Clinical Practice Skills III (CPSIII), a required third professional year course.
METHODS: We collaborated with UI Information Technology Services and the Iowa Drug Information Service (IDIS) to develop an online database of 780 indexed, de-identified patient cases searchable by several categories, including drug, disease, drug therapy problem(s), case complexity, and care setting. Users can submit new or modified cases and associated ancillary teaching materials online. In 2006, CPSIII instructors replaced the required published casebook with IowaTeach cases. Each student (n=108) was assigned three cases and was expected to identify drug therapy problems (DTPs) and treatment goals, provide referenced recommendations for treating DTPs, and present the case recommendations orally and written to the

instructor and other students in small groups. Students were surveyed to evaluate their perceptions of IowaTeach cases compared with the published casebook used in earlier CPSI and CPSII courses.
RESULTS: Fifty-six students responded to the survey. On a 5-point Likert scale, 82% agreed/strongly agreed the cases seemed real, and 79% agreed/strongly agreed they were the type they would see in real life. Sixty-two percent agreed/strongly agreed that the amount of unknown information was similar to actual pharmacy practice. Ninety-one percent agreed/strongly agreed the cases challenged their thinking skills. In a general question, 75% felt that IowaTeach cases were more helpful for learning than cases used in other classes.
CONCLUSIONS: IowaTeach assists faculty in providing active learning that simulates the practice environment. Students perceive learning value in using real-life cases from the database.

72. Assessment of an advanced cardiac life support simulation in a pharmacotherapeutics laboratory course. *Shawn J. Boyle, Pharm.D.*, Michael J. Cawley, Pharm.D., RRT, CPFT, Cynthia A. Sansoki, Pharm.D.; University of the Sciences in Philadelphia, Philadelphia, PA.

PURPOSE: Pharmacists are routinely involved as members of rapid response teams to participate in Advanced Cardiac Life Support (ACLS). Prior to entering clerkship, pharmacy students are typically exposed to principles of ACLS in a didactic setting only. Therefore, students may not fully appreciate the stress associated with managing patients in a "code blue" setting. The purpose of this activity was to enable pharmacy students in their 3rd professional year to incorporate calculations, therapeutic knowledge, and elements of both basic life support and ACLS in a pharmacotherapeutics laboratory course.
METHODS: Critical care pharmacy faculty staged an ACLS simulation using a mannequin attached to a cardiac monitor. Each simulation involved a group of 6–8 students. Students were expected to identify the arrhythmia and administer cardiopulmonary resuscitation, as well as select and calculate the dose of the appropriate drug therapy. Criteria for patient survival were established to allow every group the possibility of successfully resuscitating the patient. After the activity, students were asked to complete a 4-question survey to assess their opinions regarding this activity.
RESULTS: Of the 230 students (29 groups) that participated, only 9 (31%) groups successfully resuscitated the patient. The most common reason for unsuccessful resuscitation was an inability to perform calculations in a timely manner. Although success in this activity was limited, of the 103 students who responded to the survey, 93% enjoyed the activity and 99% recommended the activity as a routine exercise for the pharmacotherapeutics laboratory course in the future.
CONCLUSIONS: Results from this simulation demonstrate a need not only to teach ACLS topics and accompanying pharmaceutical calculations in a didactic setting, but also to place students in real-life scenarios to enable them to use these important skills. ACLS simulations should be a routine pharmacotherapeutic exercise to assist students with the skills required as a practicing pharmacist.

73. Students' sense of calling and emotional quotient influenced by clinical pharmacist preceptors. Chanuttha Ploylearmsang, *Ph.D.*, Siritree Suttajit, Ph.D., Bhuddhipong Satayavongthip, Ph.D.; Faculty of Pharmacy, Mahasarakham University, Kantaravichai, Maha Sarakham Province, Thailand.

PURPOSE: Sense of calling and emotional quotient (EQ) are important factors for being successful pharmacy practitioners. The objective was to examine the effect of pharmacy education on students' sense of calling and EQ. The effect of pharmacy education included the institutional socialization and the integration during clerkship rotations with clinical pharmacy preceptor.
METHODS: In the academic year of 2005, Pharmacy students of Mahasarakham University (MSU) were surveyed using a 1-year analytical cross-sectional study. Overall, 134 pharmacy students from 4th to 6th years were selected to receive the self-administered questionnaire. The effect of pharmacy education on sense of calling and EQ were analyzed using multiple regression.
RESULTS: A total of 97 (72.4%) usable questionnaires were returned for analysis. Significant factors affecting students' sense of calling were their pride in the pharmacy profession (β=0.150, $p<0.0001$) and the integration with clinical pharmacist preceptors (β=0.252, p=0.045). These two variables accounted for 44.7% of the variance in sense of calling. Students' EQ was also affected by the integration with clinical pharmacist preceptors (β=0.868, p=0.005). This variable accounted for 8.0% of the variance in students' EQ. There was no significant difference of sense of calling and EQ among the 3 study years. The 6th-year students showed the highest level of sense of calling and EQ, whereas the 5th-year students showed the lowest in both variables.
CONCLUSIONS: It was concluded that clinical pharmacist preceptors and the pride in profession were important factors for developing and enhancing students' sense of calling and EQ. Pharmacy schools should take account of these factors and use them as resources for setting the educational plan for their students.

74. Impact of research requirements on pharmacy resident abilities and interests. *Kelly M. Smith, Pharm.D.*, Melody Ryan, Pharm.D., Frank Romanelli, Pharm.D.; University of Kentucky College of Pharmacy, Lexington, KY.

PURPOSE: To assess the impact of residency research requirements on pharmacy resident attitudes towards, experience with and confidence in conducting research.
METHODS: Postgraduate year 1 (PGY1) residents (n=6) from one academic medical center completed a 14-point anonymous survey at residency onset (prior to 5 seminars and required research project) and conclusion. Data included anticipated career paths, prior research experiences/training, and experience and confidence in conducting research (Likert scale; 1=none, 5=extensive experience/mastery). Attitudes towards and experience with research, and the required research experiences' impact on career goals and research ability (1=strongly disagree, 5=strongly agree), were captured.
RESULTS: At baseline, 5 (83.3%) residents had previously conducted research; 3 (50%) had undergone formal research training. At exit, all were pursuing second-year residencies and anticipated obtaining clinical specialist positions with research components. Experiences with and confidence in 10 and 3 of 19 research-related areas, respectively, increased significantly, including: experience in selecting statistical tests (1.2 ± 0.4 baseline mean; 3.2 ± 0.8 exit; p=0.003) and constructing a research manuscript (1.3 ± 0.05; 3.5 ± 0.8; p=0.003), and confidence in developing methods (2.2 ± 0.08; 3.0 ± 0.6; p=0.004) and presenting results in a poster (2.7 ± 1.0; 3.8 ± 0.4; p=0.01). At exit, residents reported the research experience improved their writing skills (6, 100%) and research knowledge (5, 83.3%); 4 (66.7%) reported improvement in poster and verbal presentation and time-management skills. Anxiety about manuscript preparation continued for four (66.7%). Ability to design, execute and report practice/educational research was rated as 3.6 ± 0.55, career goal alteration by the research experience as 3.3 ± 0.82.
CONCLUSIONS: A required project/seminar series improved pharmacy resident experience and confidence in many research areas. Findings will be used to alter the residency research requirements to optimize future residents' research abilities.

75. Evaluation of the effectiveness of a pharmacotherapeutics preparatory program on subsequent exam grades. *Maria C. Foy, B.S., Pharmacy*[1], Andrew Peterson, Pharm.D.[2], Cynthia A. Sanoski, Pharm.D.[2]; (1)Doylestown Hospital, Doylestown, PA; (2)Philadelphia College of Pharmacy, University of the Sciences in Philadelphia, Philadelphia, PA.

PURPOSE: A 4-day preparatory program was offered to Pharm.D. candidates following their second professional year to try to improve student performance and decrease anxiety related to the intensive nature of the 1-year pharmacotherapeutics course delivered in the third professional year. The purpose of this project was to determine whether such a program had an effect on exam grades in the first pharmacotherapeutics course.
METHODS: Thirty-two students electively participated in a pharmacotherapeutics preparatory program (PPP) approximately 2 months prior to the start of the first required pharmacotherapeutics course (PTC). Students who took the PPP were matched to a control (C) group who did not take the course, based on age (± 3 years), grade point average (GPA) (± 10%), and gender. A General Linear Model (GLM) univariate analysis was used to determine whether there was a difference in the overall mean adjusted PTC grade between the PPP and C groups. The model used group as the fixed factor, GPA as the covariate, and age and gender as random factors. The first exam grade in the PTC was also evaluated in the PPP and C groups as a secondary outcome.
RESULTS: Twenty-eight of the 32 students were matched (n=56; 73.2% female; average age = 24.1 ± 3.1 years). The average GPAs for the PPP and C groups were 2.81 ± 0.44 and 2.85 ± 0.46, respectively (p=0.787). The mean adjusted overall PTC grades for the PPP and C groups were 68.3% and 66.8%, respectively (p=0.435). The mean adjusted scores for the first exam in the PTC were 79.0% and 75.2% for the PPP and C groups, respectively (p=0.071).
CONCLUSIONS: When comparing the prep course experimental group with a matched control group, no significant differences were observed in either the overall grade or the first exam grade in the initial, required pharmacotherapeutics course.

76. Assessing the self-learning ability in a third professional year therapeutics course. *Julie A. Brousil, Pharm.D.*, Patrick M. Finnegan, Pharm.D.; St. Louis College of Pharmacy, St. Louis, MO.

PURPOSE: Self-learning is defined as exhibiting intellectual curiosity, taking responsibility for developing abilities, and conducting continual self-assessment of abilities in order to develop and enact a plan to improve

performance. This study evaluated students' performance on self-learning assignments and assessed students' attitudes toward self-learning.
METHODS: Self-learning is an ability outcome that is assessed in the Therapeutics III course in the third professional year. Students, in groups of five, were required to complete two written toxicology cases during the semester, without having received a formal lecture on the topics. Groups were assessed on the accuracy of their responses. Formative and summative feedback was provided to the students after completion of the first and second cases, respectively. A survey was administered to the students before the first case (pre-survey), between the first and second cases (intermediate-survey), and after the completion of the second case (post-survey).
RESULTS: One hundred forty-eight students were enrolled in Therapeutics III in 2005. The class averages on the first and second case were 79.3% and 79.4%, respectively. On the pre-, intermediate-, and post-surveys, the response rates were 93%, 88.5%, and 75.7%, respectively. The pre-survey demonstrated that 71.5% of responders thought that it was very important to be a self-motivated, independent life-long learner. On the intermediate-survey, although 47.3% of responders enjoyed this approach to learning, 26.7% prefer a traditional lecture format. Although 46.4% of responders on the post-survey would like to see self-learning as a component of most courses, 53.6% would not like to see this learning technique used again.
CONCLUSIONS: The students' performance on the self-learning assignments did not change over the course of the semester. The surveys indicated that although a majority of students understand the importance of being a self-motivated, independent life-long learner, when given the opportunity to practice this ability, their attitudes changed.

77. Student opinions about the use of a "peripheral brain" in the therapeutics sequence of a pharmacy curriculum. *Julie A. Brousil, Pharm.D.*, Patrick M. Finnegan, Pharm.D., Alicia B. Forinash, Pharm.D., Suzanne G. Bollmeier, Pharm.D.; St. Louis College of Pharmacy, St. Louis, MO.

PURPOSE: Students have assembled a pocket reference book, "peripheral brain" (PB), to increase opportunities to practice higher-order thinking skills on exams in the therapeutics sequence. There was question as to whether the PB was necessary to achieve this outcome and whether students fully understood the purpose of the PB. For one group, use of the PB was allowed in the second professional year, but not during the third. This study evaluated the same group of students' opinions about the PB both before and after it was removed from the therapeutics sequence.
METHODS: A similar survey was administered to the same group of students after one semester of allowing the PB on exams and after one semester of not allowing the PB on exams. Students could answer yes, no, or not sure to the following: do you view the PB as a valuable learning tool, does the PB enhance your learning of therapeutics, and do you understand the purpose of the PB. The difficulty of the exams was not altered during this transition. Differences were evaluated using Chi-square and Fisher's exact test.
RESULTS: One hundred fifty students were eligible to respond to the survey. During the second and third professional years, 84% and 69% of the students responded, respectively. The results of the survey demonstrate that students' opinions about the PB were altered from the second to the third professional years, respectively, as follows: they view the PB as a valuable learning tool (88% to 68%, p=0.0002); they feel the PB enhances their learning of therapeutics (79% to 56%, p=0.0006); and they understand the purpose of the PB (98% to 90%, p=0.0126).
CONCLUSIONS: Student opinions about the PB were altered after it was removed from the therapeutics sequence. If the PB is reinstated, understanding of its purpose needs to be confirmed.

78E. An interdisciplinary diabetes self-care simulation experience for medical students. L. Brian Cross, Pharm.D., CDE, John E. Delzell, M.D., MSPH, *Andrea S. Franks, Pharm.D., BCPS*; University of Tennessee, Memphis, TN.

Presented at the Annual Predoctoral Education Conference of the Society of Teachers of Family Medicine, Albuquerque, NM, January 2005.

79. Evaluation of a pharmacy school-wide Web-based clinical intervention system. *Margarita DiVall, Pharm.D., BCPS*, Debra Copeland, Pharm.D., Michael Gonyeau, Pharm.D., BCPS; Northeastern University School of Pharmacy, Boston, MA.

PURPOSE: To implement and evaluate a global, electronic clinical intervention system (CIS) to document types and impact of clinical activities of pharmacy preceptors and students during advanced pharmacy practice experiences (APPEs).
METHODS: A faculty-validated clinical intervention form was developed and placed on a secure Web site using Education Management System (EMS) software. All pharmacy students were trained on the use, purpose and methods to appropriately document interventions. Participation in the pilot phase was voluntary for preceptors. Students and preceptors were surveyed at the end of the APPE cycle to assess overall form utility and data utilization.
RESULTS: During an academic year, 83 students at 58 sites (28 community (48%), 23 institutional (40%), 7 ambulatory care (12%)) documented 3,707 interventions. The most common interventions included: new drug for untreated indication (17%); patient/health care provider education (14%); drug information (13%); and inappropriate dose (12%). Ninety-one percent were accepted, and 92% were categorized as clinically significant. Sixty-two percent of interventions were student initiated. Overall, interventions potentially prevented 1,208 adverse drug reactions; 330 medication errors; 1511 had long-term impact. Surveys revealed that preceptors required CIS on 3 or more APPEs; agreed that CIS is important and should be required for all students; and most included intervention reports as part of their annual merit review. Students surveyed reported that most felt well oriented to the CIS, found CIS easy to use and documentation process valuable. However, the majority stated that they would not document their clinical interventions if not required by preceptors.
CONCLUSIONS: Our school-wide system allows students and preceptors to document clinical activities, which can serve a number of purposes, including incorporation into student portfolios, faculty merit, and promotion dossiers. Future use of these data includes illustrating the clinical and economic impact of students/preceptors in establishing new APPE sites for our school.

80. Relationships between undergraduate institution ranking and academic performance in a doctor of pharmacy program. Roger L. White, Pharm.D., *Philip Hall, Pharm.D.*; Medical University of South Carolina, Charleston, SC.

PURPOSE: Undergraduate GPA and PCAT scores are major criteria for admission to Pharm.D. programs. Because applicants may take prerequisite courses from institutions with varying degrees of academic rigor, they may be disadvantaged if they receive a lower GPA from a more competitive program. Thus, consideration of undergraduate institution ranking may improve the ability to predict academic performance in a Pharm.D. program.
METHODS: We evaluated relationships between college ranking and GPAs of 2003-2006 graduates of the MUSC Pharm.D. program. Undergraduate institutions at which these graduates completed prerequisite courses were categorized according to Barron's Profiles of American Colleges (26th edition, 2005) and assigned a ranking as follows: most competitive (MC=5), highly competitive (HC=4), very competitive (VC=3), competitive (C=2), and less competitive (LC=1). The relationships between undergraduate (UG) indices (cumulative UG GPA, PCAT composite percentile, Barron's rankings) and cumulative GPA from each year of the Pharm.D. program (P1-P4, 2003-06 data pooled) were assessed by univariate and multivariate analyses. A $p<0.05$ was considered significant.
RESULTS: Records were available for 167 students from 55 different UG institutions. The number of students per category was: MC=2, HC=79, VC=33, C=43, LC=10. By univariate analysis, UG GPA and PCAT ($p<0.0001$) were associated with MUSC GPA in each year (P1-P4); however, Barron's ranking was only significant for P4 ($p=0.0013$). R^2 values were consistent for UG GPA (0.328-0.355) and PCAT (0.248-0.285) for P1-P3, but lower for P4 (UG GPA=0.0161, PCAT=0.126). Barron's rankings R^2 were low (0.009-0.061), but were highest for P4. With multivariate analysis, only UG GPA and PCAT were significant for P1-P3; however, in P4, only Barron's ranking and UG GPA were significant.
CONCLUSIONS: When UG GPA and PCAT are used, the addition of Barron's ranking improves the relationship with Pharm.D. GPA only in the P4 year. Additional studies are needed to verify these findings.

81. Description of a pharmacist-managed toxicology consult service at the Ottawa Hospital: evaluation of program and impact from an educational perspective. Gisia L. Pisegna, B.Sc.Pharm., Salmaan Kanji, Pharm.D., *Sabrina Natarajan, B.Sc.Pharm.*, Chole Campbell, B.Sc.Pharm., Bob MacLean, B.Sc.Pharm., Céline Corman, M.Sc., Rakesh Patel, MD, Pharm D.; The Ottawa Hospital, Ottawa, ON, Canada.

PURPOSE: The Toxicology Service at The Ottawa Hospital is a unique consult service operated by pharmacy residents 24 hours per day. We conducted a formal evaluation of our consults and the impact of the program from an educational perspective.
METHODS: In the first part of this study, physician opinion was solicited using an informal questionnaire to determine the essential components of an ideal written consult. In the second part of this study, consecutive patients (June 2005–May 2006) for which toxicology consults were sought were prospectively identified. Data pertinent to demographics, overdose etiology, clinical outcome, and written consult components were extracted from medical records. The third part was a Web-based survey designed to collect self-reported values and skills gained from past pharmacy residents who completed the program during the previous 10 years.
RESULTS: Users of the service identified four essential components of the written consult: medication history, overview of toxidrome, severity of overdose and pharmacological treatment recommendations. Fifty-four toxicology consults were conducted over the 1-year period (16% of all

overdoses) and represent a wide variety of overdoses. More than 80% of written consults had 3 of 4 essential components. Greater than 90% of past pharmacy residents found that participation in the program enhanced their confidence, independence, sense of responsibility, communication skills, and ability to work in a stressful environment. Although 61% of past pharmacy residents found it a significant source of stress, 88% felt that their participation did not compromise their learning experience.
CONCLUSIONS: This study describes the diversity of overdoses for which the Toxicology Program is consulted at The Ottawa Hospital and identifies essential components of the written consult. Most past pharmacy residents felt that participation in the program was an important part of the residency and that the skills and values developed were useful in subsequent careers.

82. Impact of formal feedback on exam grades during two consecutive semesters of therapeutics. *Zachary A. Stacy, Pharm.D., BCPS*, Alicia B. Forinash, Pharm.D., BCPS, CCD, Suzanne G. Bollmeier, Pharm.D., BCPS, AE-C; St. Louis College of Pharmacy, St. Louis, MO.

PURPOSE: This retrospective study analyzed the effect of case presentation feedback on exam grades in Therapeutics I (TI) and Therapeutics II (TII).
METHODS: Upon entering the Therapeutics sequence, students form groups consisting of five students. These groups work together to complete patient cases highlighting specific topic areas. Patient cases are divided into five sections: assess, evaluate, select and recommend, monitor, and educate. Students enrolled in TI (second professional year of Fall 2005) presented a different section of a patient case each week during discussion and received informal verbal formative feedback and no summative feedback. Students enrolled in TII (second professional year of Spring 2006) presented one entire case once during the semester and received formal written formative and summative feedback. Exams in both courses were structured similarly with a multiple choice content portion (50%) and patient case application portion (50%). The primary outcome compared overall final exam scores in both courses. Secondary outcomes included a comparison of content, application, and differences in content and application scores on all exams for both courses. A paired student-t test was used for statistical analysis.
RESULTS: This analysis included 163 students co-enrolled in TI and TII. Overall final exam grades were significantly improved with formative and summative feedback (60.0% vs. 63.4%, respectively; $p<0.001$). Content (37.2% vs. 33.7%; $p<0.001$) and application (33.4% vs. 35.3%; $p<0.001$) scores were significantly different in TI and TII, respectively. The difference in content and application scores (3.8 vs. -1.8, respectively; $p<0.001$) demonstrated that students performed better on content in T1 and application in T2.
CONCLUSIONS: Performance on application sections and overall final exam grades significantly improved when students received formal formative and summative feedback.

83. A pilot study to assess the long term effectiveness of a community based smoking/tobacco cessation training program for healthcare practitioners: a 3-month interim analysis. *Timothy C. Chen, Pharm.D.*[1], Pamela Matten, R.N., O.C.N.[2], Dana Rutledge, R.N., Ph.D.[2], Eunice P. Chung, Pharm.D.[1], Siu-Fun Wong, Pharm.D.[1]; (1)Western University of Health Sciences, College of Pharmacy, Pomona, CA; (2)St. Joseph Hospital of Orange, Orange, CA.

PURPOSE: A tobacco cessation training program (based on the Rx for Change program) for practitioners with an initial focus on inpatient nurses was initiated. To ensure the effectiveness of a tobacco cessation training program, this study was developed to determine whether or not the practitioners retain the objectives of the training program over a 12 month duration.
METHODS: A single center, prospective outcomes trial where participants will complete pre-, post-, and follow-up surveys at 3, 6, and 12 months. The study will evaluate the participants' self-rated abilities in: the first 4 of 5 key competency facets of smoking cessation (Ask, Advise, Assess, Assist) and overall ability in cessation counseling at baseline, 3-, 6-, and 12- months. Five-point scales (1 = poor, 2 = fair, 3 = good, 4 = very good, 5 = excellent) will be used. Paired samples t-test will be used to compare non-parametric scaled scores where appropriate.
RESULTS: Twenty participants completed the first training session. Sixteen completed pre- and post- surveys. Six surveys at 3 month were completed. Pre- and post- self-reported abilities improved significantly for Advise (2.88 vs 4.06, $p<0.001$), Assess (2.81 vs 3.88, $p<0.001$) and Assist (2.33 vs 3.75, $p<0.001$). No difference was seen for Ask, and the reported mean scores of Advise, Assess, Assist were 3.83, 3.67, 3.6 respectively for the 3-month study. Mean scores on overall counseling ability for pre-, post-, and at 3 months were 2.69, 4.25, and 3.0 respectively.
CONCLUSIONS: The training program significantly improved participants' perceived overall ability and key facets of tobacco cessation immediately following the training program. At 3 months, trends for improvement were also seen. Strategies to improve compliance of follow-up surveys will be conducted. Linkable surveys and a knowledge assessment will be used in future training sessions.

84. Gender differences in self-learned therapeutics material. *Alicia B. Forinash, Pharm.D., BCPS, CCD*, Suzanne G. Bollmeier, Pharm.D., BCPS, AE-C, Claude J. Gaebelein, Ph.D.; St. Louis College of Pharmacy, St. Louis, MO.

PURPOSE: This retrospective analysis explored differences in self-learning (SL) performance as a function of gender.
METHODS: Second-year pharmacy students completed two SL tasks as part of a therapeutics experience. Students independently completed two cases on unfamiliar material. Pre- and post-quizzes were administered prior to each SL task. Students were surveyed prior to these tasks concerning SL and valuing feedback.
RESULTS: Females performed significantly higher than males on the first self-learning pre-quiz (8.5 vs 7.9 out of 10, respectively; $p=0.01$) and on the post-quiz (9.6 vs. 9.1 out of 10, respectively; $p=0.001$); however, on the case assignment no significant difference occurred (female 14.5 vs. male 12.8 out of 20; $p=0.06$). There was no significant difference in performance on the second SL task or quizzes. The survey indicated potential gender differences in SL: 1) 27% of males categorized themselves as a confident self learner vs. 16% females, 2) 28% of males look up unknown material vs. 43% of females, 3) 20% of males use feedback for self improvement vs. 34% of females, 4) 50% of males use keys to correct work vs. 62% of females. Ten percent of males were more concerned about getting a pharmacy degree than learning new things compared with only 2% of women.
CONCLUSIONS: There may be a significant gender difference regarding the development of SL skills. This analysis shows that females performed better on the initial self-learning quizzes despite ranking themselves as less confident. Females also report the use of SL skills, such as using feedback and keys to improve, more often than males. Men rated themselves as more confident but performed lower than females initially. Further studies are needed to define how these possible gender differences in SL affect overall student learning.

Endocrinology

85E. Colesevelam HCl improves glycemic control in patients with type 2 diabetes (T2DM): a pilot study. *Sherwyn L. Schwartz, M.D.*[1], Franklin Zieve, M.D.[2], Marcia Kalin, M.D.[3], Michael Jones, Ph.D.[4], William Bailey, Pharm.D.[4]; (1)Diabetes & Glandular Disease Research Associates, San Antonio, TX; (2)Hunter Holmes McGuire VA Medical Center, Richmond, VA; (3)Memorial Sloan-Kettering Cancer Center, New York, NY; (4)Daiichi Sankyo, Inc., Parsippany, NJ.

Presented at the Annual Meeting of the American Diabetes Association, Washington, D.C., June 9-13, 2006.

86E. Colesevelam HCl reduces postprandial glucose in patients with type 2 diabetes mellitus (T2DM). *Franklin Zieve, M.D.*[1], Sherwyn L. Schwartz, M.D.[2], Marcia Kalin, M.D.[3], Michael Jones, Ph.D.[4], Isabelle Raymond-Shaw, Pharm.D.[5]; (1)Hunter Holmes McGuire VA Medical Center, Richmond, VA; (2)Diabetes & Glandular Disease Research Associates, San Antonio, TX; (3)Memorial Sloan-Kettering Cancer Center, New York, NY; (4)Daiichi Sankyo, Inc., Parsippany, NJ; (5)Daiichi Sankyo, Inc., Parsippany, NJ.

Presented at the Annual Meeting of the American Diabetes Association, Washington, D.C., June 9-13, 2006.

87E. Lipid-lowering effects of colesevelam hydrochloride (HCl) in patients with type 2 diabetes. *Marcia Kalin, M.D.*[1], Franklin Zieve, M.D.[2], Sherwyn L. Schwartz, M.D.[3], Michael Jones, Ph.D.[4], Angelica Munoz, Pharm.D.[4]; (1)Memorial Sloan-Kettering Cancer Center, New York, NY; (2)Hunter Holmes McGuire VA Medical Center, Richmond, VA; (3)Diabetes & Glandular Disease Research Associates, San Antonio, TX; (4)Daiichi Sankyo, Inc., Parsippany, NJ.

Presented at the Annual Meeting of the American Diabetes Association, Washington, D.C., June 9-13, 2006.

88. Colesevelam HCl for the management of type 2 diabetes mellitus: rationale for a clinical trial program. *William Bailey, Pharm.D.*, Michael Jones, Ph.D., Stacey Abby, Pharm.D, CED; Daiichi Sankyo, Inc., Parsippany, NJ.

PURPOSE: Type 2 diabetes mellitus (T2DM) is a well-known cardiovascular risk factor, and there remains a need for additional therapeutic options to help clinicians manage this increasingly prevalent disease. Colesevelam is a non-absorbed agent specifically designed to bind bile acids and is currently

indicated to be used alone or in combination with statins as adjunctive therapy for the reduction of elevated LDL-C. The objective of this analysis was to assess the effect of colesevelam on fasting plasma glucose (FPG) concentration.
METHODS: A post-hoc analysis was conducted on the colesevelam 24-week pivotal efficacy and safety data in primary hypercholesterolemia subjects reported by Insull (2001). Subjects included in this post-hoc analysis were either diagnosed with diabetes or not diagnosed with diabetes but met ADA criteria for diabetes, based on baseline FPG ≥ 126 mg/dL.
RESULTS: Due to the small number of subjects meeting the criteria for diabetes, subjects receiving the two highest doses of colesevelam 3.8 g or 4.5 g daily were combined (n=12). This group had a mean baseline FPG 140 mg/dL which was reduced to 122 mg/dL, a 12% reduction from baseline (p=0.005) after 24 weeks treatment with colesevelam. In comparison, subjects receiving placebo (n=5) had a mean baseline FPG 140 mg/dL and had no change in FPG after 24 weeks.
CONCLUSIONS: Following the findings from this exploratory analysis that suggested colesevelam could improve glycemic control, a 12-week, prospective, double-blind, placebo-controlled, pilot study was conducted and later demonstrated colesevelam's A_{1c} lowering effect. Subsequently, a clinical trial program with three well-designed Phase III studies was initiated to assess the A_{1c} lowering effect of colesevelam in uncontrolled T2DM subjects on stable insulin and/or oral antidiabetic (OAD) agents. These studies will be used to help determine the approved use of colesevelam as an unexpectedly novel OAD agent.

89. Safety tolerability of colesevelam HCl in patients with type 2 diabetes. *William Bailey, Pharm.D.*[1], Sherwyn L. Schwartz, M.D.[2], Franklin Zieve, M.D.[3], Marcia Kalin, M.D.[4], Michael Jones, Ph.D.[1]; (1)Daiichi Sankyo, Inc., Parsippany, NJ; (2)Diabetes & Glandular Disease Research Associates, San Antonio, TX; (3)Hunter Holmes McGuire VA Medical Center, Richmond, VA; (4)Memorial Sloan-Kettering Cancer Center, New York, NY.

PURPOSE: Medical treatment of type 2 diabetes mellitus (T2DM) is often complicated by poor drug tolerability. Elderly patients or those with comorbidities compose a large population of "difficult-to-treat" patients in whom safe and well-tolerated treatment is essential. Clinical studies in primary hypercholesterolemia have established that colesevelam HCl is safe and well tolerated, with favorable adverse event and drug-drug interaction profiles.
METHODS: The safety and tolerability of colesevelam in T2DM were evaluated in a prospective, randomized, double-blind, placebo-controlled, parallel-group pilot study, consisting of 4 weeks of placebo run-in followed by 12 weeks of active treatment. Eligibility criteria included a diagnosis of T2DM, HbA1C 7.0%–10.0%, inclusive, at randomization, and at least 3 months of treatment with a stable dose of sulfonylurea, metformin or their combination. Eligible patients were randomized to colesevelam (3.75 g/day) or placebo (6 tablets/day). Sixty-five patients (31 receiving colesevelam and 34 receiving placebo) were randomized; 59 (27 receiving colesevelam and 32 receiving placebo) completed the study.
RESULTS: Treatment emergent adverse events (TEAEs) were experienced by 64.5% of colesevelam and 64.7% of placebo-treated patients. Nine (29.0%) patients in the colesevelam and 3 (8.8%) in the placebo group experienced a drug-related TEAE. For both groups, the severity of most TEAEs was mild-to-moderate, involving gastrointestinal, metabolic or nutritional disorders. No patients in the colesevelam group experienced a serious AE. Two (6.5%) patients in the colesevelam and 1 (2.9%) in the placebo group withdrew due to clinical or laboratory TEAEs. No clinically meaningful changes in safety laboratory parameters, vital signs, or physical findings were observed for either treatment group overall. Only 3 patients experienced SAEs during run-in or while on treatment; none were determined by the investigator to be related to the study medication.
CONCLUSIONS: Compared with placebo, colesevelam represents a safe and well-tolerated treatment option in patients with T2DM.

90. Evaluation of the relationship between body composition, systemic inflammatory markers, and bone mineral density in men with severe chronic obstructive pulmonary disease. *Sheryl F. Vondracek, Pharm.D.*, Connie Valdez, Pharm.D., Norbert F. Voelkel, M.D., Michael T. McDermott, M.D.; University of Colorado Health Sciences Center, Denver, CO.

PURPOSE: To identify the relationship between body composition, various systemic inflammatory markers, and bone mineral density (BMD) in men with severe, stable chronic obstructive pulmonary disease (COPD).
METHODS: Cross-sectional pilot study of 25 men, ≥45 years of age, with severe, stable COPD (forced expiratory volume in 1 sec [FEV1] <50% predicted). The following were obtained on all subjects: (1) dual energy x-ray absortiometry for determination of body composition and BMD; (2) serum testosterone, estradiol, and 25-OH vitamin D; (3) bone turnover markers: serum osteocalcin and urinary N-telopeptide; and (4) serum concentrations of various inflammatory markers (e.g., tumor necrosis factor-alpha). This report summarizes the results evaluating the relationship between body composition and BMD.
RESULTS: Twenty-four subjects completed the study. The average age was 65 ± 9 years. The average FEV1% predicted was 33 ± 11%. Nineteen subjects (79%) had low BMD by T-score; 8(33%) had osteoporosis and 11(46%)had osteopenia. Subjects with osteoporosis(n=8) compared with subjects without osteoporosis (n=16) were on average 5 years younger, had a significantly lower FEV1 % predicted (26 ± 10% vs. 36 ± 11%; p=0.03) and a lower total body mass (66.4 kg ± 7.0 kg vs. 83.8 kg ± 22.1 kg; p=0.0096). Subjects with osteoporosis also had higher % predicted thoracic gas volumes (210 ± 45 vs. 176 ± 41) and % predicted residual volumes (256 ± 81 vs. 197 ± 67); however, these were not statistically significant. When considering all COPD subjects, total lean body mass (spearman r=0.7167; p<0.0001), and total body fat (spearman r=0.535; p<0.0071) were significantly positively correlated with total body BMD.
CONCLUSIONS: Men with severe COPD have a high incidence of osteoporosis. Reduced lean body mass and total body fat is significantly correlated with reduced total body BMD in this population.

91. Screening by pharmacists for prediabetes in patients at high risk for diabetes and heart disease. *Brian K. Irons, Pharm.D.*[1], Kathleen A. Snella, Pharm.D.[2], Ann E Canales, Pharm.D.[1], Rebecca B Sleeper, Pharm.D.[1], Shane Greene, Pharm.D.[1], Arthur A Nelson, Ph.D.[1]; (1)Texas Tech School of Pharmacy, Lubbock, TX; (2)UMKC School of Pharmacy, Columbia, MO.

PURPOSE: To identify patient characteristics that correlate with impaired fasting glucose (IFG), a form of prediabetes, in patients at high risk for diabetes and heart disease. Subjects were screened by pharmacists in pharmacies and non-health care settings.
METHODS: Post-hoc analysis from a multicenter, prospective, observational trial where pharmacists screened patients for blood glucose, total cholesterol, high-density lipoprotein cholesterol (HDL-C), and blood pressure. Screened patients had one or more of the following risk factors: first-degree relative with diabetes, age 55 years or older, obesity, or previous diagnosis of either dyslipidemia or hypertension. Of the 782 subjects screened as part of the original project, 299 were fasting. Subjects with fasting plasma glucose levels < 100 mg/dL were compared with subjects with IFG. The student t-test was used to compare ratio data and chi-square statistics were used to analyze nominal data.
RESULTS: Of those screened, 121 (15%) of subjects on a single occasion had glucose levels consistent with IFG. Those participants were more likely to be male (p=0.039), have a body mass index > 30 kg/m^2 (p=0.004), a higher diastolic blood pressure (DBP) (p=0.020), or a lower HDL-C (p=0.002) compared with patients with normal fasting blood glucose (n=139). There were no statistical differences between the two groups regarding age greater than 65 years, ethnicity, screening site, and those with a first-degree relative with diabetes.
CONCLUSIONS: Screening by pharmacists for prediabetes (IFG) in those at risk for diabetes and heart disease identifies patients who may require additional lifestyle modification to limit progression from IFG to type 2 diabetes. Patients who are overweight, male, have increased DBP, and low HDL-C may be at a higher risk for IFG than those with other known risk factors for diabetes.

92E. A simple predictor of Vitrase® efficacy for BCVA improvement in diabetic patients with severe vitreous hemorrhage. Abdhish R. Bhavsar, M.D.[1], Maurice B. Landers III, M.D.[2], Ronald K. Pearson, Ph.D.[3], Alan M. Hochberg, BSEE[3], *Timothy R. McNamara, Pharm.D.*[4], James A. Gow, M.D.[4], Lisa R. Grillone, Ph.D.[4]; (1)Retina Center, PA and Phillips Eye Institute, Minneapolis, MN; (2)UNC Ophthamology Department, Chapel Hill, NC; (3)Prosanos Corporation, Harrisburg, PA; (4)ISTA Pharmaceuticals, Inc., Irvine, CA.

Presented at the Annual Meeting of the Association for Research in Vision and Ophthalmology, Fort Lauderdale, FL, April 30-May 4, 2006.

93E. Preliminary evaluation of an early surrogate marker for successful laser treatment in ovine hyaluronidase-treated subjects with diabetes and severe vitreous hemorrhage. Edgar L. Thomas, M.D.[1], Lisa R. Grillone, Ph.D.[2], *Timothy R. McNamara, Pharm.D.*[2], James A. Gow, M.D.[2], Alan M. Hochberg, BSEE[3], Ronald K. Pearson, Ph.D.[3]; (1)Retina-Vitreous Associates Medical Group, Beverly Hills, CA; (2)ISTA Pharmaceuticals, Inc., Irvine, CA; (3)Prosanos Corporation, Harrisburg, PA.

Presented at the Federal Drug Administration Science Forum, Washington, D.C., April 18-20, 2006.

94. The influence of race and ethnicity on patient access to thiazolidinediones for the treatment of type 2 diabetes. *Christina L. Aquilante, Pharm.D.*, Weiming Zhang, M.S., Marianne McCollum, Ph.D.; Department of

Clinical Pharmacy, University of Colorado School of Pharmacy, Denver, CO.

PURPOSE: Thiazolidinediones (TZDs) are effective agents for the treatment of type 2 diabetes (DM). The objective of this retrospective study was to determine whether access to TZDs differs between Whites, Blacks, and Hispanics.
METHODS: Data for adults (age > 18 years) were obtained from the 2003 Medical Expenditure Panel Survey, a nationally representative database. Diabetes was defined by ICD-9-CM codes or self-reported DM. Race/ethnic groups were defined as: White/not-Hispanic; Black/not-Hispanic; or Hispanic. TZD access was defined as at least one prescription of rosiglitazone or pioglitazone (alone or in combination with other antidiabetic therapy). Covariates included insurance status (insured versus uninsured), sex, age, and having a usual source of care (yes/no). Categorical data were compared by χ^2 tests. Logistic regression was used to determine the joint effect of covariates on access to TZDs.
RESULTS: Of 1757 persons with DM identified as Whites, Black, or Hispanics, the estimated proportions were 0.70, 0.17, and 0.13, respectively. The number of patients with DM who had access to TZDs was 362. In univariate analyses, the estimated proportion of patients who had access to TZDs did not differ significantly between Whites, Blacks, and Hispanics (0.24, 0.20, and 0.22, respectively; p=0.33). Access to TZDs was greater in patients with insurance versus those without insurance (p=0.03), but did not differ significantly by race, sex, or having a usual source of care. In logistic regression analysis, race/ethnicity was not a significant predictor of access to TZDs (p=0.53). In the adjusted analyses, patients without a usual source of care were less likely to have access to TZDs compared with those with a usual source of care (p=0.016).
CONCLUSIONS: These data suggest that access to TZDs does not differ based on race/ethnicity. Educational efforts targeting persons with DM should stress the importance of obtaining and maintaining a primary care provider.

95. Improved A1c, blood pressure, and lipid control and assessment of diabetic patient satisfaction of clinical pharmacy services. *Alicia B. Forinash, Pharm.D., BCPS, CCD*[1], Mounir Shenouda, M.D.[2], Todd A. Armstrong, Pharm.D., BCPS[3]; (1)St. Louis College of Pharmacy, St. Louis, MO; (2)Fairview Heights Medical Group, Fairview Heights, IL; (3)Pfizer, Inc., St. Louis, MO.

PURPOSE: The purpose of this project was to measure the impact of clinical pharmacy diabetic services on hemoglobin A1c (A1c), blood pressure (BP), and lipid panels, as well as assess patients' satisfaction with these services.
METHODS: All new and referred diabetic patients who had a visit with clinical pharmacy services from July 2004 – June 2005 were included in this retrospective analysis. Baseline and most recent A1c, BP, and fasting lipid panels were obtained from the patients' electronic medical records. A satisfaction survey for pharmacy services was designed to address diabetes services and mailed to all patients. This one-page form allowed patients to rate satisfaction on a five-point Likert scale, provide basic demographic data, and number of pharmacy visits for diabetes in that year. Both HIPAA compliant data collection forms were scanned using TELEforms scan technology into an Access database and then imported into Microsoft Excel and SPSS (version 14) for analysis.
RESULTS: One hundred sixty-six patients with a mean age of 61 years old (range 28–88) were seen a mean of 2.4 visits, and 68 (40%) satisfaction surveys were returned. A significant reduction in mean A1c (8.01 to 7.18%, p<0.001) LDL (97 to 87.1 mg/dL, p<0.02), total cholesterol (175 to 162 mg/dL, p<0.01), TG (155 to 136 mg/dL, p<0.01), systolic (136 to 131 mm Hg, p<0.001), and diastolic BP (78 to 75 mm Hg, p<0.002) occurred from pre- to post-pharmacy visits, respectively. ADA goal attainment also improved for A1c (p<0.001), LDL, and BP. Of the surveyed patients, 95% were willing to recommend clinical pharmacy service to others, and 60% were willing to pay for the visits.
CONCLUSIONS: Mean A1c, BP, and lipid parameters, as well as the number of diabetic patients achieving goals of these parameters significantly improved after pharmacy interventions. Further studies are still needed to determine correlation of patient satisfaction and goal attainment.

Gastroenterology

96. Administering lansoprazole as a 2-minute intravenous injection provides a similar pharmacokinetic, pharmacodynamic, and safety profile as a 30-minute infusion. *John W. Devlin, Pharm.D.*[1], David C. Metz, M.D.[2], Majid Vakily, Ph.D.[3], Stuart Atkinson, M.D.[3], Eric Lloyd, M.S.[3]; (1)Northeastern University, Boston, MA; (2)University of Pennsylvania, Philadelphia, PA; (3)TAP Pharmaceutical Products Inc., Lake Forest, IL.

PURPOSE: The ability to administer intravenous (IV) lansoprazole as a 2-min injection rather than over 30 min may offer potential advantages. We compared the pharmacokinetics, pharmacodynamics, and safety of an investigational formulation of IV lansoprazole 30 mg infused over 30 min vs a 2-min injection for 7 days.
METHODS: In this randomized, crossover study, 38 healthy subjects were sequentially administered: lansoprazole 30 mg/10 mL 0.9% NaCl (NS) as a 2-min injection, a 10-mL NS placebo as a 2-min injection, or lansoprazole 30 mg/60 mL NS as a 30-min infusion. A five-day washout separated regimens. For each regimen, blood samples were obtained for pharmacokinetic analysis on days 1 and 7; 24-h intragastric pHmetry was performed on day 1. Safety was evaluated daily.
RESULTS: As expected, the mean peak plasma concentration (C_{max}) of lansoprazole was approximately 2-fold higher after the 2-min injection compared with the 30-min infusion on days 1 (3038 vs 1301 ng/mL) and 7 (2816 vs 1391 ng/mL). On days 1 and 7, the 90% confidence intervals for the ratio of the *AUCs* for the 2 lansoprazole regimens fell within the 80%–125% range, indicating similar systemic exposures. Analysis of integrated gastric acidity revealed significantly greater acid suppression with the 2-min injection during the 1st hour after administration ($p \leq 0.05$), possibly because of the higher C_{max}. The 24-hour integrated gastric acidity was similar for both regimens. The mean percentages of time the 24-hour intragastric pH was > 4 were 53%, 47%, and 12% for the lansoprazole 2-min, 30-min, and placebo regimens, respectively. All 3 regimens had similar safety profiles. All treatment-related adverse events were mild; the most common were injection-site and infusion-site reactions.
CONCLUSIONS: An investigational formulation of lansoprazole 30-mg IV administered as a 2-min injection demonstrated a pharmacokinetic, pharmacodynamic, and safety profile similar to that of a 30-min infusion.

97. Gastrointestinal transit of solid oral dosage forms: imaging studies using Magnetic Marker Monitoring technique. *Henning H. Blume, Prof., Dr.*[1], Maria Anschütz, B.Sc.[1], Katja Schmücker, B.Sc.[1], Barbara S. Schug, Dr.[1], Jens Haueisen, Prof.Dr.-Ing.[2], Werner Weitschies, Prof.Dr.[3]; (1)SocraTec R&D Oberursel, Germany; (2)Technische Universität Ilmenau, Ilmenau, Germany; (3)Ernst-Moritz-Arndt-Universität Greifswald, Greifswald, Germany.

PURPOSE: Aim of this study was to compare in-vivo performance and intestinal drug delivery of essentially similar enteric-coated sulfasalazine tablets. Magnetic Marker Monitoring (MMM) was used to visualize gastrointestinal transit and tablet disintegration in the intestine. Gastric residence, intestinal transit, and colonic arrival should be compared and correlated with plasma profiles of sulfasalazine and its metabolite sulfapyridine.
METHODS: This open-label, randomized, 2-period crossover study was performed in six healthy male volunteers. All subjects received both products in fasted state. Prior to administration, tablets were magnetically marked by incorporation of 5 mg of black iron oxide (E172) and subsequent magnetization. This procedure did not affect biopharmaceutical properties. Monitoring was performed in a magnetically shielded room. Transit and disintegration of the tablets were localized by measuring magnetic flux density using very sensitive sensors (SQUIDs). Plasma concentrations of sulfasalazine and sulfapyridine were determined using a validated HPLC procedure with MS/MS detection.
RESULTS: Gastric residence times were comparable for both products (32.5 min vs. 40 min) whereas intestinal transit differed with 190 min and 289 min, respectively. Disintegration of the tablets was observed either in terminal ileum or colon. Onset of sulfasalazine absorption (lag-times of 105 and 130 min, respectively) could be correlated with gastric emptying and tablet disintegration monitored by MMM. As expected, first sulfapyridine concentrations in plasma were obtained with certain delay (lag-times: 303 min vs. 295 min) due to necessary cleavage of sulfasalazine by intestinal bacteria.
CONCLUSIONS: MMM is an appropriate technique to visualize gastro-intestinal transit and localize intestinal drug delivery of solid oral dosage forms. Differences in in-vivo performance could be easily characterized. Sulfasalazine and sulfapyridine plasma profiles could be correlated with MMM findings. Both investigational products showed similar in-vivo performance with comparable rate and extent of the drug delivery.

98. Is continuous intravenous proton pump inhibitor therapy needed after dndoscopic treatment of high-risk bleeding peptic ulcers? *J. Drew Zimmer, R.Ph.*[1], Scott T. Micek, Pharm.D.[1], Chandra Prakash, M.D.[2]; (1)Barnes-Jewish Hospital, St. Louis, MO; (2)Washington University School of Medicine, St. Louis, MO.

PURPOSE: The incidence of recurrent bleeding in high-risk peptic ulcers after hemostasis via endoscopic intervention ranges from 5%–50%. The objective of this study was to compare re-bleeding rates in patients managed with continuous intravenous or intermittent proton pump inhibitor (PPI) therapy after successful endoscopy.
METHODS: A retrospective study of gastric and duodenal ulcers proven by esophagogastroduodenoscopy (EGD)conducted at Barnes-Jewish Hospital from 2004-2005. High-risk peptic ulcers (spurting/oozing, visible vessel, adherent clot or pigmented material) with hemostasis by either injection of

epinephrine and/or coagulation via heater probe were included. Patients had at least 48 hours of PPI therapy and remained in the hospital for 72 hours after successful EGD. Primary end point was re-bleeding within 7 days of successful endoscopy. Re-bleeding was defined by repeat endoscopy or a drop in hemoglobin of 2 g/dL from the peak level measured after EGD.
RESULTS: 122 patients were included in the analysis (gastric, n=71; duodenal, n=51). The overall incidence of re-bleeding was 34.4% within 3–7 days of successful EGD. 34 patients were initially managed with continuous IV PPI, 88 with intermittent PPI. The re-bleeding rate was 41.2% (n=14) in the continuous IV PPI group and 31.8% (n=28) in the intermittent PPI group (p=0.329). The median (interquartile range) number of packed red blood cells transfused post-EGD was 2 (0-3.75) units in the continuous IV PPI group and 2 (0-3) units in the intermittent group (p=0.539). Eight patients subsequently underwent surgery for refractory bleeding (n=5 continuous IV PPI, n=3 intermittent PPI; p=0.024).
CONCLUSIONS: After successful EGD intervention, recurrent bleeding remained high despite use of parenteral PPI. The re-bleeding rate and median units of packed red blood cells transfused was not statistically different between the two groups.

Geriatrics

99. Underuse of prophylaxis for opioid induced constipation in elderly long long-term care residents. *Ellina K. Max, Pharm.D.*[1], Ilene H. Zuckerman, Pharm.D., Ph.D.[2], Jose J. Hernandez, R.Ph., M.P.H.[2], Deborah A. Sturpe, Pharm.D.[2]; (1)Brigham & Women's Hospital, Boston, MA; (2)University of Maryland School of Pharmacy, Baltimore, MD.

PURPOSE: Opioid-induced constipation is a preventable adverse effect; therefore laxative prophylaxis is recommended for patients taking opioids. Our objective was to determine national estimates of laxative use, with and without concurrent opioid use, in the long-term care population (LTC) and to determine factors associated with the use of laxatives among residents receiving opioids.
METHODS: The study population was derived from the 2001 Medicare Current Beneficiary Survey (MCBS), a comprehensive source of health information of the entire spectrum of Medicare beneficiaries. Patients ≥ 65 years of age residing in nursing homes were included in the analysis. Information from the Medication Administration Records, which provides information on medications prescribed and administered for each patient, was available for the LTC sample. Monthly and annual measures of laxative and opioid usage were developed to estimate prevalence of drug use in the LTC population. Multivariable logistic regression analysis was used to determine factors associated with the use of laxatives among residents receiving opioids.
RESULTS: Among our sample of 867 MCBS beneficiaries, 32.4% received opioids at some time during 2001. Only 66.2% of patients on opioids also received a laxative at any time of the year, and the mean monthly prevalence of concurrent use was only 55%. Results of the multivariable analysis indicated that white, female and married patients respectively spend 226% ($p<0.007$), 52% ($p<0.008$), and 39% ($p<0.02$) more months with both a laxative and opioid prescription than their non-white, male, unmarried counterparts. No association was found between prophylaxis and medical co-morbidities or functional status.
CONCLUSIONS: Although laxative use is recommended for patients taking opioids, not all LTC patients receive this care. As a result, patients may experience constipation. Because functional status and medical co-morbidites were not associated with prophylaxis, LTC facility factors may play a role. Future research should examine such associations.

100E. Quality of life and safety with transdermal oxybutynin in patients 85 years and older with overactive bladder: results from the MATRIX study. Ruth A. Hamad, M.D.[1], Roger R. Dmochowski, M.D.[2], *Naomi V. Dahl, Pharm.D.*[3], MATRIX Investigators[3]; (1)Private Practice, Glendora, CA; (2)Dept of Urology, Vanderbilt University, Nashville, TN; (3)Watson Laboratories, Morristown, NJ.

Presented at the Annual Meeting of the American Geriatrics Society, Chicago, IL, May 3–7, 2006.

101. Risk for delirium associated with psychotropic medications in nursing home residents with and without dementia. *Lisa C. Hutchison, Pharm.D., M.P.H.*, Song H. Hong, Ph.D.; University of Arkansas for Medical Sciences College of Pharmacy, Little Rock, AR.

PURPOSE: The aims were to determine the risk for delirium in nursing home (NH) residents with dementia compared with NH residents without dementia and identify whether exposure to psychotropic medications is associated with increased risk for delirium in NH residents with dementia compared with residents without dementia.
METHODS: The study uses a historical cohort design from a database of residents from Beverly Enterprises NHs. 500 residents with dementia and 500 residents matched for age without dementia were randomly selected from the database. Information from the Minimum Data Set (MDS), demographic data, and diagnoses were analyzed.
RESULTS: The study cohort was 70.9% female, 84.3% white, and 11.7% black; the mean age was 83.9 years. Delirium was noted in 5% of residents on the admission MDS completed within 7 days of admission (MDS-7D); 13.1% had delirium within 1 year of admission (MDS-1Y). Residents with dementia were more likely to have an assessment of delirium on MDS-7D than those without dementia (6.6% vs. 3.4%, p=0.02). This difference was not seen on MDS-1Y (15.0% vs. 11.2%, p=0.08). Exposure to psychotropic drugs occurred in 72.7% of the cohort. Those with dementia were more likely to be exposed to psychotropic medications (80.0% vs. 65.4%, p=0.0001). In residents without dementia, those exposed to psychotropic drugs were more likely to have delirium noted on MDS-1Y than those not exposed to psychotropic drugs (14.4% vs. 5.2%, p=0.002). However, in residents with dementia, the difference was not significant (11.0% vs. 16%, p=0.21).
CONCLUSIONS: The risk for delirium at the time of admission to the NH and exposure to psychotropics is greater in NH residents with dementia than in residents without dementia. However, in residents without dementia, those with exposure to psychotropic medications are more likely to have delirium assessed within 1 year of admission.

102. Investigation of a pharmacist intervention on serum 25-hydroxyvitamin D levels in geriatric outpatients. *Joseph P. Vande Griend, Pharm.D.*[1], Sunny A. Linnebur, Pharm.D.[1], J. Mark Ruscin, Pharm.D.[1], Sheryl F. Vondracek, Pharm.D.[1], Pamela Wolfe, M.S.[2], Michael T. McDermott, M.D.[2]; (1)University of Colorado Health Sciences Center, School of Pharmacy, Denver, CO; (2)University of Colorado Health Sciences Center, School of Medicine, Denver, CO.

PURPOSE: This study evaluated the effect of a clinical pharmacist educational intervention on serum 25-hydroxyvitamin D levels in geriatric outpatients insufficient in vitamin D.
METHODS: Eighty subjects age 65–89 years from the University of Colorado Hospital Seniors Clinic were enrolled 12/05–1/06. Baseline vitamin D and parathyroid hormone (PTH) levels were obtained. Deficient subjects (vitamin D < 12 ng/mL) and those with abnormal PTH levels were excluded. Subjects who were vitamin D insufficient (12–31 ng/mL) were randomized to receive a short educational intervention or no intervention. The intervention instructed subjects to obtain 1200 IU of vitamin D from dietary and supplementary sources. Subjects returned in 12 weeks to reevaluate vitamin D and PTH levels.
RESULTS: Twenty-three subjects received the intervention and 22 did not. At 12 weeks, vitamin D levels in the intervention group increased from a mean (± SD) of 23.5 (± 5.0) to 30.4 (± 6.3) ng/ml. Vitamin D levels in the non-intervention group increased from a mean of 22.8 (± 5.4) to 26.9 (± 6.2) ng/ml. The difference in change from baseline between the groups did not reach statistical significance (p=0.068). However, 12 subjects (55%) in the intervention group achieved sufficient vitamin D levels, compared with five subjects (24%) in the non-intervention group (p=0.039). The change in mean PTH levels trended towards significance with a decrease from 48.6 (± 13.5) to 37.5 (± 22.3) pg/mL in intervention subjects compared with 49.6 (± 15.5) to 46 (± 20.7) pg/mL in nonintervention subjects (p=0.065). At 12 weeks, vitamin D intake reported by intervention subjects increased by a mean of 647 IU/day compared with 92 IU/day in the nonintervention group ($p<0.0001$).
CONCLUSIONS: Despite a significant increase in reported vitamin D intake in the intervention group, vitamin D levels between groups did not reach significance. However, the intervention was successful at increasing the number of subjects who achieved sufficient vitamin D levels.

Health Services Research

103. Member cost sharing is inversely associated with statin persistency: pharmacy benefit implications. *Patrick P. Gleason, Pharm.D., FCCP, BCPS*[1], Alan H. Heaton, Pharm.D.[2], Carol Walters, MBA[1], David Lassen, Pharm.D.[1]; (1)Prime Therapeutics LLC, Eagan, MN; (2)Blue Cross Blue Shield of Minnesota, Eagan, MN.

PURPOSE: Recent studies indicate that increasing a member's out-of-pocket contribution (copayment) may be associated with decreased drug persistency. Using medical and pharmacy administrative claims data from a 1.8 million-member BCBS plan, we assessed new start statin utilizers to determine the independent relationship that member contribution had on drug persistency.
METHODS: New statin starts were identified in a 3-month period, January 1, 2005, through March 31, 2005. New start was defined as lacking any claim in the drug category within the previous 180 days. Persistency was defined as a continuous drug supply within the drug category from the initial claim forward 180 days using a 1.5 days supply multiplier. Each member's duration

of therapy was terminated on the first 1-day gap. Multivariate linear regression was used to adjust for covariates known to influence persistency, including age, gender, mail order use, total out-of-pocket prescription expenses, Charlson severity of illness score, and drug classes used. Linear regression equations were developed.
RESULTS: 9,318 new-start statin utilizers, with a typical 30-day supply member contribution of $30 (25% and 75% quartiles, $15 to $69), met study criteria. The model R-squared was 0.13. Significant (p<0.01) independent predictors were member contribution, age, mail order use, total prescription out-of-pocket expenses, Charlson severity of illness score, gender, and unique drug classes used by member. Persistency decreased 15% among statin utilizers when holding all independent predictors constant while increasing member contribution from $30 to $60 for a 30-day supply. Halving member contribution improved persistency by 7%.
CONCLUSIONS: These findings add to recent publications by defining the magnitude statin persistency is associated with member contribution. Pharmacy benefit designs calling for increasing member contribution are likely to result in decreased statin drug persistency potentially diminishing the drugs benefits. Health plans should consider drug persistency trends when making pharmacy benefit design decisions.

104. Member cost sharing is inversely associated with antihypertensive persistency: pharmacy benefit implications. *Patrick P. Gleason, Pharm.D., FCCP, BCPS*[1], Alan H. Heaton, Pharm.D.[2], Carol Walters, M.B.A.[1], David Lassen, Pharm.D.[1]; (1)Prime Therapeutics LLC, Eagan, MN; (2)Blue Cross Blue Shield of Minnesota, Eagan, MN.

PURPOSE: Recent studies indicate that increasing a member's out-of-pocket contribution (copayment) may be associated with decreased drug persistency. Using medical and pharmacy administrative claims data from a 309,000 member BCBS plan, we assessed new-start angiotensin coverting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB) utilizers to determine the independent relationship that member contribution had on drug persistency.
METHODS: New ACEI/ARB starts were identified in a 3-month period. New start was defined as lacking any claim in the drug category within 180 days. ACEI/ARB new starts excluded members with CAD or CHF. Persistency was defined as a continuous drug supply within the drug category from the initial claim forward 180 days using a 1.5 days supply multiplier. Each member's duration of therapy was terminated on the first gap date. Multivariate linear regression was used to adjust for covariates known to influence persistency including age, gender, mail-order use, total out-of-pocket prescription expenses, Charlson severity of illness score, and number drug classes used. Linear regression equations were developed.
RESULTS: 944 new-start ACEI/ARB members, with a typical member contribution of $15 (25% and 75% quartiles, $9 and $22), met study criteria. Model R-squared was 0.13. Significant (p<0.01) independent predictors were member contribution, age, mail-order use, total prescription out-of-pocket expenses, and number of unique drug classes used. Persistency decreased 18% among ACEI/ARB utilizers when holding all independent predictors constant while increasing member contribution from $15 to $30 per 30 day supply. Halving the typical 30-day supply member contribution improved persistency by 7%.
CONCLUSIONS: These findings add to recent publications by defining the magnitude ACE/ARB persistency is associated with member contribution. Pharmacy benefit designs calling for increasing member contribution are likely to result in decreased ACEI/ARB persistency, potentially diminishing medication benefits. Health plans should consider drug persistency when making benefit design decisions.

105. The global impact of pharmacist interventions on patient care and costs - A descriptive study at a Trinidad hospital. *Feroza Sircar-Ramsewak, M.S., Pharm.D.*, Sherryl Baliramsingh, B.Sc.Pharm., Vaneeta Seepersad, B.Sc.Pharm., Shakti Sasenarine-Persad, Pharm.D.; The University of the West Indies. Pharmacy School. Trinidad, MT. Hope, Trinidad and Tobago.

PURPOSE: The primary objective of the study was to analyze pharmacist-documented interventions in order to determine the frequency and the clinical significance of the interventions. The secondary objective was to relate the interventions to economic outcomes.
METHODS: A retrospective study was conducted at a local institutional pharmacy in Trinidad, a southerly developing Caribbean country. An approved organized form was used to collect 1-year of documented data that was entered in an "Intervention Record Book." Data analysis was performed using SPSS Version 8 for Windows. The study used descriptive statistics.
RESULTS: Over the 1-year period pharmacists had screened 47,382 prescriptions with an intervention rate of 5.2% (2,466). 65.29% of the interventions were due to unavailability of formulary drugs, followed by 24.74% for inappropriate dosing of drugs. Approximately 31% could have resulted in a negative patient outcome. The interventions, in relation to published studies, have a good potential to result in cost savings.
CONCLUSIONS: This study has concluded that pharmacist interventions on drug-related problems could have a positive impact on quality patient care and costs to the health care system.

106. Impact of pharmacist assistance with obtaining medications through pharmaceutical company programs in achieving therapeutic goals in hypertension, diabetes and dyslipidemia. *Dawn E. Havrda, Pharm.D.*, Jessica Trompeter, Pharm.D.; Bernard J. Dunn School of Pharmacy, Shenandoah University, Winchester, VA.

PURPOSE: To determine whether patients without prescription insurance who obtain medications with pharmacist help and pharmaceutical company assistance programs(PCAP) achieve therapeutic goals in hypertension, diabetes, and dyslipidemia similar to patients with prescription insurance.
METHODS: Family practice patients were identified by CPT-codes for hypertension, diabetes and dyslipidemia over 6-months and PCAP records. Patients ≥ 18-years on one medication for hypertension, diabetes, or dyslipidemia were included. Eligible patients' records were reviewed for demographics and disease state information, including medication(s) and information to assess goal achievement. Therapeutic goals were defined by national guidelines available in 2005. Changes in continuous variables were assessed using Kruskal-Wallis test and categorical variables with chi-square; logistic regression was performed.
RESULTS: 458 patients were eligible: 250 with prescription insurance, 208 using PCAP. PCAP patients were older, more often female and with multiple disease states. Achievement of hypertension goals didn't differ between groups and was met in 41.9%; PCAP patients were taking more hypertension medications(2.35 ± 0.92 vs. 1.88 ± 0.89, p<0.0001). Reaching hypertension goals wasn't predicted by PCAP, presence of diabetes, or medication type. PCAP patients were more likely to reach HbA1C goal(67.1% vs. 39.6%, p=0.002) despite taking less diabetic medications(1.91 ± 0.61 vs. 2.00 ± 0.89, p=0.018). Achieving HbA1C goal was predicted by using PCAP(p=0.029), but not by reaching fasting blood glucose goal or medication type. PCAP patients had lower LDL values(95.8 ± 28.0 vs. 111.8 ± 37.5, p<0.0001); achieving LDL goals was only significant for LDL goal<130(p=0.007) and < 160 mg/dL (p=0.007). Diabetics were less likely to be at LDL goals compared with non-diabetics in both groups. Reaching LDL goals were predicted by using PCAP(p=0.021) and goal LDL category(p=0.002).
CONCLUSIONS: Patients without prescription insurance who receive pharmacist and PCAP assistance in obtaining medications were more likely to reach diabetic/HbA1C goal and have lower LDL values compared with patients with prescription insurance. Pharmacist involvement with PCAP significantly predicted achieving HbA1C goals and LDL goals.

107. Sex-based differences in health care use and provider advice for U.S. adults with and without diabetes. *Marianne McCollum, Ph.D., R.Ph.*, Laura B. Hansen, Pharm.D., Vahram Ghushchyan, Ph.D., Patrick W. Sullivan, Ph.D.; University of Colorado School of Pharmacy, Denver, CO.
PURPOSE: Sex-based differences in U.S. health-care utilization exist. Analysis of resource use in specific disease states such as diabetes is lacking. This study compared routine preventive care and provider advice to U.S. women and men with and without diabetes.
METHODS: Data were obtained from the 2001 and 2003 Medical Expenditure Panel Survey (MEPS). Diabetes was identified by self-report or ICD-9-CM code. Demographic, clinical, utilization, and provider advice data (e.g., age, sex, cholesterol and blood pressure checks, regular check-ups, advice concerning diet and exercise) were examined. Analyses were stratified by sex and conducted for the U.S. adult population and those with diabetes.
RESULTS: A total of 47,178 U.S. adult respondents (25,412 women) and 3,640 respondents with diabetes (883 women) were identified. Women were more likely than men to report having a routine check-up (67% versus 52%), cholesterol check (56% versus 49%), and blood pressure check (91% versus 81%) within the last year (all p<0.001). Compared to men, women reported receiving more advice to exercise more (39% versus 33%) and stop smoking (59% versus 42%; current smokers only, p<0.001). More men than women reported being told to restrict high fat/cholesterol foods (31.9% versus 31.8%, p=0.01). In the diabetes cohort, women and men reported increased and similar rates of routine check-ups (89%), cholesterol checks (85%), and blood pressure checks (98% for women, 97% for men, all p>0.05) within the last 12 months. Similar increases with no sex-based differences in physician advice regarding diet, exercise, and smoking were observed for adults with diabetes.
CONCLUSIONS: U.S. women use and receive more preventive care and advice than do men. Sex-based differences do not persist among those with diabetes. These results warrant further investigation, and efforts to increase preventive care for U.S. adults without diabetes should be undertaken.

Hematology/Anticoagulation

108E. Use of low molecular weight heparin (LMWH) during pregnancy: a retrospective analysis. *Nancy L. Shapiro, Pharm.D.*, Michelle A. Kominiarek, M.D., Soula M Angelopoulos, Pharm.D., Edith A. Nutescu, Pharm.D., Aimee

B. Chevalier, Pharm.D., Judith U. Hibbard, M.D.; University of Illinois at Chicago, Chicago, IL.

Presented at the 73rd Annual Meeting of the Central Association of Obstetricians and Gynecologists, Las Vegas, NV, October 18-21, 2006.

109E. Low molecular weight heparins in pregnancy: a case-control study. Michelle A. Kominiarek, M.D., Soula M. Angelopoulos, Pharm.D., *Nancy L. Shapiro, Pharm.D.*, Laura Studee, M.P.H., Edith A. Nutescu, Pharm.D., Judith U. Hibbard, M.D.; University of Illinois at Chicago, Chicago, IL.

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110. Pharmacy education and interventions increase appropriate venous thromboembolism prophylaxis in medically ill patients at a large teaching hospital. *Ruomei Wang, Pharm., D.*, Sheila M. Wilhelm, Pharm.D.; Harper University Hospital, Detroit, MI.

PURPOSE: The American College of Chest Physicians (ACCP) recommends venous thromboembolism (VTE) prophylaxis with unfractionated heparin (UFH) or a low-molecular-weight-heparin (LMWH) for medically ill patients. Our objective was to assess the current VTE prophylaxis rates of medically ill patients and evaluate the impact of pharmacist-driven education and interventions on prescribing patterns at a large teaching hospital.
METHODS: A Phase 1 prospective chart review of patients admitted to internal medicine services at a large teaching hospital was conducted between 11/15/05 and 2/26/06 to establish baseline VTE prophylaxis rates. Patients were classified as eligible or ineligible for VTE prophylaxis. In March, the medical staff was educated about VTE prophylaxis recommendations via lectures, informational posters, and pharmacist-delivered inservices. A Phase 2 prospective chart review was done between 3/29/06 and 5/24/06 to assess whether prescribing patterns had changed. During phase 2, pharmacists reviewing patient charts made interventions regarding appropriate VTE prophylaxis.
RESULTS: 218 and 185 patients were screened for VTE prophylaxis eligibility in Phase 1 and 2, respectively (n=403); 137 and 134 patients were eligible for VTE prophylaxis in Phase 1 and 2, respectively (n=271). There were no significant differences between Phase 1 and Phase 2 patients with respect to age, gender, or VTE risk factors. Appropriate VTE prophylaxis for eligible patients increased significantly in Phase 2 compared with Phase 1 (57.7% vs 73.1%, p=0.011). Pharmacist interventions further increased VTE prophylaxis rates in Phase 2 to 93.3% (p<0.001 vs Phase 1). The medical team accepted 75% percent of VTE prophylaxis recommendations made by the pharmacists.
CONCLUSIONS: Pharmacist-driven education and interventions significantly improved the rate of appropriate VTE prophylaxis for medically ill patients in a large teaching hospital.

111. Use of a bleeding risk assessment tool in an anticoagulation service. Kathleen E. Horner, Pharm.D., *Beth B. Phillips, Pharm.D.*, Deanna McDanel, Pharm.D., Phyllis Hemerson, Student Pharmacist, Erin Newkirk, Pharm.D.; University of Iowa Hospitals and Clinics, Iowa City, IA.

PURPOSE: The Outpatient Bleeding Risk Index (OBRI) is an assessment tool that has been described and validated in newly anticoagulated patients. The objective of this study was to determine how the OBRI may be used to evaluate bleeding risk of chronically anticoagulated patients in a pharmacist-managed Anticoagulation Case Management Service (ACMS).
METHODS: Patients included were followed in the University of Iowa Hospitals and Clinics Internal Medicine ACMS and experienced a bleeding event between January 1 and December 31, 2004. Each bleeding event was classified as major or minor. The OBRI was retrospectively completed for each patient at the time of initial ACMS enrollment, 2 months prior to the bleeding event and at the time of the event.
RESULTS: A total of 364 patients were evaluated. There were 108 patients with 146 bleeding events. Of these, 24 (16%) were classified as major and 122 (84%) as minor. Overall, the most common bleeding events were epistaxis [39 (27%)], bruising [23 (16%)], rectal [21 (14%)], and genitourinary [19 (13%)]. The most common types of major bleeding events were genitourinary [8 (33%)], hematoma [4 (17%)], and gastrointestinal [3 (13%)]. The most common indication for anticoagulation was atrial fibrillation (40%). At the time of the bleeding event, 4 patients (4%) were classified as high risk, and of this group 3 (75%) had a major bleeding event. Patients classified as high risk at the time of the bleeding event or 2 months prior were significantly more likely to experience a major bleeding event than those classified as low risk [OR 18.750 (95% CI 1.543–227.776), OR 19.500 (95% CI 1.607–236.607) respectively].
CONCLUSIONS: Major bleeding events occurred more often in patients classified as high risk for bleeding. The OBRI may be a useful assessment tool to identify chronically anticoagulated patients at high risk for bleeding.

112. Case-control analysis of prophylactic enoxaparin use in obese patients. Evan R. Horton, Pharm.D., *Amy Pai, Pharm.D.*, Lisa Anselmo, Pharm.D., David Garcia, M.D.; University of New Mexico Health Sciences Center, Albuquerque, NM.

PURPOSE: Obesity has been cited as a risk factor for developing venous thromboembolism (VTE), however, few studies have addressed the efficacy of prophylactic enoxaparin in obese patients. The purpose of this study was to determine the frequency of treatment failure in obese patients (Body Mass Index [BMI] > 30 kg/m^2) on standard, fixed-dose prophylactic therapy and to identify possible associated risk factors.
METHODS: This was a single-center, case-control analysis. Patients with VTE (cases) were matched 1:3 with patients with no VTE (controls) based on age, sex, and reason for prophylaxis. Medical record data were reviewed to determine BMI, enoxaparin dose, indication and length of prophylaxis, time to first dose of enoxaparin and concomitant aspirin use. Frequency of VTE among obese and non-obese patients was compared using chi-square analysis, and risk factors for development of VTE were determined using multivariate logistic regression.
RESULTS: A total of 104 patients were enrolled (26 cases, 78 controls). Orthopedic surgery (Ortho) patients who developed VTE had higher mean ± SD BMI values compared with controls (36.3 ± 9.4 vs. 28.5 ± 6.6 kg/m^2, respectively, p=0.003) BMI > 30 kg/m^2 was associated with an increased frequency of VTE in Ortho (p=0.042) but not in general surgery patients or those receiving prophylaxis for other indications. In multivariate analysis of Ortho patients, BMI > 30 kg/m^2 was independently associated with an increased risk of VTE (OR 5.3, 95% CI 1.22–23.16).
CONCLUSIONS: BMI > 30 kg/m^2 was associated with a markedly increased risk for developing VTE in orthopedic surgery patients receiving prophylactic enoxaparin therapy. Further studies of optimal prophylactic dosing in obese patients are warranted.

113E. Erythroid response (ER) rates in myelodysplastic syndromes (MDS) patients treated with epoetin alfa (EPO): a meta-analysis using the international working group criteria (IWGc) for MDS response. *Victor Moyo, M.D.*[1], Patrick Lefebvre, M.A.[2], Mei-Sheng Duh, M.P.H., Sc.D.[3], Ahmed Bourezak, M.A.[2], Behin Yektashenas, Pharm.D.[1], Richard C. Woodman, M.D.[1], Suneel Mundle, M.D.[1]; (1)Ortho Biotech Clinical Affairs, LLC, Bridgewater, NJ; (2)Groupe d'Analyse, Ltée., Montreal, QC, Canada; (3)Analysis Group, Inc, Boston, MA.

Presented at the 42nd Annual Meeting of the American Society of Clinical Oncology, Atlanta, GA, June 2-6, 2006.

114. Patient and provider satisfaction with a pharmacist versus nurse-managed outpatient anticoagulation management service. *Heather C. Ulrich, Pharm.D., BCPS, CDE*, Samuel E. Ellis, Pharm.D., BCPS, CDE, Marianne McCollum, Ph.D., R.Ph.; University of Colorado at Denver and Health Sciences Center, School of Pharmacy, Denver, CO.

PURPOSE: To compare patient and provider satisfaction with an anticoagulation service before and after a transition from a pharmacist-managed to a nurse-managed model.
METHODS: After 5 years of operation, a university-affiliated pharmacy-managed anticoagulation service (PMAS) was transitioned to a nurse-managed anticoagulation service (NMAS). A written Likert scale satisfaction survey was administered to patients on chronic anticoagulation therapy enrolled in the PMAS at the time of the pharmacy-to-nursing transfer (baseline survey) and again at 3 and 12 months following the transition of their care to the NMAS. A similar written survey assessed provider satisfaction with the PMAS compared with the NMAS.
RESULTS: A total of 173 patients who were enrolled in the PMAS at the time of transfer were surveyed at baseline. There were 12 patients excluded from the 3 month and 28 patients from the 12 month surveys because they were discharged from the NMAS. Patient response rates at baseline, 3 and 12 months were 63%, 45%, and 35%, respectively. The mean score for overall satisfaction with PMAS care at baseline was 4.71, higher than with NMAS care at 3 months (4.25, p=0.001) and at 12 months (4.56, p=0.18). Patients rated pharmacist knowledge of anticoagulation therapy higher (baseline, 4.82) than that of the nurses at 3 months (4.11, p<0.001) and 12 months (4.44, p=0.01). The mean provider overall satisfaction score was greater for PMAS (4.63) than NMAS at 3 and 12 months (4.18, p=0.098 and 4.23, p=0.093, respectively).
CONCLUSIONS: Patient and provider satisfaction was higher with a pharmacist-managed anticoagulation service than with a nurse-managed anticoagulation service. Survey scores with the NMAS increased over time, suggesting that any transition in care may initially decrease satisfaction. It is likely that satisfaction improved as patients and providers gained more experience with the new model.

Herbal/Complementary Medicine

115. Antiulcer and antioxidant effect of Benincasa hispida (Thunb.) Cogn. fruit extract. *Manish A. Rachchh, M., Pharm*[1], Sunita M. Jain, M.Pharm, Ph.D.[2]; (1)S. J. Thakkar Pharmacy College, Munjaka, Rajkot, India; (2)L. M. College of Pharmacy, Ahmedabad, India.

PURPOSE: The present study was designed to evaluate the antiulcer and antioxidant potential of petroleum ether and methanolic extract of fruit of Benincasa hispida (Thunb.) Cogn.
METHODS: The antiulcer activity was evaluated using ethanol-induced gastric mucosal damage model, pylorus ligated (PL) ulcer model and cold restraint-stress (CRS)-induced ulcer model in rats. Petroleum ether and methanolic extract were administrated orally at the dose of 300 mg/kg, while omeprazole (reference standard) was administered at the dose of 20 mg/kg, orally. Ulcer index was common evaluating parameter in all the models. Additionally, antioxidant potential was evaluated by finding out the level of lipid peroxidation, superoxide dismutase (SOD), and catalase (CAT) in case of CRS-induced ulcer model.
RESULTS: Petroleum ether and methanolic extract showed 49.03% and 67.36% inhibition in ulcer index (UI) respectively, compared with omeprazole (61.26%) in ethanol-induced gastric mucosal damage model. Both showed 85.26% and 75.96% reduction in UI respectively, as compared with omeprazole (78.69%), in case of PL ulcer model. There was 62.13% and 51.52% reduction in UI respectively, as compared with omeprazole (47.83%), in case of CRS-induced ulcer model. The level of lipid peroxidation was significantly lower in case of petroleum ether (0.307 ± 0.002) and methanolic (0.308 ± 0.025) group compared with control group (0.740 ± 0.056). The level of catalase (CAT) was significantly higher in case of petroleum ether (4.39 ± 0.341) and methanolic (5.18 ± 0.273) group compared with control group (2.88 ± 0.217). However, no significant difference was observed in the level of superoxide dismutase (SOD).
CONCLUSIONS: Petroleum ether and methanolic extract of Benincasa hispida (Thunb.) Cogn possess significant antiulcer as well as antioxidant property as evident by significant reduction in UI and in lipid peroxidation level while increase in the level of CAT level. Henceforth, they are more effective than omeprazole in the treatment of peptic ulcer disease.

116. Dietary supplement use among anticoagulation clinic patients. *Ann K. Wittkowsky, Pharm.D., CACP, FASHP, FCCP*[1], Henry I. Bussey, Pharm.D., FCCP, FAHA[2], Christopher R. Frei, Pharm.D., M.S.[3], Marie Walker, B.B.A.[4], Mary Pubentz, Pharm.D.[5], Tina G. Hipp, Pharm.D.[6], Rebecca J. Szymanski, Pharm.D.[6]; (1)University of Washington School of Pharmacy, Seattle, WA; (2)University of Texas, San Antonio, TX; (3)University of Texas at Austin College of Pharmacy, San Antonio, TX; (4)Clotcare.com, San Antionio, TX; (5)Advocate Lutheran General Hospital, Park Ridge, IL; (6)NorthEast Medical Center, Concord, NC.

PURPOSE: Many dietary supplements, including natural products and herbal medicinals, can interact with warfarin and increase the risk of bleeding or thrombosis. The extent of dietary supplement use among patients treated with warfarin has not been well described.
METHODS: A written survey was administered to patients enrolled at four anticoagulation clinics in the United States. Patients completed surveys during routine anticoagulation clinic visits. Patients were stratified into two groups (users or nonusers) on the basis of dietary supplement use. For the purposes of this study, vitamins, minerals, and amino acids were not classified as dietary supplements. Groups were compared using Chi-square for dichotomous variables and Student's t-test for continuous variables.
RESULTS: A total of 1203 patients completed the survey. Respondents had a mean (± SD) age of 68 ± 15 years; 57% were female, and 32% had a college degree. One-third (31%) of patients reported routine use of dietary supplements, including glucosamine/chondroitin (11%), fish oil (10%), cranberry extract (6%), and coenzyme Q10 (5%). More than one-third (35%) of patients indicated that no health care practitioner had discussed with them the possibility of interactions between dietary supplements and warfarin. Alarmingly, 11% of patients reported that they did not take dietary supplements, yet they later listed medicinal preparations on other parts of the survey that were considered to be dietary supplements by the study investigators.
CONCLUSIONS: Dietary supplement use is common among patients enrolled in anticoagulation clinics; however, one-third of patients have not discussed potential drug-supplement interactions with their healthcare providers. Finally, up to 10% of supplement users may not recognize that they currently take dietary supplements.

117. Green tea polyphenol mediated induction of xenobiotic efflux transporters. *David R. Foster, Pharm.D.*, Rong Huang, Ph.D., Xiaomei Zheng, M.S.; Purdue University, Department of Pharmacy Practice, Indianapolis, IN.

PURPOSE: Green tea polyphenols (GTPs) are currently under investigation for cancer prevention and as treatments for inflammatory disorders. GTPs may be substrates for the xenobiotic efflux transporters p-glycoprotein (MDR1) and multidrug resistance associated protein 2 (MRP2). These transporters are important in the disposition of a number of drugs and play an important role in resistance to chemotherapy. Because transporter substrates often influence transporter expression, we conducted a series of experiments to determine whether GTPs influence the expression of these transporters in cultured human intestinal cells (Caco2 cells).
METHODS: Caco2 cells were treated for 72 hours with blank media (controls) and in media containing 100 μM of the following individual GTPs: epigallocatechin gallate (EGCG), epicatechin gallate (ECG), epigallocatechin (EGC), epicatechin (EC), and catechin gallate (CG). Cells were also treated with a GTP mixture with GTP content similar to that of tea (added based on EGCG content). Total RNA was extracted, and gene expression of MDR1 and MRP2 (normalized to GAPDH) was determined using quantitative real time RT-PCR.
RESULTS: GTPs significantly induced both MDR1 and MRP2; EGCG, the GTP that has generated most interest as a therapeutic agent, induced MDR1 and MRP2 4-fold and 7-fold, respectively (table). Table: Transporter fold-induction relative to control (n=3/group, mean ± SD). *p<0.05 vs. controls (post-hoc analysis).

GTP/Gene	EGCG	ECG	EGC	EC	CG	Mix	p (ANOVA)
MDR1	3.8 ± 1.4*	10.7 ± 1.6*	2.2 ± 0.8	2.7 ± 0.6	4.1 ± 0.9*	2.9 ± 0.2	<0.01
MRP2	7.3 ± 2.1*	14.0 ± 1.6*	5.4 ± 0.6*	5.3 ± 1.5*	6.1 ± 1.1*	6.2 ± 0.2*	<0.01

CONCLUSIONS: GTPs significantly induce the expression of MDR1 and MRP2 in Caco2 cells. This may have implications regarding acute vs. chronic (i.e., post induction) intestinal absorption of GTPs. Moreover, because MDR1 and MRP2 are also involved in the action and disposition of many pharmacologic agents, these data suggest that GTPs may contribute to drug interactions when coadministered with transporter substrates. Further evaluation of these phenomena is warranted.

HIV/AIDS

118E. The effects of coadministered low-dose ritonavir and food on absolute bioavailability of TMC114. *Deborah H. Schaible, Pharm.D.*[1], Ron Falcon, M.D.[1], Vanitha Sekar, Ph.D.[2]; (1)Tibotec Therapeutics, Bridgewater, NJ; (2)Tibotec Inc., Yardley, PA.

Presented at the 10th European AIDS Conference, Dublin, Ireland, November 17-20, 2005.

119. Effectiveness and tolerability of atazanavir in an urban, indigent, coinfected population. *Ian R. McNicholl, Pharm.D., BCPS*, Vanita A. Parrish; University of California, San Francisco Positive Health Practice, San Francisco, CA.

PURPOSE: Atazanavir (ATV) was approved by the Food and Drug Administration in June 2003. Data submitted to the FDA report an incidence of grade 3-4 hyperbilirubinemia, grade 3-4 transaminitis and rash of 35%–49%, 3%–4% and 21%, respectively. Data for co-infected patients are not currently available. The objective was to conduct a retrospective investigation into the effectiveness and tolerability of ATV in a diverse urban population with a high incidence of hepatitis C coinfection.
METHODS: A search from Jan 2000 to February 2006 for all patients who were prescribed ATV was conducted. Exclusion criteria: never started ATV or lost to follow-up. Patients were randomly selected and stratified by hepatitis status. Data collected: demographics, medication regimen, refill history, CD4 count, viral load (VL), liver function tests. Descriptive statistics and Student's t-test were used to analyze data.
RESULTS: At time of report, 145 patients were eligible for inclusion. Population mean age 46.3 years, 83% male, 49% Caucasian, 28% African-American, 18% Latino, 57% hepatitis C coinfected and 92% receiving 300 mg ATV/100 mg ritonavir. Prior to starting ATV, mean CD4 count and VL were 276 cells/mm^3 and 77508 copies/mL, respectively. After mean 15.6 months, CD4 count and VL were 354 cells/mm3 and 6634 copies/mL, respectively. Overall, grades 3-4 hyperbilirubinemia, jaundice and transaminitis were 31%, 3%, and 3%, respectively. Time to first bilirubin > 1.2 mg/dL occurred in a median of 63 days with median bilirubin of 2.7. Patients were more likely to discontinue ATV due to jaundice than rash. After extensive comparisons of coinfected patients (n=83) to non-coinfected patients (n=62), no clinical or statistical differences were noted in demographics, CD4 count (median 314 vs 312 cells/mm3), VL (median 75 copies/mL), ATV duration or incidence of adverse reactions.
CONCLUSIONS: With the high rate of coinfection, the relative effectiveness and incidence of adverse events is comparable to non-coinfected patients.

120E. Pharmacokinetic studies of TMC114/r and coadministered medications in healthy, HIV-negative volunteers. *Raymond Pecini, Pharm.D.*[1],

Ron Falcon, M.D.[1], Vanitha Sekar, Ph.D.[2]; (1)Tibotec Therapeutics, Bridgewater, NJ; (2)Tibotec Inc., Yardley, PA.

Presented at the International Workshop on Clinical Pharmacology of HIV Therapy, Lisbon, Portugal, April 20-22, 2006.

121. Evaluation of darbepoetin versus erythropoietin for the treatment of HIV-related anemia in hospitalized patients. *Elizabeth González, Pharm.D.*[1], Keith A. Hecht, Pharm.D., BCOP[1], Dennis K. Fuller, Pharm.D.[2], Jingyang Fan, Pharm.D., BCPS[1]; (1)University of Southern Nevada, College of Pharmacy, Henderson, NV; (2)University Medical Center of Southern Nevada, Las Vegas, 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 data evaluating darbepoetin (DARBE) in this patient population. We previously reported interim results of this evaluation, which compared DARBE versus EPO in hospitalized patients with HIV-related anemia. These are the final results from our analysis.
METHODS: We conducted a prospective observational evaluation of DARBE in hospitalized patients with HIV-related anemia compared with a retrospective control group previously treated with EPO. The study population included all 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: Patients with HIV-related anemia were identified (DARBE, n=42; EPO, n=42). 7 DARBE and 3 EPO patients were excluded. Baseline characteristics were similar, except that more patients in the EPO group had ESRD (3 vs. 0). The mean Hgb increase for the DARBE group was 1.20 ± 1.57 g/dL and for the EPO group 0.88 ± 1.97 g/dL (p=0.4). The percentage of patients transfused in the DARBE and EPO groups was 24% and 44%, respectively (p=0.098). 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.
CONCLUSIONS: The final results of this analysis continue to support 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. Randomized, controlled trials should be performed to verify these results.

Infectious Diseases

122E. Vancomycin MIC creep in non-VISA, vancomycin susceptible clinical MRSA blood isolates from 2001-2005. Gregory Steinkraus, Ph.D.[1], Roger L. White, Pharm.D.[2], *Lawrence Friedrich, Pharm.D.*[3]; (1)New Hanover Regional Medical Center, Wilmington, NC; (2)Medical University of South Carolina, Charleston, SC; (3)Cubist Pharmaceuticals, Mt. Pleasant, SC.
Presented at the 106th General Meeting of the American Society for Microbiology, Orlando, FL, May 24, 2006.

123. Clinical efficacy of ertapenem for treatment of extended-spectrum, beta-lactamase-producing, Gram-negative infections. *Melody L. Berg, Pharm.D.*[1], Christopher W. Crank, Pharm.D.[2], Alexander H. Philbrick, Pharm.D.[1], Mary K. Hayden, M.D.[2]; (1)Midwestern University, Downers Grove, IL; (2)Rush University Medical Center, Chicago, IL.

PURPOSE: The objective of this study was to examine the clinical and microbiological outcomes associated with ertapenem therapy of extended spectrum beta-lactamase (ESBL)-producing *Escherichia coli*, *Proteus* species, and *Klebsiella* species.
METHODS: This study utilized a retrospective, chart review design. Inpatients from Rush University Medical Center with an ESBL-producing gram negative isolate treated with ertapenem during 2003–2005 were included. Data collected included patient demographics, risk factors for ESBL infection, antibiotic and infection histories, and microbiological and clinical outcomes.
RESULTS: Twenty-two patients received treatment with ertapenem for an ESBL infection. Twenty-seven percent (6/22) of patients received ertapenem as initial treatment. Forty-one percent of patients were treated with imipenem or meropenem prior to receiving ertapenem. *E. coli* was isolated in 65% of patients while *Klebsiella* species and *Proteus* species represented 26% and 9%, respectively. The urinary tract and blood were the most common sites of infection representing 55% and 32% of patients, respectively. Of the 7 patients evaluable for microbiological outcome, 6 were considered a cure (defined as clearance of the pathogen from the original culture site). Approximately, 95% (21/22) of patients had a positive outcome, cure or improvement, defined as full or partial resolution of signs and symptoms of infection while on ertapenem therapy. There were no deaths during this study but one patient was determined to be a clinical failure. Of the 6 patients who initially received ertapenem, there were 2 clinical cures, 3 improvements, and 1 clinical failure.
CONCLUSIONS: For this small case series, ertapenem therapy appears to be a reasonable option for the management of ESBL-producing gram-negative organisms. Most patients received consolidation therapy with ertapenem while only a small proportion received ertapenem for initial therapy. The results of this study warrant a prospective analysis of the clinical efficacy of ertapenem for this indication.

124. Molecular characterization of *Aspergillus fumigatus* isolates with elevated intraconazole, voriconazole, and posaconazole minimum inhibitor concentrations. *Carlos A. Alvarez, Pharm.D.*, Jodi L. Grabinski, Pharm.D., M.S., Robert L. Talbert, Pharm.D., Nathan P. Wiederhold, Pharm.D.; University of Texas at Austin College of Pharmacy, San Antonio, TX.

PURPOSE: Invasive aspergillosis is a leading cause of infectious disease related mortality in patients with hematologic malignancies. Although rare, antifungal resistance in *A. fumigatus* species may hinder treatment and result in suboptimal patient outcomes. The objective of this study was to evaluate the pharmacodynamics of itraconazole, voriconazole, and posaconazole against three *A. fumigatus* isolates with elevated minimum inhibitory concentrations (MICs), and to characterize point mutations at specific codons in the gene encoding 14 α-demethylase using a pyrosequencing assay.
METHODS: MICs were determined according to CLSI M38-A microdilution methodology and verified using Etest strips. Pharmacodynamic analysis was performed in duplicate using the XTT viability assay at antifungal concentrations ranging from 0–16 µg/mL. IC50 and IC90 values were calculated by fitting viability data to a four parameter logistic model and compared with AF 293, the strain used in the *A. fumigatus* genome sequencing project. DNA was extracted from mycelial cultures grown for 18 hours at 37°C. Base-pair regions of the *A. fumigatus* CYP51A gene (GenBank AF338659) were amplified by PCR. Sequence data of codons 54 and 220 for each isolate were acquired by pyrosequencing and compared with the corresponding sequences in AF 293.
RESULTS: Each isolate tested had significantly elevated MIC, IC50, and IC90 values for itraconazole, voriconazole, posaconazole, or all three compared with AF 293. In one of the isolates tested with elevated MICs to each azole, a point mutation was identified in codon 220, resulting in the replacement of methionine by lysine (M220K).
CONCLUSIONS: The activity of itraconazole, voriconazole, and posaconazole were significantly reduced in the isolates studied. One isolate did demonstrate a mutation in the CYP51A gene resulting in amino acid substitutions at codon 220 of 14 α-demethylase. Further assessments of resistance mechanisms, including assessment of changes in gene expression of CYP51A, are ongoing.

125E. Aerosolized itraconazole as prophylaxis against invasive pulmonary aspergillosis due to *Aspergillus fumigatus*. *Carlos A. Alvarez, Pharm.D.*[1], Nathan P. Wiederhold, Pharm.D.[1], Jason T. McConville, Ph.D.[2], Jay I. Peters, M.D.[3], Laura K. Najvar, B.S.[3], John R. Graybill, M.D.[3], David Marks, M.D.[3], Robert L. Talbert, Pharm.D.[1], David S. Burgess, Pharm.D.[1], Rosie Bocanegra, B.S.[3], Keith P. Johnston, Ph.D.[4], Robert O. Williams III, Ph.D.[2]; (1)University of Texas at Austin College of Pharmacy, San Antonio, TX; (2)University of Texas at Austin College of Pharmacy, Austin, TX; (3)University of Texas Health Science Center at San Antonio, San Antonio, TX; (4)University of Texas at Austin College of Engineering, Austin, TX.

Presented at the 46th Annual Interscience Conference on Antimicrobial Agents and Chemotherapy, San Francisco, CA, September 27–30, 2006.

126. Interaction of daptomycin with two prothrombin time reagents leads to false prolongation of patient results. *Scott Levy, Pharm.D.*; Cubist, Royal Oak, MI.

PURPOSE: A cluster of patients having experienced marked elevations of International Normalized Ratio without evidence of bleeding diatheses in temporal association with daptomycin therapy was identified during routine postmarketing safety surveillance. A common risk factor among these patients was the thromboplastin reagent used to assess prothrombin time. The objective is to evaluate the effect of daptomycin on measured prothrombin time using commercially available thromboplastin reagent kits commonly used in the United States.
METHODS: Thirty prothrombin time reagent kits were obtained. Daptomycin was added to pooled normal human plasma samples to achieve final concentrations of 0–200 µg/mL, a clinically relevant range. Quality control ranges were established for each reagent kit using normal and abnormal control plasmas. Triplicate assays of prothrombin time were performed on the daptomycin-spiked plasma samples using each of the 30 reagent kits. Activated partial thromboplastin time and thrombin time were

also assessed. Statistical comparisons of interest were performed using ANOVA with Bonferroni *t*-test for multiple comparisons. An alpha of 0.05 was used.
RESULTS: Addition of daptomycin to human plasma samples dose-dependently prolonged measured prothrombin times when 2 of 30 different commercially available thromboplastin reagents were utilized for the assays. The findings were both statistically and clinically significant. No clinically significant effect was observed with the other 28 reagents. Activated partial thromboplastin time and thrombin time were not affected.
CONCLUSIONS: The effect of daptomycin on measured prothrombin time results is highly reagent-specific. Healthcare providers should consider the possibility of a drug-laboratory test interaction if prolonged prothrombin time or elevated International Normalized Ratio values are observed in patients receiving daptomycin.

127. Changes in antimicrobial susceptibility of *Escherichia coli* and *Klebsiella pneumoniae* documented by antibiograms and isolates: the antibiogram resistance method or isolate-based resistance monitoring (ARMOR) study group. *Benjamin J. Epstein, Pharm.D.*[1], John G. Gums, Pharm.D.[1], Philip Turner, Ph.D.[2]; (1)University of Florida, Gainesville, FL; (2)Astra Zeneca, Macclesfield, United Kingdom.

PURPOSE: To compare susceptibility data from 1999-2004 generated by two methodologically unique antibiotic surveillance studies, the Antimicrobial Resistance Management (ARM) and Meropenem Yearly Susceptibility Test Information Collection (MYSTIC) programs.
METHODS: ARM is a Web-based, queriable, real-time repository of bacterial susceptibility data submitted by US hospitals as antibiograms. MYSTIC is monitoring resistance worldwide among individual isolates; antimicrobial susceptibility tests are performed by broth microdilution in a reference laboratory (for U.S. institutions) in accordance with the Clinical Laboratory Standards Institute (CLSI). For the years 1999-2004, we compared national susceptibility rates from ARM and MYSTIC for *E. coli* and *K. pneumoniae* to ciprofloxacin, levofloxacin, ceftriaxone, and gentamicin.
RESULTS: For *E. coli*, ARM and MYSTIC reported declining susceptibility to the fluoroquinolones during the study period. For ciprofloxacin, susceptibility in ARM decreased from 95.7% in 1999 to 84.3% in 2004 versus MYSTIC, 96% to 78.9%. The average, absolute decrease in susceptibility was 2.3% per year in ARM and 3.4% per year in MYSTIC. Susceptibility to ceftriaxone was high and nearly identical levels of activity were documented. Susceptibility to gentamicin in 1999 was 97% and 96.5% in ARM and MYSTIC, respectively, and decreased to 92.1% and 89.8%, respectively, by 2004. For *K. pneumoniae*, resistance patterns were more stable. (Table 2) In ARM, susceptibility to ciprofloxacin was 94.7% in 1999 and 92.2% in 2004, while, in MYSTIC, susceptibility was 94.1% and 94.7%, respectively. Resistance to ceftriaxone and gentamicin among *K. pneumoniae* was low (< 5%) and stable, with similar levels of activity in both programs.
CONCLUSIONS: An antibiogram-based surveillance system and an isolate-based initiative identified similar patterns of resistance from 1999-2004. Despite application of unique surveillance methods, both systems detected a similar rate of increasing fluoroquinolone resistance, lesser changes in aminoglycoside resistance and stable third-generation cephalosporin activity. Surveillance can be performed confidently with either method.

128. Usage and associated outcomes of IV antifungal agents for candidemia. *Paul Juang, Pharm.D.*[1], Rob MacLaren, Pharm.D.[2], Rose Jung, Pharm.D.[2], Doug N. Fish, Pharm.D.[2]; (1)St. Louis College of Pharmacy, St. Louis, MO; (2)University of Colorado Health Sciences Center, Denver, CO.

PURPOSE: Infections caused by Candida species are increasing. Several new antifungal agents have become available for treatment. The purpose of this study was to assess the use of specific antifungal agents and associated outcomes of antifungal therapy for candidemia.
METHODS: Single-center, retrospective evaluation of 44 patients with positive Candida blood cultures from January 2004 to December 2004. The primary outcome was the appropriateness of antifungal selection based on published IDSA guidelines. Secondary outcomes were duration of therapy, incremental drug cost of inappropriate therapy, length of hospital stay, patient disposition, and adverse events of antifungal agents. Mean, median, and standard deviation were evaluated.
RESULTS: Patients were 54 ± 15 years old with median APACHE II score of 14 and 3.6 ± 1.5 risk factors for developing candidiasis. Patients were most commonly on the pulmonary (25%), oncology (14%), or medicine (11%) services. Antifungal therapy was started 10.5 ± 9.9 days after admission and 8.5 ± 9.6 days after start of antibiotics. The most common species were Candida albicans (44%) and Candida glabrata (35%). The most common empiric agents were caspofungin (59%) and fluconazole (34%). Empiric and culture-specific therapies were appropriately selected for 72% and 75% of patients, respectively. Duration of inpatient antifungal therapy was 16.2 ± 17.9 days at a total cost of $131,809 while total duration was 25.5 ± 32.2 days. The incremental inpatient cost of inappropriate therapy was $31,446. Hospital length of stay was 29.1 ± 29.1 days with 30% mortality. Four adverse events were recorded: increased creatinine with amphotericin lipid complex (2 cases), rise in liver function tests with voriconazole (1), and thrombocytopenia with caspofungin (1).
CONCLUSIONS: Most patients with candidemia were initially placed on appropriate antifungal therapy, but inappropriate use resulted in a high cost burden to the hospital. Appropriately switching antifungal agents based on culture results and limiting duration of therapy could substantially improve overall appropriateness and cost of therapy.

129. Alternative antimicrobials for methicillin-resistant *Staphylococcus aureus*. *Christopher R. Frei, Pharm.D., MSc*, Nathan P. Wiederhold, Pharm.D., David S. Burgess, Pharm.D.; Center for the Advancement of Research and Education in Infectious Diseases. (CARE-ID), University of Texas at Austin; University of Texas Health Science Center at San Antonio, San Antonio, TX.

PURPOSE: Methicillin-resistant *Staphylococcus aureus* (MRSA) poses a significant public health threat due to its increasing prevalence and acquired resistance to most antimicrobial classes. Vancomycin, the traditional drug of choice, has no oral formulation and resistance concerns have prompted the CDC to develop guidelines for prudent use. Newer agents, such as linezolid and quinupristin/dalfopristin, have resistance concerns, serious adverse effects, and substantially higher costs. Hence, there is a critical need for alternative agents against MRSA.
METHODS: MICs for vancomycin, VAN; quinupristin/dalfopristin, SYN; linezolid, LZD; doxycycline, DOX; minocycline, MIN; and trimethoprim/sulfamethoxazole, SXT were determined against 40 clinical MRSA isolates. Time-kill experiments were performed using a standard inoculum ($5x10^5$ cfu/mL) for 5 clinical isolates at clinically achievable concentrations (µg/mL): LZD 7, DOX 4, MIN 7, SXT 7/35, VAN 15, and SYN 1/2. Samples were withdrawn at 7 time-points over 24h, plated onto agar plates, and incubated for 24h at 35°C. Bacteriocidal activity was defined as a reduction of at least 99.9% in the starting inoculum.
RESULTS: $MIC_{50/90}$ (µg/mL) and percent susceptible were: VAN 2/4, 100%; LZD 4/4, 100%; MIN 0.125/0.5, 100%; DOX 0.5/2, 93%; SXT 0.5/32, 80%; and SYN 1/2, 78%. SXT rapidly achieved (6h) and maintained bacteriocidal activity against all susceptible isolates. SXT also demonstrated bacteriostatic activity against an intermediate isolate. VAN achieved (12-24h) and maintained bacteriocidal activity against 4/5 susceptible isolates and demonstrated bacteriostatic activity against the remaining isolate. Finally, LZD, SYN, DOX, and MIN maintained bacteriostatic activity for all susceptible isolates.
CONCLUSIONS: This study suggests that SXT may be a suitable alternative for the treatment of patients with susceptible MRSA isolates due to its good activity, favorable pharmacodynamic profile, availability as an oral formulation, and relatively low cost.

130E. Clinical characteristics and health outcomes associated with methicillin-resistant *Staphylococcus aureus* infective endocarditis. Alejandro Jimenez, M.D.[1], *Christopher R. Frei, Pharm.D., M.Sc.*[2], Marcos I. Restrepo, M.D., M.Sc.[3]; (1)San Antonio Bacterial Endocarditis Res. (SABER), University of Texas Health Science Center at San Antonio, San Antonio, TX; (2)SABER, University of Texas Health Science Center at San Antonio; Univ. TX at Austin Coll. of Pharmacy, San Antonio, TX; (3)SABER, University of Texas Health Science Center; Veterans Evidence-Based Research Dissemination Implementation Center (VERDICT), South Texas Veterans Health Care System, San Antonio, TX.

Presented at the 46th Interscience Conference on Antimicrobial Agents and Chemotherapy, San Francisco, CA, September 27-30, 2006.

131E. Discrepancies in international susceptibility criteria for the carbapenems vs. Gram-negative aerobes and the role of pharmacokinetic-pharmacodynamic (PK-PD) modeling with Monte Carlo simulation. *Christopher R. Frei, Pharm.D., M.Sc.*, Nathan P. Wiederhold, Pharm.D., David S. Burgess, Pharm.D.; Center for the Advancement of Research and Education in Infectious Diseases (CARE-ID), University of Texas at Austin; University of Texas Health Science Center at San Antonio, San Antonio, TX.

Presented at the 46th Annual Interscience Conference on Antimicrobial Agents and Chemotherapy, San Francisco, CA, September 27-30, 2006.

132E. In vitro activity of daptomycin and vancomycin lock solutions on staphylococcal biofilms in a central venous catheter model. *Kerry L. LaPlante, Pharm, D.*[1], Leonard A. Mermel, M.D.[2]; (1)University of Rhode Island and Veterans Affairs Medical Center, Providence, RI; (2)Division of Infectious Diseases, Rhode Island Hospital and Department of Medicine, Brown Medical School, Providence, RI.

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Chemotherapy, San Francisco, CA, September 26-30, 2006.

133. Assessment of a standard cefepime dosing strategy for serious, Gram-negative infections at a large, tertiary academic medical center. *Eli Deal, Pharm.D.*, Scott T. Micek, Pharm.D., Richard M. Reichley, R.Ph., David J. Ritchie, Pharm.D.; Barnes-Jewish Hospital, St. Louis, MO.

PURPOSE: Multiple dosing strategies have been proposed for cefepime in severe, gram-negative infections. The objective of this study was to determine the impact of a institutional, standardized dose of cefepime (1 gram intravenously every 8 hours, interval adjusted for renal impairment) on clinical outcomes for pulmonary and bloodstream infections caused by *Pseudomonas aeruginosa, Enterobacter* spp. or *Citrobacter freundii*.
METHODS: Patients hospitalized at Barnes-Jewish Hospital (St. Louis, MO) with bacteremia or pneumonia caused by *Pseudomonas aeruginosa*, *Enterobacter aerogenes*, *Enterobacter cloacae*, or *Citrobacter freundii* were prospectively evaluated. Patients receiving appropriate and adequate monotherapy against the studied isolate within 24 hours of culture were segregated according to treatment success, improvement, or failure. Univariate analysis and multiple logistic regression were performed to determine independent risk factors associated with clinical failure.
RESULTS: Over a 1-year period (October 2004–October 2005), 120 infections were identified and analyzed. Clinical failure occurred in 42.5% of these cases [n=51; 36/74 (48.6%) of patients receiving cefepime vs. 15/46 (32.6%) with other antibiotic treatments (p=0.084)];. Univariate analysis revealed that clinical failure was more likely to occur in patients with higher markers of disease severity (ICU care, APACHE II, SOFA, and CPIS scores), Pseudomonas infection, and in those with decreased renal function (p<0.05). Multiple logistic regression analysis identified infection with *Pseudomonas aeruginosa* (AOR, 1.4; 95% CI=1.0-2.01) and mechanical ventilation on the index date (AOR, 7.5; 95% CI=1.8-31.3) were associated with treatment failure among patients receiving cefepime.
CONCLUSIONS: Clinical success rates did not differ between patients receiving standard dose cefepime or other antibiotics. Further prospective studies using pharamcodynamic parameters are necessary to determine the optimal dosing of cefepime at our institution, particularly in infections caused by *Pseudomonas aeruginosa* and in patients requiring mechanical ventilation.

134. Angiotensin converting enzyme inhibitors (ACEI) reduce pneumonia risk. *Donald P. Alexander, Pharm.D.*, Nancy A Nickman, Ph.D., Gary M Oderda, Pharm.D., Gregory J. Stoddard, M.Ph., Mark A Munger, Pharm.D.; University of Utah, Salt Lake City, UT.

PURPOSE: Community-acquired pneumonia is a major cause of elderly morbidity and mortality. Oropharyngeal aspiration, due to reduced respiratory defense mechanism, is an important etiologic factor to increased pneumonia risk. ACEI activity is associated with maintenance of substance P concentrations, a protective respiratory defense hormone. A study in an elderly Asian inpatient population showed a significant risk reduction in nosocomial pneumonia with ACEI exposure. The present cohort study was conducted to quantify risk for community-acquired pneumonia in adults, ≥ 65 years, without select neurological disorders, exposed to ACEI in the United States (U.S.).
METHODS: A prescription and medical claims de-identified dataset was created from a U.S. database; Medstat MarketScan®/Medicare Supplemental and Coordination of Benefits (2000-2002). Claims for patients age ≥ 65 years, who were prescribed an ACEI versus no ACEI were analyzed for the event end point of pneumonia ICD-9-CM code. Patients with select neurological disorders associated with dsyphagia and prior antibiotic use were excluded. The cohorts were filtered for select concomitant medications. A multivariable Cox regression model was fitted to the data.
RESULTS: A total of 668,281 subjects were included in the study with 151,342 (22.6%) receiving an ACEI. Relative to the comparison cohort, chronic ACEI use reduced pneumonia risk: Hazard Ratio (HR) 0.79 [95% CI=0.77–0.82] (p<0.0001). ACEI chemical structure, female gender, age, concomitant HMGCoA-reductase inhibitors use, and NSAID use were predictive of pneumonia risk reduction. Corticosteroid use was a negative predictor.
CONCLUSIONS: Chronic ACEI significantly reduced the risk of pneumonia in a U.S. cohort of elderly individuals without select neurological disorders associated with dysphagia. ACEI protection may be applicable to a wider elderly and diverse ethnic population than has previously been reported. In consideration of the rising importance of this population, a prospective, controlled study of chronic ACEI use should be conducted to confirm these results.

135. Caspofungin induces expression of the beta-1,3-glucan synthase gene FKS2 (GSC2) in an SLT2-dependent fashion in *Candida glabrata*. *Kelly D. Earhart, Pharm.D.*[1], Santosh K. Katiyar, Ph.D[2], Katherine S. Barker, 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 College of Medicine, Philadelphia, PA.

PURPOSE: The echinocandin antifungal agents target the fungal cell wall by inhibiting beta-1,3-glucan synthase (Fks2p). In the closely related yeast *Saccharomyces cerevisiae*, we have shown that caspofungin induces the expression of genes in the cell integrity pathway, including those encoding beta-1,3-glucan synthase (Fks2p), the transcriptional regulator Rlm1p, the cell wall protein Crh1p, and the MAP kinase Slt2p. The present study was undertaken to determine if in the fungal pathogen *Candida glabrata* 1) these genes are up-regulated in response to caspofungin, 2) whether their up-regulation is dependent upon Slt2p, and 3) if perturbation of this pathway affects susceptibility to caspofungin.
METHODS: *C. glabrata* strain 200989Δslt2 (SLT2 deleted) was derived from ATCC strain 200989 using the PRODIGE method. Both strains were exposed to either medium alone or caspofungin at a concentration four-times the MIC (0.5 µg/mL for 3 hours). Total RNA was isolated, and mRNA abundance for FKS2, RLM1, CRH1, and SLT2 were measured by real-time RT-PCR. Caspofungin susceptibilities for these strains were determined at 18 and 48 hours.
RESULTS: Caspofungin-induced expression of FKS2 (15-fold), RLM1 (8-fold), CRH1 (7.5-fold) and SLT2 (9-fold). Disruption of SLT2 abrogated caspofugin-induced expression of FKS2, RLM1, and CRH1, and led to increased susceptibility to caspofungin at 18 and 24 hours.
CONCLUSIONS: These results demonstrate that *C. glabrata* responds to caspofungin exposure by up-regulating genes of the cell integrity pathway, including the echinocandin target FKS2. Slt2p is required for caspofungin-induced activation of these genes, and this response is integral to the susceptibility of *C. glabrata* to caspofungin. Components of the cell integrity pathway represent potential drug targets for the enhancement of the activity of the echinocandins.

136. Nomogram for relationships between vancomycin (V) AUC/MIC values and steady-state trough serum concentrations. *Roger L. White, Pharm.D.*; Medical University of South Carolina, Charleston, SC.

PURPOSE: V troughs are often monitored by clinicians; however, relationships with clinical efficacy have been poor. Recent studies suggest a V AUC/MIC ≥ 400 is correlated with both clinical and microbiological success in patients with S. auerus lower respiratory infections. Furthermore, healthcare-associated pneumonia guidelines recommend V troughs of 15–20 mg/L, which are higher than those previously recommended. With changing V dosing and monitoring recommendations, clinicians need to understand the relationships between AUC/MIC target values and V trough concentrations.
METHODS: One-compartment model steady-state simulations were performed with the following V doses: 1g, 2g, 15 mg/Kg, 19 mg/Kg with the following intervals: q12h for CrCl > 60–120 mL/min, q24h for CrCl > 30–60 mL/min, and q48h for CrCl 15–30 ml/min. Simulations were performed for each regimen on a range of patient body weights (70–80 Kg) and volumes (0.7–0.9 L/Kg) using a weighted (based on number of subjects) regression of CrCl vs.Cl relationships to predict trough values. From the daily dose and Cl values, AUCs (0–24 hr) were calculated. From these, AUC/MIC values were calculated for MICs of 0.5, 1, 2, and 4 mg/L. Relationships between troughs and AUC/MICs were fit by linear and non-linear regression.
RESULTS: From the 72 regimens simulated, t 1/2 (hrs) ranged from 7–54 hours. Ranges for troughs and AUC/MICs were 7–50 mg/L and 91–3,104, respectively. Relationships between troughs and AUC/MICs were fit well by both linear and non linear methods (R2 from 0.826-0.985). To achieve an AUC/MIC ≥ 400, target trough concentration ranges for MICs of 0.5, 1, 2, and 4 are 4.3–4.8, 7.2–11.7, 21.3–25.0, and 46.7–58.1 mg/L, respectively.
CONCLUSIONS: There is no direct correlation between AUC/MICs and trough concentrations; however, V target trough concentrations within a relatively narrow range were found to correlate well with AUC/MIC target values. Knowledge of these relationships should be useful to clinicians using V for the treatment of lower respiratory tract infections.

137E. Efficacy and safety of daptomycin (DAP) in patients (Pts) treated for non-catheter related bacteremia (nCRB). George Sakoulas, M.D.[1], Jack Brown, Pharm.D.[2], *Kenneth C. Lamp, Pharm.D.*[2], Lawrence V. Friedrich, Pharm.D.[2]; (1)New York Med. Coll., Valhalla, NY; (2)Cubist Pharmaceuticals, Lexington, MA.

Presented at the Interscience Conference on Antimicrobial Agents and Chemotherapy, San Francisco, CA, September 27-30, 2006.

138E. Clinical experience with daptomycin (DAP) for the treatment of osteomyelitis in patients with post-therapy follow-up. *Kenneth C. Lamp, Pharm.D.*, Lawrence V. Friedrich, Pharm.D.; Cubist Pharmaceuticals, Lexington, MA.

Presented at the Interscience Conference on Antimicrobial Agents and Chemotherapy, San Francisco, CA, September 27-30, 2006.

139E. Retrospective evaluation of daptomycin (DAP) use in patients (pts) with osteomyelitis (osteo). Laurence Balter, M.D.[1], *Brian J. Donovan, Pharm.D.*[2], Donald S. North, Pharm.D.[2], Kenneth C. Lamp, Pharm.D.[2], Lawrence V. Friedrich, Pharm.D.[2]; (1)Kane and Davis Associates, Washington, DC; (2)Cubist Pharmaceuticals, Lexington, MA.

Presented at the Annual Meeting of the Infectious Diseases Society of America, Toronto, ON, Canada, October 12-15, 2006.

140E. Daptomycin (DAP) use in patients with septic arthritis (SA): post-marketing experience from CORE 2005. Graeme Forrest, M.B.B.S.[1], *Brian J. Donovan, Pharm.D.*[2], Kenneth C. Lamp, Pharm.D.[2], Lawrence V Friedrich, Pharm.D.[2]; (1)Univ. of Maryland, Baltimore, MD; (2)Cubist Pharmaceuticals, Lexington, MA.

Presented at the Interscience Conference on Antimicrobial Agents and Chemotherapy, San Francisco, CA, September 27-30, 2006.

141. Clinical outcomes of daptomycin (DAP) as first-line therapy (FLT) versus subsequent therapy (ST). George Sakoulas, M.D.[1], *Jack Brown, Pharm.D.*[2], Kenneth C. Lamp, Pharm.D.[2], Lawrence V Friedrich, Pharm.D.[2]; (1)New York Med. Coll., Valhalla, NY; (2)Cubist Pharmaceuticals, Lexington, MA.

PURPOSE: DAP is approved for complicated skin and skin structure infections (cSSSI) and bacteremia including right-sided endocarditis. Limited data is available evaluating DAP as FLT verses ST.
METHODS: The Cubicin® Outcomes Registry and Experience (CORE 2005) is a retrospective, post-marketing study of DAP experience. Outcomes were assessed clinically (cure, improvement, failure) at the end of therapy; adverse events were not classified as failures; 225 nonevaluable patients were excluded.
RESULTS: DAP Outcomes were reported for 947 pts; 212 FLT and 735 ST. FLT and ST demographics were similar, except more FLT pts were in the community 2 days prior to beginning DAP than ST (63% vs 40%, p<0.0001) and uncomplicated SSSI were more common in the FLT group (23% vs 12%, p=0.0002). Pathogens were similar between groups, MRSA (FLT 47%, ST 44%) was most frequent. The mean dose for both groups was 4.9 mg/kg with an average duration of therapy of 20.5 days and 20.8 days for FLT and ST, respectively. Outcomes were similar overall (FLT 95%, ST 92%) or within infection types. The mean time to clinical response was similar; FLT 6.3 days, ST 6.9 days. DAP clinical success was statistically lower (p<0.01) in those ST pts (n=123) that failed prior vancomycin (86%) compared with FLT or those that did not fail non-vancomycin prior antibiotics (95%). Multiple factors were statistically higher in the prior vancomycin failure group compared with FLT; age, hospital associated location, chronic kidney disease, low renal function, dialysis, bacteremia infections, MRSA, and concomitant antibiotic use. Vancomycin MIC distributions for MRSA were similar between groups.
CONCLUSIONS: DAP outcomes were comparable when used as FLT or ST. ST patients who failed vancomycin had lower DAP outcomes, but this is likely explained by the differences noted in comorbidities and infection types. Further studies are needed to confirm these findings.

142. Assessment of meropenem and amikacin activity against *Acinetobacter baumannii* in an in vitro pharmacodynamic model. Natalie Boyd, Pharm.D.[1], *Nathan P. Wiederhold, Pharm.D.*[1], Michael F. Carden, B.A.[2], David S. Burgess, Pharm.D.[1]; (1)University of Texas at Austin College of Pharmacy, San Antonio, TX; (2)University of Texas Health Science Center, San Antonio, TX.

PURPOSE: *Acinetobacter baumannii* infections are an increasing cause of life-threatening infections in intensive-care settings. Our limited understanding of the pharmacodynamics of available antibiotics against infections caused by this organism and its ability to develop resistance can result in suboptimal outcomes. The objective of this study was to assess the pharmacodynamic activity of meropenem and amikacin, alone and in combination against susceptible and resistant *A. baumannii* isolates.
METHODS: MICs were determined for 3 *A. baumannii* isolates, including 2 resistant strains, using microdilution methodology (CLSI M7-A7). Time-kill studies were performed in duplicate to assess rate and extent of activity of each agent. A one-compartment in vitro pharmacodynamic model was used to simulate the serum pharmacokinetic profile achieved clinically for various regimens: meropenem 1 g and 2 g q8, and amikacin 15 mg/kg q24. Each regimen was tested in duplicate. Samples were serially removed over 24 hours for enumeration of colony-forming units (CFU). Antibiotic concentrations were determined by bioassay.
RESULTS: In time-kill studies, meropenem was able to maintain bactericidal activity against the susceptible strain. However, against resistant isolates, regrowth was observed by 24 hours. Against the susceptible strain in the pharmadocynamic model, both meropenem 1 g and 2 g q8 were able to reduce colony-counts from the starting inoculum by > 2 log CFU/mL after 4–8 hours of exposure. The addition of amikacin 15 mg/kg did initially enhance the activity of meropenem. Despite early reductions in CFU counts, regrowth of 2 to 3 log CFU/mL was observed at 24 hours for each regimen tested against each isolate.
CONCLUSIONS: Clinically relevant meropenem and amikacin dosing strategies, alone and in combination, showed initial activity against *A. baumannii*, including resistant isolates. However, these regimens were unable to maintain activity over time at clinically achievable pharmacokinetic parameters.

143. Community-associated methicillin-resistant *Staphylococcus aureus* (CAMRSA) hospitalized skin and soft tissue infection (cSSTI): assessment of daptomycin (DAP) vesus vancomycin (VAN). *Levi Hall, Pharm.D.*[1], Michael Rybak, Pharm.D., M.P.H.[2], Susan L. Davis, Pharm.D.[3], George Delgado Jr., Pharm.D.[4], Warren Rose, Pharm.D.[5], Robert Wilson, MD[6], Peggy McKinnon, Pharm.D.[7]; (1)Detroit Receiving Hospital and University Health Center, Detroit, MI; (2)Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University and Detroit Receiving Hospital, Detroit, MI; (3)Henry Ford Hospital and Wayne State University, Detroit, MI; (4)Detroit Receiving Hospital, Detroit, MI; (5)Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University, Detroit Receiving Hospital, Detroit, MI; (6)Detroit Receiving Hospital and University Health Center, Wayne State University School of Medicine, Detroit, MI; (7)Barnes-Jewish Hospital, St. Louis, MO.

PURPOSE: We assessed the impact of DAP versus VAN treatment on the outcome of patients with CAMRSA cSSSI.
METHODS: Patients hospitalized for cSSSI and documented CAMRSA treated with DAP 4 mg/kg IV q24h were compared with historical controls treated with VAN. DAP and VAN patients were matched 1:2 on age, APACHE II, Charlson score, and infection type. CAMRSA isolates were evaluated for SCCmec type and antibiotic susceptibilities. Outcomes included blinded assessment of clinical resolution, treatment duration and costs.
RESULTS: 42 patients, 14 DAP and 28 VAN, were assessed. Demographics in DAP, VAN: median age, 43, 43; APACHE II, 3, 2; Charlson, 0, 1; cellulitis 15%, 4%; abscess 46%, 27%; cellulitis + abscess 31%, 54%; wound (other) 8%, 15% (p=NS for all). Microbiology in DAP, VAN (p=NS) - CAMRSA alone: 92%, 92%; Polymicrobial: 8%, 8%. Patients achieving complete resolution of cSSSI on days 3, 5, 7, 10 and EOT were 31% v 0%, 54% v 15%, 69% v 19%, 69% v 27%, and 92% v 31% respectively, (p<0.05 for all). 100% of patients in both groups achieved at least partial resolution of cSSSI. In patients achieving complete resolution of cSSSI, average day of clinical cure was 4(2–7) vs. 7(4–8) in DAP and VAN, respectively (p=0.012). Median(range) total LOS was 5(3–7) and 7(3–26) days in DAP and VAN (P<0.01) corresponding to hospitalization costs of $4260 and $5964 (p<0.01). Duration of IV therapy was 3(3–6) and 7(3–14) days (p<0.01), with antibiotic cost of $567(500–930) and $574($310–$2820) (p=NS).
CONCLUSIONS: Duration of IV therapy was significantly shorter for DAP vs. VAN. Overall costs, treatment duration and LOS were all significantly lower for DAP. Rate of complete resolution was greater and time to cure was shorter in patients receiving DAP. This study supports the speed of resolution observed in clinical trials of DAP for cSSSI.

144. Treatment of candidemia at a tertiary medical center. *Stephanie Costante, Pharm.D.*, Jason Gallagher, Pharm.D., Christina Rose, Pharm.D.; Temple University Hospital, Philadelphia, PA.

PURPOSE: The objective of this study was to determine whether appropriate empiric and definitive therapy is being used in patients diagnosed with candidemia in the hospital, in addition the presence of specific risk factors for candidemia were assessed.
METHODS: Medical records of 50 patients with ICD-9 codes and/or a positive blood culture for candidemia were retrospectively reviewed during admission to Temple University Hospital from January 2003 to April 2006. Data collected included type of Candida species identified, antifungal agent, and specific risk factors were assessed up to thirty days prior to the first positive blood culture. Primary end points were the number of days of inappropriate therapy, defined as the use of fluconazole in a fluconazole-resistant species. Inappropriate definitive therapy was defined as treatment of a fluconazole-sensitive species with an alternative agent when fluconazole could have been used.
RESULTS: A total of fifty-three Candida sp. were isolated. Overall, 62% of the 53 isolates were non-albicans species. *C. albicans* represented 38% of the isolates, *C. glabrata* 33%, *C. parapsilosis* 15%, *C. tropicalis* 12%, and *C. lusitaniae* 2%. The most common risk factor was the use of broad-spectrum antibiotics (39 patients), along with the use of TPN (31 patients). Overall, 28% received inappropriate empirical therapy. In addition, 20% of patients received inappropriate definitive therapy. No correlation between a risk factor and a species could be found. In the 10 patients with inappropriate definitive therapy, a potential cost savings of $27, 941 could have been saved if treated with intravenous fluconazole in place of caspofungin.
CONCLUSIONS: Due to one-third of species being *C. glabrata*, it may be

reasonable to initiate empiric therapy with high-dose fluconazole or caspofungin. However, it is important to narrow the initial choice once a species is identified.

145. Antimicrobial usage in *C. glabrata* and *C. albicans* bloodstream infection. *Erika J. Ernst, Pharm.D.*, Nolan N. Ngo, Pharm.D., candidate, Joshua G. Miller, Pharm.D., Michael J. Klevay, M.D., Ryan Jepson, B.S., Michael Pfaller, M.D., Daniel J. Diekema, M.D.; Universiy of Iowa, Iowa City, IA.

PURPOSE: *Candida glabrata* is increasingly recognized as a nosocomial pathogen exhibiting antifungal resistance. Knowing risk factors specific to *C. glabrata* compared with *C. albicans* infection could help guide empiric antifungal therapy.
METHODS: We compared antimicrobial usage in patients with nosocomial *C. glabrata* bloodstream infection (BSI) with *C. albicans* BSI. All patients admitted to a university hospital between 1997 and 2004 with *C. glabrata* BSI were included (n=55). Patients with *C. albicans* BSI were identified from laboratory records and selected to match cases (1:1) based upon date of hospitalization. All antifungal and other antimicrobials administered before the first positive blood culture (T0) were recorded. Defined daily doses (DDD) were calculated for each antimicrobial class, according to the WHO/ATC DDD index. The Wilcoxan Signed Rank Test was used to compare antimicrobial usage between groups. Antifungal susceptibility testing was performed according to methods described by the CLSI.
RESULTS: The frequency of fluconazole susceptibility among *C. glabrata* isolates was 34.5%, 50.9%, and 14.5% for susceptible, susceptible dose-dependent and resistant isolates, respectively. For the *C. albicans* isolates, 98% were susceptible to fluconazole and 2% (1 isolate) displayed dose-dependent susceptibility. There was no difference in antifungal use or other antimicrobial use before T0 between the two groups. 15 patients in the *C. glabrata* group received an azole prior to T0 compared with 10 in the *C. albicans* group. Azole DDDs administered did not differ between groups (3.9 vs. 3.5, p>0.1).
CONCLUSIONS: Up to 85% of *C. glabrata* isolates in this study displayed full or dose-dependent susceptibility to fluconazole. Antimicrobial usage, including azole use prior to infection, was not a significant risk factor for infection with *C. glabrata* compared with *C. albicans*. Identification of risk factors other than prior azole exposure is needed to better predict the likelihood of *C. glabrata* compared with *C. albicans* infection.

146E. Phenotypic characterization of heterogeneous methicillin-susceptible *Staphylococcus aureus* correlates to patient outcomes. *Vanthida Huang, Pharm.D.*[1], Mary B. Perri, M.Ph[2], Dora Vager, B.S.[2], Marcus J. Zervos, M.D.[3]; (1)Mercer University Southern School of Pharmacy, Department of Clinical and Administrative Sciences, Atlanta, GA; (2)Henry Ford Health System, Detroit, MI; (3)Henry Ford Health System and Wayne State University School of Medicine, Detroit, MI.

Presented at the 16th European Congress of Clinical Microbiology and Infectious Diseases, Nice, France, April 1-4, 2006.

147E. Molecular epidemiology of community-associated methicillin-resistant *Staphylococcus aureus*. *Vanthida Huang, Pharm.D.*[1], Susan M. Donabedian, M.Ph.[2], Ajay K. Singh, M.D.[3], Susan L. Davis, Pharm.D.[4], Mary B. Perri, M.Ph[2], Dora Vager, B.S.[2], Karen Speirs, D.O.[3], Barbara Robinson-Dunn, Ph.D.[3], Mary K. Hayden, M.D.[5], Robert Muder, M.D.[6], Marcus J. Zervos, M.D.[7]; (1)Mercer University Southern School of Pharmacy, Department of Clinical and Administrative Sciences, Atlanta, GA; (2)Henry Ford Health System, Detroit, MI; (3)William Beaumont Hospital, Royal Oak, MI; (4)Henry Ford Hospital and Wayne State University, Detroit, MI; (5)Rush University Medical Center, Chicago, IL; (6)Veterans Affairs Medical Center, Pittsburgh, PA; (7)Henry Ford Health System and Wayne State University School of Medicine, Detroit, MI.

Presented at the 16th European Congress of Clinical Microbiology and Infectious Diseases, Nice, France, April 1-4, 2006.

148E. Stereotypical changes in the gene expression profile of *Candida albicans* in response to the sterol biosynthesis inhibitors fenpropimorph, ketoconazole, and terbinafine. Teresa T. Liu, B.S.[1], Sadri Znaidi, Ph.D.[2], Katherine S. Barker, Ph.D.[1], Lijing Xu, M.S.[1], Ramin Homayouni, Ph.D.[1], Martine Raymond, Ph.D.[2], *P. David Rogers, Pharm.D., Ph.D.*[1]; (1)University of Tennessee, Memphis, TN; (2)Institute of Research in Immunology and Cancer, Montreal, QC, Canada.

Presented at the 16th Congress of the International Society of Human and Animal Mycology, Paris, France, June 25-30, 2006.

149E. Identification of transcriptional activation targets of the transcription factor Tac1p associated with azole resistance in clinical isolates of *Candida albicans*. Teresa Liu, B.S[1], Sadri Znaidi, Ph.D.[2], Katherine S. Barker, Ph.D.[1], Lijing Xu, M.S.[1], Ramin Homayouni, Ph.D.[1], Joachim Morschhauser, Ph.D.[3], Martine Raymond, Ph.D.[1], *P. David Rogers, Pharm.D., Ph.D.*[1]; (1)University of Tennesse College of Pharmacy, Memphis, TN; (2)Institute of Research in Immunology and Cancer, Montreal, QC, Canada; (3)University of Wuerzburg, Wuerzburg, Germany.

Presented at the 8th Conference on Candida and Candidiasis of the American Society of Microbiology, Denver, CO, March 13-17, 2006.

150E. Genome-wide expression profile analysis reveals genes differentially expressed in association with fluconazole resistance in clinical isolates of *Candida glabrata*. *Kelly D. Earhart, Pharm.D.*[1], John-Paul Vermitsky, Ph.D.[2], Lijiug 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.

Presented at the 16th Congress of the International Society of Human and Animal Mycology, Paris, France, June 25-30, 2006.

151. Ganciclovir-resistant cytomegalovirus disease in heart transplant recipients. *Fanny Li, Pharm.D.*[1], Kenneth Kenyon, Pharm.D., BCPS[1], Kate Kirby, M.S.[2], Ajit P. Limaye, M.D.[1]; (1)University of Washington Medical Center, Seattle, WA; (2)Fred Hutchinson Cancer Research Center, Seattle, WA.

PURPOSE: The incidence, clinical and virologic aspects of susceptible and ganciclovir-resistant (Gan-R) cytomegalovirus (CMV) disease have not been well characterized in heart transplant recipients who receive antiviral prophylaxis.
METHODS: We performed an IRB-approved, retrospective analysis of all patients who received their first heart transplant between January 1, 1995, and June 30, 2005, at the University of Washington Medical Center. Clinical and virologic information was extracted from medical records using standardized data collection forms. Cox proportional-hazard regression was used to assess the relationship between clinical variables and CMV disease. Portions of the UL97 gene corresponding to ganciclovir resistance were sequenced.
RESULTS: Cytomegalovirus disease developed in 11.7% (32 of 274 patients), with a median onset time of 4.9 months post transplant (range 1.8–11.6 months). CMV serostatus of D+R- was independently associated with the development of CMV disease (syndrome and tissue-invasive) (adjusted HR=5.95, p<0.001), while graft rejection was a time-dependent risk factor for tissue-invasive CMV disease only (adjusted HR=3.44, p<0.001). The incidence of ganciclovir-resistant CMV was 1.5% (4 of 274) overall and significantly associated with CMV serostatus: D+R- (3 of 79 [4%]), R+ (1 of 154 [0.6%]), and D-R- (0 of 41 [0%]), p=0.04.
CONCLUSIONS: The incidence of ganciclovir-resistant CMV in heart transplant recipients is similar to other solid-organ transplant recipients. D+R- recipients are at highest risk for development of both CMV and Gan-R CMV disease after discontinuation of antiviral prophylaxis. Strategies to reduce the incidence of CMV disease, such as extension of duration of initial CMV prophylaxis and employment of CMV prophylaxis during episodes of graft rejection, require further research.

152. Clinical outcomes of using intravenous colistin for multi-drug resistant Gram-negative pathogens. *Jason C. Gallagher, Pharm.D.*; Deanne F. Moyer, Pharm.D. candidate; Katie Ang, Pharm.D., candidate; Temple University School of Pharmacy, Philadelphia, PA.

PURPOSE: Increasing prevalence of antibiotic resistance in Gram-negative organisms has led to a revisiting of systemic use of the polymyxins, including colistin. However, reports of their utility in the treatment of multi-drug resistant Gram-negative infections are limited. This study was performed to describe the use, efficacy, and safety of intravenous colistin at our institution.
METHODS: Records of patients who had received intravenous colistin during 2004-2005 were reviewed. Data collected included demographic, microbiological, laboratory, and clinical information to observe efficacy and toxicity. Outcomes of cure and improvement were considered positive, and death within 7 days and worsening were considered negative. Nephrotoxicity was defined as an increase in serum creatinine of 50% or greater and was not evaluated in patients already receiving dialysis.
RESULTS: Intravenous colistin was administered to 61 patients during the study period, of which 58 had sufficient chart data to evaluate. These patients received colistin 62 times. Colistin was started an average of 38.8 days into a hospital stay, for a mean of 10.3 days. Patients had an average length of stay of 92.6 days. Mean dose used was 3.4 mg/kg/day. Doses were judged appropriate in 30 episodes, too low in 26 episodes, and too high in 6. The most common organisms were species of *Acinetobacter* (26 episodes), *Pseudomonas* (26), and *Klebsiella* (14). Pneumonia was the most common indication. Positive

outcomes were seen in 25 infections (40%), negative outcomes in 22 infections (35%), and little clinical change was seen in 15 episodes (25%). Nephrotoxicity developed in 24/57 (42%) evaluable patients. Neurotoxicity was not observed in this study.
CONCLUSIONS: Intravenous colistin is an agent of last resort for the treatment of multi-drug resistant Gram-negative infections. It has delirious renal effects that must be monitored.

153E. Risk factors associated with *Candida albicans* and non-*albicans Candida* species for candidemia at UCI Medical Center. *Helen H. Kim, Pharm.D.*, Helen S. Lee, Pharm.D., BCPS, Lauri Thrupp, M.D.; University of California, Irvine Medical Center, Orange, CA.

Presented at the Western State Conference, Pacific Grove, CA, May 23-26, 2006.

Managed Care

154. Off-label dosing of multiple sclerosis drugs. *Kjel A. Johnson, Pharm.D.*, Ranga R. Kanumuri, M.S., Chandrika N. Kanumuri, M.B.A.; ICORE Healthcare, LLC, Orlando, FL.

PURPOSE: This study was performed to evaluate patterns of off-label dosing of multiple sclerosis (MS) drugs being used to treat MS patients insured by a commercial payor.
METHODS: 28,819 claims for injectable MS drugs for patients diagnosed with MS, paid between January 1, 2005, and September 30, 2005, were reviewed for five large commercial payors. By virtue of FDA approved guidelines and confirmation by expert opinion, an upper limit was established for FDA approved dosing. Patients were dosed "off-label" if their stable dose was greater than the established upper limit. All of the claims for off-label doses were examined to identify patients consistently being dosed off-label. Physicians associated with these patients were also identified. A cross-sectional mail survey of 120 physicians was conducted. Sixty randomly selected physicians formed the control group while the experimental group consisted of 60 physicians identified as using off-label doses to treat MS.
RESULTS: We identified a total of 8,010 MS patients in plans representing 14.8 million lives. Of these, 72 patients (0.9%) were prescribed off-label doses by 68 different physicians. Fifty-one of the 72 patients (71%) being dosed off-label were receiving the low-dose/low-frequency interferon. Physicians in the experimental group were more inclined to increase the dose beyond standard for patients on a low-dose/low-frequency interferon in an effort to better manage their patients (68% vs 28%, p<0.05). No such difference was found for the other injectable MS drugs.
CONCLUSIONS: Off-label dosing of MS products is an infrequent finding, but is most commonly associated with the low-dose/low-frequency interferon.

Medication Safety

155E. Duloxetine in the long-term management of diabetic peripheral neuropathic pain: results from three clinical trials. Joel Raskin, M.D.[1], Smriti Iyengar, Ph.D.[2], Funjun Wang, Ph.D.[2], Amy Chappell, MD[2], Deborah D'Souza, Ph.D.[2], *Andrea Collier-Johnson, Pharm.D.*[2], Timothy Smith, M.D.[3], Joachim Wernicke, M.D.[2]; (1)Eli Lilly Canada, Scarborough, ON, Canada; (2)Eli Lilly and Company, Indianapolis, IN; (3)Mercy Health Research; Ryan Headache Center, Chesterfield, MO.

Presented at the Annual Meeting of the American Pain Society, San Antonio, TX, May 3-6, 2006.

156E. A fixed-dose study of the efficacy and safety of duloxetine for the treatment of generalized anxiety disorder. Hannu Koponen, M.D., Ph.D.[1], Christer Allgulander, M.D.[2], Janelle Erickson, Ph.D.[3], Michael Detke, M.D.[3], *Lisa Jaton, R.Ph., BCPP*[4], Susan Ball, Ph.D.[5], James Russell, M.D.[3]; (1)University of Kuopio, Kuopio, Finland; (2)Karolinska Institutet, Stockholm, Sweden; (3)Eli Lilly and Company, Indianapolis, IN; (4)Eli Lilly and Company, Sioux Falls, SD; (5)Indiana University School of Medicine, Indianapolis, IN.

Presented at the Annual Conference of the Anxiety Disorder Assocation of America, Miami, FL, March 23-26, 2006.

157. Pharmacist monitoring program reduces clinically significant QTc prolongation in medical intensive care unit. *Adrienne Craven, Pharm.D.*, Chandra Hong, Pharm.D., Jill M Hara, Pharm.D., Tanya T Lindsay, B.S., Karine N Danskey, B.S., Tien MH Ng, Pharm.D.; University of Southern California, Los Angeles, CA.

PURPOSE: Patients in the intensive care unit (ICU) are often prescribed drugs known to prolong QTc interval duration and increase proarrhythmic risk. The purpose of this study was to assess the clinical benefit of a formal pharmacist QTc monitoring protocol for patients in the medical ICU.
METHODS: In a prospective, parallel-group study, 149 consecutive medical ICU patients prescribed a prespecified QTc prolonging drug at the LAC + USC Medical Center were followed using a monitoring algorithm which utilizes daily assessments of ECGs and laboratory data to generate pharmacotherapeutic recommendations. Patients were assigned on alternating days to an intervention group (clinical pharmacist assigned to physician team monitored QTc drugs using the algorithm) or a standard care group (physician team without a pharmacist utilizing the algorithm), respectively. The primary end point was the frequency of electrophysiologic adverse events, defined as prolonged QTc interval > 500 ms at any time or a QTc increase > 60 ms over baseline. Secondary end points included: absolute QTc > 470 ms in women or > 450 ms in men, mean increase in QTc at 48 hours, and number of drug discontinuations for prolonged QTc interval.
RESULTS: Algorithm generated recommendations were accepted 70% of the time by the intervention group physician team. Electrophysiologic adverse events occurred less frequently in the intervention group compared with the standard care group (12.0 vs 42.9%, p<0.001). Incidence of both absolute QTc > 500 ms (9.5 vs 32.3%, p=0.001) and QTc increase > 60 ms over baseline (8.6 vs 24.6%, p=0.013) was lower in the intervention group. Increase in QTc at 48 hours (6.0 ± 29.9 vs 21.1 ± 32.7 ms, p=0.28) and number of drug discontinuations for QTc prolongation were not statistically different.
CONCLUSIONS: In this pilot study, pharmacist monitoring of QTc prolonging drugs using a simple algorithm reduced the risk of significant QTc prolongation. Cost-effectiveness requires evaluation in a multicenter study.

158E. Antibiotics worsen quality of life for patients with upper respiratory illnesses. George G. Bergus, M.D., Cindy Weber, Pharm.D., Michael E. Ernst, Pharm.D., *Erika J. Ernst, Pharm.D.*; Universiy of Iowa, Iowa City, IA.

Presented at the 28th Annual Meeting of the Society for Medical Decision Making, Boston, MA, October 14-18, 2006.

159E. Anesthesia and ocular tolerability of topical non-steroidal anti-inflammatory drugs: a direct comparison between bromfenac and nepafenac. *Peter J. G. Maris, Jr., M.D.*, Henry D. Perry, M.D., Eric D. Donnenfeld, MD, Timothy Chou, M.D.; Ophthalmic Consultants of Long Island, Rockville Centre, NY.

Presented at the Annual Meeting of the Association for Research in Vision and Ophthalmology, Fort Lauderdale, FL, April 30-May 4, 2006.

160. Inappropriate dosing of antiplatelet and antithrombin agents for acute coronary syndrome in an electronic order entry system. *David Parra, Pharm.D., BCPS*[1], Venkataraman Balu, M.D., FCCP[1], Daniel Woods, M.D.[1], Roy Coakley, M.S.[1], Julio Camacho, B.S.[2], Amy Colon, B.S.Pharm.[1]; (1)Veterans Affairs Medical Center (119), West Palm Beach, FL; (2)Lloyd L. Gregory School of Pharmacy, Palm Beach Atlantic University, West Palm Beach, FL.

PURPOSE: A prospective observational analysis of 30136 patients reported that patients with acute coronary syndrome often receive excess doses of antiplatelet and antithrombotic therapy. However, the effect of electronic order entry or decision support tools on dosing was not analyzed. Estimate the frequency of inappropriate dosing of unfractionated heparin (UFH), low-molecular weight heparin (LMWH) and glycoprotein IIb/IIIa inhibitors in patients with ACS in a system that relies upon electronic order entry and decision support tools to promote appropriate prescribing of these agents.
METHODS: A retrospective medication use evaluation was performed on 50 random patients presenting with acute coronary syndrome in 2005. Dosing was defined using criteria described in the previous prospective observational study and was categorized as recommended, mild excess, major excess, and underdosed.
RESULTS: Twenty-one patients had UFH ordered utilizing a standard electronic order set, and were dosed appropriately with the exception of one patient. Identical results were observed with 34 patients receiving glycoprotein IIb/IIIa inhibitors which are also ordered using standard electronic order sets. In contrast, we observed a high rate of inappropriate dosing with enoxaparin. Of 28 patients receiving enoxaparin, 5 received a mild excess and 11 were underdosed. We hypothesized that because the displayed list of available doses for enoxaparin reflects packaging sizes, providers may inadvertently have rounded the dose, assuming that one of the displayed doses had to be selected. Subsequently, the software was modified to minimize the potential for this error. However, a follow-up review of 32 patients who presented after this modification revealed no improvement (4 received a mild excess, and 11 were underdosed).
CONCLUSIONS: Utilization of electronic order sets appears to be associated with improved dosing of UFH and glycoprotein IIb/IIIa inhibitors. However, rates of inappropriate prescribing with LMWH remained high, demonstrating

that the presence of such systems still requires rigorous evaluation.

161. Evaluation of medication discrepancies at hospital discharge. *Jacqueline Wong, B.Sc.Phm*[1], Olavo Fernandes, Pharm.D.[1], Jana Bajcar, M.Sc.Phm., Ed.D., FCSHP[2], Shabbir Alibhai, M.D.[1], Gary Wong, B.Sc.Phm.[1], Annemarie Cesta, B.Sc.Phm.[1], Stephanie Ong, B.Sc.Phm.[1], Jin Huh, B.Sc.Phm.[1], Jeff Nagge, Pharm.D[1], Kelly Gomes, B.Sc.[1], Tim Tripp, B.Sc.MLIS.[1]; (1)University Health Network, Toronto, ON, Canada; (2)University of Toronto, Toronto, ON, Canada.

PURPOSE: Hospital discharge is an interface of care where patients are at a high risk of medication discrepancies as they transition from hospital to home. This study aimed to identify and characterize medication discrepancies at hospital discharge.
METHODS: All consecutive patients admitted for at least 72 hours to the general internal medicine wards at a tertiary care teaching hospital were prospectively assessed. Patients were excluded if they were discharged with verbal prescriptions from the physician, transferred from a nursing home or another institution, transferred from or to another hospital unit, or passed away during hospital stay. The primary end point of the study was to determine the number of patients with at least one unintended medication discrepancy on hospital discharge. Medication discrepancies were assessed through a comparison of a best possible medication discharge list and the actual discharge medication prescriptions. The discrepancies were characterized according to standardized criteria.
RESULTS: From March 14, 2006, to June 1, 2006, 468 patients were screened for eligibility and 149 patients were included in the study. Sixty-two patients (41.6%) had at least one unintended medication discrepancy at hospital discharge. The most common medication discrepancies were an incomplete prescription requiring clarification that may result in a patient delay in obtaining medications (48.6%) and the omission of medications (24.3%).
CONCLUSIONS: Medication discrepancies occur commonly on hospital discharge. Understanding the type and frequency of discrepancies can be used to help health care professionals better understand ways to prevent them. This study highlights the need for structured medication reconciliation to prevent discharge medication discrepancies.

Nephrology

162. Dosing vancomycin during high-flux hemodialysis. *Heather A. Nyman, Pharm.D.*[1], Adhish Agarwal, M.D.[2], Harry O Senekjian, M.D.[2], Janice Gilson, Diploma[3], Alfred K. Cheung, M.D.[4], J. Ken Leypoldt, Ph.D.[4]; (1)University of Utah Dialysis Program, Salt Lake City, UT; (2)Northern Utah Nephrology, Odgen, UT; (3)VA SLC Healthcare System, Salt Lake City, UT; (4)University of Utah Dialysis Program, VA SLC Healthcare System, Salt Lake City, UT.

PURPOSE: Previous work has shown that a substantial portion of an intradialytic dose of vancomycin (VCN) may be removed during high-flux hemodialysis (HD). We wished to examine the equivalent dosages for intra-dialytic and post-dialytic administration using a first-use large surface area dialyzer (Polyflux® 24R, Gambro Renal Products).
METHODS: A crossover study was performed in 7 chronic HD patients (5 males and 2 females, 62–105 kg body weight). All patients received 1 g of VCN infused over 1 hour immediately post-HD (Phase 1) and 1.5 g through the venous tubing during the last hour of HD (Phase 2) with a 3-week washout period between doses. In both phases, VCN concentrations were measured prior to drug administration and at 0.25, 0.5, 1.0, 1.5, 2.0 and 3.0 hours following the start of the infusion and prior to the start of the next HD treatment.
RESULTS: The calculated fraction of the VCN dose removed when administered during HD was 34.9 ± 14.6% (mean ± SD, range 17.5-56.0%). Mean VCN concentrations prior to the next HD session were similar between the treatment groups (13.1 ± 2.7 mg/L in Phase 1 and 12.3 ± 3.3 mg/L in Phase 2; p=0.55). Although the mean serum concentration versus time profiles for the two phases were different (p=0.037), there was no difference in the average log-trapezoidal area under the curve (AUC) between the phases ($AUC_{0\text{-}44.5hr}$ 929 ± 33 mg-hr/L in Phase 1 and 856 ± 209 mg-hr/L in Phase 2; p=0.72).
CONCLUSIONS: VCN can be readily administered during the last hour of HD using a high-flux Polyflux 24R dialyzer, resulting in serum drug levels comparable to those achieved by post-HD administration if the VCN dose is increased by 50%.

163. Darbepoetin alfa requirement in adult chronic hemodialysis patients. *Timothy V. Nguyen, Pharm.D.*, Rosario Lazzaro, M.S., R.Ph., Robert Rigolosi, M.D.; Holy Name Hospital, Teaneck, NJ.

PURPOSE: Anemia management in chronic hemodialysis patients often requires regular administration of erythropoietic growth factors (EGF) along with iron. There are two EGFs currently available in the United States, epoetin alfa (EPO) and darbepoetin alfa (DA, Aranesp). Due to DA's newer status, it is not used extensively in End Stage Renal Disease (ESRD) patients. However, its popularity is increasing since it has a longer half-life and requires less frequent dosing. Data on DA maintenance dose are scarce. This abstract provides data on average DA maintenance-dose requirements for adult chronic hemodialysis patients.
METHODS: Retrospective data were collected for 120 adult chronic hemodialysis patients who received regular maintenance DA from October 2005 through May 2006. Target hemoglobin levels were set to achieve at least 11 g/dL or greater. Patients must have received DA at least 3 months prior to data collection. Intravenous iron was given to reach target ferritin levels 100 ng/mL or greater and transferring saturation (TSAT) levels 20% or greater. Monthly laboratory values were drawn for hemoglobin (hgb), albumin, urea reduction rate (URR), and quarterly for iron. Average DA doses were tracked weekly.
RESULTS: The average weekly DA dose was 55 µg (95% CI, mean ± 1.12). On average, 80% (95% CI, mean ± 1.62) of patients (n=96) achieved hemoglobin 11 g/dL or greater. The percentages of patients with ferritin levels 100 ng/mL or greater were 90% (n=108), TSAT levels 20% or greater were 80% (n=96), albumin levels 3 g/dL or greater were 83% (n=100), and URR 65% or greater were 93% (n=112).
CONCLUSIONS: Using darbepoetin alfa in anemia management for adult chronic hemodialysis patients achieved a target hemoglobin level of 11 g/dL or greater for the majority of patients, and the average DA weekly requirement was 55 µg.

164E. Trace element clearance in critically ill patients receiving continuous venovenous hemodiafiltration (CVVHDF). *Mariann D. Churchwell, Pharm.D.*[1], Deborah A. Pasko, Pharm.D.[2], Imad Btaiche, Pharm.D.[2], Jinesh C. Jain, Ph.D.[3], Bruce A. Mueller, Pharm.D.[4]; (1)University of Toledo College of Pharmacy, Toledo, OH; (2)University of Michigan College of Pharmacy and University Hospital, Ann Arbor, MI; (3)University of Notre Dame, South Bend, IN; (4)University of Michigan College of Pharmacy, Ann Arbor, MI.

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165. Reporting of an estimated creatinine clearance: effect on physician recognition of chronic kidney disease in elderly hospitalized patients. *Stephen J. Schafers, Pharm.D.*, Jennifer M. Quartarolo, M.D., Mark Thoelke, M.D., Ph.D.; Barnes-Jewish Hospital at Washington University Medical Center, St. Louis, MO.

PURPOSE: Early recognition of chronic kidney disease (CKD) has been shown to slow disease progression and limit complications. Serum creatinine (SrCr) levels are an inadequate screening test for CKD, especially in elderly patients. A study investigating the effect of reporting an estimated creatinine clearance (CrCl), in elderly patients with SrCr levels in the normal laboratory range, on physician recognition of chronic kidney disease was undertaken on an internal medicine floor in a large academic medical center.
METHODS: A computer database identified patients over a 2-year period with the following characteristics: age > 65, estimated CrCl < 60 ml/min, and excluded patients with creatinine values > 1.6 mg/dL or with a > 0.4 mg/dL variation in SrCr level during hospitalization. A retrospective chart review was conducted evaluating evidence of physician documentation of CKD, followed by a prospective study using the same patient parameters with the intervention of placing a CrCl notice with a CKD staging outline in the patient's chart. Fishers' Exact Test was used to analyze the association between the intervention and physician documentation of CKD in the chart.
RESULTS: Prior to the study intervention, CKD was recognized in only 10 of 260 patients (3.85%), and following the intervention, recognition rates increased to 25 of 198 patients (12.63%). The data indicate a strong association between the intervention and increased CKD recognition ($p \leq 0.001$).
CONCLUSIONS: Physician recognition and documentation of CKD were extremely low in hospitalized elderly patients with SrCr levels in the normal laboratory range. The reporting of an estimated CrCL facilitated improved CKD recognition rates by physicians; however, further study is indicated to identify pragmatic educational tools or feedback mechanisms to further improve CKD recognition rates.

166. Variation in medication prescription for anemia management of chronic kidney disease in a nationally representative sample of outpatient settings in the United States. *Rafia S. Rasu, Ph.D.*[1], Harold J. Manley, Pharm.D., BCPS[2], Rajesh Balkrishnan, Ph.D.[3], Tonya Crawford, Pharm.D., Candidate[1]; (1)University of Missouri Kansas City School of Pharmacy, Kansas City, MO; (2)Albany College of Pharmacy, Albany, NY; (3)The Ohio State University College of Pharmacy, Columbus, OH.

PURPOSE: This study examined medication prescribing variation for anemia management of chronic kidney disease (CKD) in outpatient settings in the U.S.

METHODS: This cross-sectional study used data from the National Ambulatory Medical Care Survey (NAMCS) from 1996-2003. Patients aged ≥ 18 years with CKD were included in the study sample. Office visits were considered CKD related if relevant ICD-9 codes were recorded and if CKD was reported as the reason for the visit. Similarly, visits were considered anemia related if anemia relevant ICD-9 codes were recorded and if anemia was reported as the reason for the visit or anemia related laboratory testing (e.g., hematocrit) was ordered. Anemia medications (erythropoietic stimulating agents or iron replacement) were retrieved using the NAMCS drug codes. All analyses were weighted to make national estimates.
RESULTS: Approximately 92 million weighted outpatient visits for CKD occurred between 1996 and 2003. The majority of these visits were for females and patients > 65 years, 63% and 54%, respectively. Only 18% of the CKD patient visits were made by a nephrologist. Nearly one-half (48%) of CKD outpatient visits anemia management issues were also recorded. Only 10% of visits for anemia management resulted in an anemia medication prescription. Significant time-related differences ($p \leq 0.05$) and regional variation ($p \leq 0.05$) were observed in erythropoietin prescribing patterns.
CONCLUSIONS: The findings of this study seem to suggest that few visits addressing anemia management are receiving anemia medications in U.S. outpatient settings, because most of the visits do not result in anemia medication prescription. More than 80% of CKD patient visits are not seen by a nephrologist who is most trained to address CKD and associated anemia management. With respect to national utilization pattern of anemia medication, erythropoietin had the highest number of prescriptions over the last 4 years of the study period.

168. Factors associated with hypocalcemia in hemodialysis (HD) patients receiving cinacalcet HCl for secondary hyperparathyroidism. *Charles R. McQuade, B.A.*, Alex V. Boyd, B.S., Ryan Burke, B.S., Alicia Chavez, B.S., Amy Pai, Pharm.D.; University of New Mexico, Albuquerque, NM.

PURPOSE: This retrospective cohort study evaluated hypocalcemia (serum calcium ≤ 8.4 mg/dL) in HD patients receiving cinacalcet and sought to identify potential factors associated with the development of hypocalcemia.
METHODS: Medical records of patients who received cinacalcet between January 1, 2004, and May 16, 2006, were evaluated. Demographic information and laboratory data including serum calcium (Ca), serum phosphorus (P), and parathyroid hormone (PTH) values were collected. Information on vitamin D analog and calcium-based phosphate binder use was obtained. Mean laboratory values among patients who developed hypocalcemia versus those who did not were analyzed by unpaired t-test. Chi square analysis was used to compare the frequency of vitamin D analog and calcium-based phosphate binder use.
RESULTS: A total of 42 patients with 370 Ca values was analyzed. The mean ± SD duration of cinacalcet therapy was 259 ± 191 days (range: 12–684 days). The mean ± SD age and time on hemodialysis of the patients analyzed was 50 ± 16 years and 5.9 ± 4.2 years, respectively. Twenty-nine (69%) patients had one or more episodes of hypocalcemia during treatment with cinacalcet. These patients had higher mean ± SD PTH values (754 ± 594 vs. 483 ± 247 pg/mL, $p<0.001$), and were more likely to be on doses > 30 mg ($p=0.003$), concomitant vitamin D analogs ($p<0.001$), and calcium-based binders ($p<0.001$).
CONCLUSIONS: Patients with moderate to severe hyperparathyroidism on cinacalcet doses > 30 mg had a high incidence of hypocalcemia despite concomitant vitamin D analog and calcium-based phosphate binder use. More vigilant monitoring may be warranted in these patients.

Neurology

169. Postmarketing modifications in the safety labeling of the new antiepileptics. *Marcia L. Buck, Pharm.D.*, Matthew J. Gurka, Ph.D., Howard P. Goodkin, M.D., Ph.D.; University of Virginia Children's Hospital, Charlottesville, VA.

PURPOSE: Between 1993 to 2000, eight antiepileptic drugs (AEDs), felbamate, gabapentin, lamotrigine, levetiracetam, oxcarbazepine, tiagabine, topiramate, and zonisamide, were approved by the Food and Drug Administration (FDA). While premarketing trials suggested a mild adverse effect profile for these drugs, limited information was available at the time of approval to accurately define their risks. To examine the significance of postmarketing adverse reaction reporting for the new AEDs, we reviewed safety labeling modifications made since their release.
METHODS: Safety labeling modifications made for the new AEDs from 1993 through December 2005 were identified using prescribing information and a search of the FDA MedWatch database. Mean cumulative function analysis was used to determine if there was a point at which safety labeling changes were complete.
RESULTS: All drugs underwent safety labeling changes. There were 38 modifications, with the median time to the first change being 2 years (range 13 months–12 years). Three changes involved the addition of a black box warning (2 for felbamate and 1 for lamotrigine). All occurred within 3 years after the drug's introduction. The remaining labeling modifications consisted of changes in the Adverse Reactions (n=14), Warnings (n=10), Precautions (n=10), and Clinical Pharmacology (n=1) sections. Although the majority of labeling modifications came within the first 6 years after approval, mean cumulative function analysis revealed no identifiable point at which additional changes were unlikely to be made.
CONCLUSIONS: Over the past 13 years, a significant number of modifications have been made in the safety labeling of the new AEDs, ranging from black box warnings to the addition of new data in the adverse reactions tables. This information, however, may still not be complete. Although these drugs offer significant advantages over traditional agents, clinicians must stay informed of new safety information to provide optimal therapy for patients with seizures.

170E. XP13512 improves symptoms in moderate to severe restless leg syndrome in a 2-week, randomized, double-blind, placebo-controlled exploratory trial. *Daniel M. Canafax, Pharm.D.*[1], Clete Kushida, M.D., Ph.D.[2], Philip M. Becker, M.D.[3], Aaron L. Ellenbogen, D.O., M.P.H.[4], Arthur S. Walters, M.D.[5]; (1)XenoPort Inc., Santa Clara, CA; (2)Stanford Center of Excellence for Sleep Disorders, Stanford University, Stanford, CA; (3)Sleep Medicine Association of Texas, Dallas, TX; (4)Quest Research Institute, Bingham Farms, MI; (5)New Jersey Neuroscience Institute at JFK Medical Center, Seton Hall University of Graduate Medical Education, Edison, NJ.

Presented at the 58th Annual Meeting of the American Academy of Neurology, San Diego, CA, April 1-8, 2006.

171E. Gabapentin exposure and pain reduction in patients with postherpetic neuralgia: analysis of a phase 2a randomized, double-blind, placebo-controlled study of Neurontin and XP13512. *Daniel M. Canafax, Pharm.D.*[1], Misha-Miroslav Backonja, M.D.[2], Kenneth C. Cundy, Ph.D.[1]; (1)XenoPort Inc., Santa Clara, CA; (2)University of Wisconsin Medical School, Madison, WI.

Presented at the 25th Annual Scientific Meeting of the American Pain Society, San Antonio, TX, May 3-6, 2006.

172E. XP13512 improves symptoms and sleep disturbance in RLS patients: results of a 2-week, randomized, double-blind, placebo-controlled crossover polysomnography trial. *Daniel M. Canafax, Pharm.D.*[1], Clete Kushida, M.D., Ph.D.[2], Philip M. Becker, M.D.[3], A. Thomas Perkins, M.D., Ph.D.[4], Stephen G. Thein, Ph.D.[5], Arthur S. Walters, M.D.[6], Thomas Roth, Ph.D.[7]; (1)XenoPort Inc., Santa Clara, CA; (2)Stanford Center of Excellence for Sleep Disorders, Stanford University, Stanford, CA; (3)Sleep Medicine Association of Texas, Dallas, TX; (4)Raleigh Neurology Associates, Raleigh, NC; (5)Pacific Research Network, Inc., San Diego, CA; (6)New Jersey Neuroscience Institute at JFK Medical Center, Seton Hall University School of Graduate Medical Education, Edison, NJ; (7)Henry Ford Hospital Sleep Disorders Center, Detroit, MI.

Presented at SLEEP 2006, the 20th Anniversary Meeting of the Associated Professional Sleep Societies, Salt Lake City, UT, June 17-22, 2006.

173. Rasagiline does not promote a tyramine pressor response in levodopa-treated patients with Parkinson's disease. *Jack J. Chen, Pharm.D.*[1], Richard C. Berchou, Pharm.D.[2], Crystal Obering, Pharm.D., M.B.A.[3]; (1)Loma Linda University, Loma Linda, CA; (2)Wayne State University, Bingham Farms, MI; (3)Kansas City VA Medical Center, Kansas City, MO.

PURPOSE: Tyramine is an indirect-acting sympathomimetic amine. The enzyme, monamine oxidase (MAO), which metabolizes and deactivates biogenic amines, has 2 immunologically distinct isoenzymes: MAO-A and B. MAO-A is predominant (80%) in the gut and metabolizes tyramine. Use of nonselective MAO inhibitors and ingestion of tyramine can provoke a life-threatening pressor response ("cheese reaction"). The objective is to assess whether rasagiline, a selective, irreversible inhibitor of MAO-B shown to be safe and effective for treatment of Parkinson's disease (PD), induces a tyramine pressor response.
METHODS: On the last day of the 26-week, double-blind study of rasagiline in 472 levodopa-treated PD patients with motor fluctuations (PRESTO), 55 patients randomized to rasagiline 0.5 or 1.0 mg/day or placebo underwent blood pressure (BP), heart rate (HR), and ECG monitoring before and for 3 hours after receiving a 50-mg oral tyramine HCl dose. The primary end point was incidence of systolic BP (SBP) increases ≥ 30 mm Hg or reflex bradycardia (HR < 40 bpm) observed in 3 consecutive measurements, or clinically significant ECG changes.
RESULTS: Before tyramine challenge, there were no significant differences in BP or HR among treatment groups. SBP elevations occurred in 3/22 (14%) patients taking rasagiline 0.5 mg/day, 0/12 patients taking rasagiline 1 mg/day, and 1/21 (5%) patients taking placebo. Incidence of BP changes was not

significantly different between rasagiline-treated and placebo-treated patients. BP changes were asymptomatic, with no associated adverse events, HR, or ECG changes.
CONCLUSIONS: Rasagiline does not promote a tyramine pressor response and can be used without dietary tyramine restrictions by levodopa-treated PD patients.

174. Transdermal rotigotine: evaluation of efficacy and continuous drug delivery in Parkinson's disease. *Jack J. Chen, Pharm.D.*[1], J. William Langston, M.D.[2], Joseph Jankovic, M.D.[3], Fen Lei Chang, Ph.D., M.D.[4]; (1)Loma Linda University, Loma Linda, CA; (2)The Parkinson's Institute, Sunnyvale, CA; (3)Baylor College of Medicine, Houston, TX; (4)Fort Wayne Neurological Center, Fort Wayne, IN.

PURPOSE: To evaluate the efficacy and absorption at different application sites of a transdermal patch formulation of rotigotine, a new dopamine agonist approved for monotherapy of Parkinson's disease (PD) in the EU and under investigation in the U.S.
METHODS: Data were collected from four double-blind, randomized, placebo-controlled trials of rotigotine (2–16 mg/24h) in early-stage and late-stage PD. Outcome was primarily assessed by the UPDRS (II +III) in early-stage PD and by the mean reduction in "off" time in late-stage PD. Given the transdermal mode of delivery, data from a separate pharmacokinetic trial with rotigotine applied to one of six application sites also are presented.
RESULTS: In two Phase III clinical trials, early-stage PD patients treated with rotigotine optimally dosed up to 6 mg/24 hrs or 8 mg/24 hrs had significantly improved Parkinsonian symptoms (assessed by the UPDRS) compared with placebo ($p<0.0001$ [n=177 rotigotine, n=96 placebo]; and $p<0.0001$ [n=213 rotigotine, n=117 placebo]). Rotigotine also led to a statistically greater mean reduction in "off" time relative to placebo in two Phase III trials of late-stage PD ($p<0.001$ [n=202 for rotigotine up to 16 mg/24 hrs, n=100 placebo]; $p<0.001$ for 8mg/24h rotigotine [n=113] and $p=0.003$ for 12 mg/24h rotigotine [n=109], both vs. placebo [n=119]). Overall, mean rotigotine plasma levels remained relatively stable throughout the 24-hour patch cycle and were similar among application sites (n=63).
CONCLUSIONS: In all four Phase III clinical trials, rotigotine resulted in statistically significant improvement on UPDRS (II+III) scores and in reduction in "off" time for patients with early-stage or late-stage PD compared with placebo, respectively. Furthermore, once-daily application of the rotigotine patch resulted in a relatively stable 24-hour plasma concentration profile regardless of application site.
Supported by SCHWARZ PHARMA.

175. Lack of rasagiline–tyramine interaction in levodopa-naïve patients with Parkinson's disease. *Jack J. Chen, Pharm.D.*[1], Richard C. Berchou, Pharm.D.[2], Crystal Obering, Pharm.D., M.B.A.[3]; (1)Loma Linda University, Loma Linda, CA; (2)Wayne State University, Bingham Farms, MI; (3)Kansas City VA Medical Center, Kansas City, MO.

PURPOSE: Two isoforms of monamine oxidase (MAO), an enzyme that deaminates bioactive amines, have been identified (MAO-A and B). MAO-A is found primarily in the GI tract where it metabolizes tyramine, an indirectly acting sympathomimetic amine. Nonselective MAO inhibition can impede tyramine metabolism in the periphery, leading to catecholamine release and provoking a life-threatening pressor response ("cheese reaction"). The objective is to evaluate the risk of inducing a pressor response to tyramine in patients receiving rasagiline, a potent, second-generation, selective, irreversible MAO-B inhibitor.
METHODS: On the last day of the 6-month, randomized, double-blind phase of the TEMPO study of rasagiline monotherapy in early PD patients, a subgroup of patients (n=55) randomized to rasagiline 1 or 2 mg/day or matching placebo received a 75-mg tyramine HCl dose within 60 minutes after a meal. Supine blood pressure (BP), heart rate (HR), and ECG were assessed before and for 4 hours after tyramine challenge. A pressor response was defined as systolic BP (SBP) increase ≥ 30 mm Hg from baseline or reflex bradycardia (HR < 40 bpm) sustained for ≥ 10 min and documented over 3 consecutive measurements, or clinically significant ECG change.
RESULTS: Mean changes from baseline SBP post-challenge were not different among treatment groups. Two patients (placebo [n=1], 2 mg rasagiline [n=1]) reported headache during tyramine challenge, but had no hemodynamic changes suggestive of a tyramine reaction.
CONCLUSIONS: No pressor responses were observed in PD patients receiving rasagiline 1 mg or 2 mg monotherapy after ingestion of supra-dietary amounts of tyramine, supporting the selective MAO-B inhibition of rasagiline at therapeutic dosages.

176E. A retrospective review of labetalol and nicardipine for acute hypertension following stroke. *Xi Liu-DeRyke, Pharm.D.*, Dennis Parker, Pharm.D., Denise Rhoney, Pharm.D.; Wayne State University, Detroit, MI.

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177E. Use of calcaneal ultrasound test as a screening device in patients taking antiepileptic agents. *Timothy E. Welty, Pharm.D.*, Andrea Pierce, Pharm.D.; McWhorter School of Pharmacy, Birmingham, AL.

Presented at the Annual Meeting of the American Epilepsy Society, Washington, D.C., December 2-6, 2005.

178. Rasagiline, a second-generation, selective, irreversible MAO-B inhibitor is effective in patients with early Parkinson's disease (The TEMPO Study). *Richard C. Berchou, Pharm.D.*[1], Jack J. Chen, Pharm.D.[2], Crystal Obering, Pharm.D., M.B.A.[3]; (1)Wayne State University, Bingham Farms, MI; (2)Loma Linda University, Loma Linda, CA; (3)Kansas City VA Medical Center, Kansas City, MO.

PURPOSE: The enzyme, monamine oxidase type B (MAO-B), is predominant in the breakdown of dopamine in the brain. Selective inhibition of MAO-B results in elevation of striatal synaptosomal dopamine concentrations, thereby improving parkinsonian symptoms. Rasagiline is a potent, irreversible, selective, second-generation MAO-B inhibitor. Unlike the older drug in its class, selegiline, rasagiline has no amphetamine metabolites. The objective is to evaluate the efficacy, safety, and tolerability of rasagiline as monotherapy in patients with early Parkinson's disease (PD).
METHODS: This 26-week, multicenter, parallel-group, randomized, double-blind, placebo-controlled trial included early PD patients (N=404) not requiring dopaminergic therapy. Patients were randomized to rasagiline 1 mg/day or 2 mg/day or matching placebo. The primary outcome was the change in total Unified Parkinson's Disease Rating Scale (UPDRS) score from baseline to end of study at 26 weeks. Secondary measures included changes in UPDRS subscale scores.
RESULTS: Rasagiline monotherapy was effective, safe, and well tolerated. Statistically significant improvements in total UPDRS scores were observed with rasagiline 1 mg vs placebo (adjusted effect size -4.20, 95%CI: -5.66, -2.73; p=0.0001), and rasagiline 2 mg vs placebo (adjusted effect size -3.56, 95%CI: -5.04, -2.08; p=0.0001). Rasagiline also significantly improved scores in the UPDRS activities of daily living and motor subscales compared with placebo. Both rasagiline dosages were equally effective. There were no statistical differences in frequency of adverse events or rate of study withdrawal among the 3 treatment arms.
CONCLUSIONS: Rasagiline monotherapy is safe and effective compared with placebo in patients with early PD who are not receiving dopaminergic therapy.

Nutrition

179. In vitro evaluation of albumin addition to parenteral nutrition: filter integrity and albumin and multivalent cation availability. *Catherine M. Crill, Pharm.D.-*[1], Lindsay R. Lester, Pharm.D.[1], Lawrence A. Robinson, M.S., Pharm.D.[2], Emily B. Hak, Pharm.D.[1]; (1)The University of Tennessee Health Science Center, Memphis, TN; (2)Methodist Alliance Home Infusion, Memphis, TN.

PURPOSE: Human serum albumin is occasionally added to pediatric parenteral nutrition (PN) solutions. This practice has not been adequately evaluated and is discouraged by albumin manufacturers. This in vitro study evaluated the effect of albumin addition to PN solutions on filter integrity and pre and post filter availability of albumin and multivalent cations.
METHODS: PN solutions (n=12) of varying formulations (maintenance volume, partially and fully volume-restricted neonatal and maintenance-volume child) and varying albumin concentrations (0, 8, and 16 g/L) were hand compounded in duplicate and allowed to infuse through a 0.2-micron in-line filter over 24 hours into receiving containers. Samples were collected from PN solution and receiving container (pre and post filter) from all solutions at baseline, 12 and 24 hours and analyzed for albumin, calcium, magnesium, and phosphorous concentration. Filter integrity was tested via bubble-point at infusion end.
RESULTS: Percent differences in pre and post filter calcium, magnesium and phosphorous concentrations were within acceptable deviation (≤ 10%). Pre and post filter albumin concentrations were different at baseline for all solutions containing albumin (mean % difference 72 ± 30, range 42%–100%). All post filter albumin concentrations were undetectable from solutions containing 8 g/L albumin and 44% ± 4% (range 42%–50%) of expected concentration from solutions containing 16 g/L albumin. Pre and post filter albumin concentrations were similar at 12 and 24 hours. The total albumin dose reaching the receiving container was not measured. All filters passed integrity testing.
CONCLUSIONS: A binding phenomenon occurs during early infusion of albumin via PN that is likely saturable because it disappears by 12 hours. This effect may be related to albumin binding to the filter, bag, or tubing, or albumin binding to other compounds, preventing it from being filtered. Albumin infusion via PN cannot be recommended as a reliable method for ensuring delivery of prescribed dosing.

180. Efficacy of pancreatic enzyme powder and sodium bicarbonate for clearance of occluded enteral feeding access devices. *Caitlin S. Curtis, Pharm.D.*[1], Kenneth A. Kudsk, M.D.[2], Gordon S. Sacks, Pharm.D., B.S.[3]; (1)University of Wisconsin Hospital and Clinics, Department of Pharmacy, Madison, WI; (2)University of Wisconsin - Madison, School of Medicine, WI; (3)The University of Wisconsin - Madison, School of Pharmacy, Madison, WI.

PURPOSE: To determine the effectiveness of pancreatic enzyme powder (Viokase®, Axcan Pharma, Birmingham, AL) and sodium bicarbonate combination (PEP/SB) in the clearance of enteral feeding access device occlusions.

METHODS: Medical records of consecutive adult patients with orders for PEP/SB during hospital admissions between July 1, 2005, and December 31, 2005, were retrospectively reviewed. Data collected and analyzed included: demographic data, tube type, bore size, and tube material, radiographic confirmation of tube placement, and surgical/interventional radiology procedure notes. Progress notes were reviewed to determine the necessity for replacing occluded enteral feeding access devices. Follow-up abdominal X-rays ordered within 48 hours after PEP/SB administration for tube placement verification were also used to indicate that PEP/SB clearance failed and that enteral feeding devices had to be replaced.
RESULTS: Medical records of 32 patients were identified with obstructed enteral access devices during the review period. Small-bore nasoenteric enteral feeding tubes (10 Fr) made of polyurethane were placed in 16 patients, latex rubber jejunostomy feeding tubes (7 Fr–18 Fr) were surgically placed in 10 patients, and silicone gastrostomy tubes (12 Fr–20 Fr) were percutaneously placed in 6 patients. The average number of PEP/SB doses was 1.5 per patient. PEP/SB administration was 90% (9/10) effective in jejunostomy tube clearance and 44% (7/16) effective in nasoenteric tube clearance. PEP/SB successfully cleared 5/6 gastrostomy tubes, and the 6th tube was manually cleared by interventional radiology and replacement was not necessary.
CONCLUSIONS: Our data suggest that PEP/SB is effective in clearing jejunostomy and gastrostomy enteral feeding access devices. PEP/SB is less effective in clearing nasoenteric feeding tubes, with approximately a 50% success rate. Increased failure rates may be due to smaller bore size or tube material.

Oncology

181. Outcome of implementing a protocol for the management of chemotherapy-induced hypersensitivity. *Carrie S. Molesa, Pharm.D.*, Kathryn Conner, Pharm.D. Candidate, Chin Y. Liu, Pharm.D., BCOP; Detroit Medical Center/Karmanos Cancer Hospital, Detroit, MI.

PURPOSE: Acute hypersensitivity reaction is an unpredictable and potentially catastrophic complication associated with chemotherapy. Clinical manifestations of hypersensitivity reactions range from uncomfortable cutaneous symptoms to respiratory arrest, cardiac collapse, and even death. Therefore, prompt intervention is paramount to minimize the potential severity of such events. A protocol for the management of hypersensitivity reactions was developed and approved by the Hematology/Oncology Pharmacy and Therapeutics Subcommittee in 2004. The aim of this study is to evaluate the outcome of implementing this protocol.
METHODS: This is a retrospective chart review study. Seventeen patients admitted to the outpatient chemotherapy infusion center between October 1, 2004, and June 30, 2005, were identified through the adverse event reporting system. Patient demographics, chemotherapy agents, hypersensitivity reactions, time to initiation of protocol and outcome of interventions were collected.
RESULTS: Platinums, taxanes, and rituximab were the most common agents to cause hypersensitivity reactions. Most patients experienced grade 2 reactions, such as itching, flushing, and pain. In the 11 patients treated per protocol, the median time to hypersensitivity reaction was 20 minutes (range: 2–90 mins) and the median time to first treatment medication administered was 10 minutes (range: 5–25 mins). In comparison, those patients treated according to physician's orders experienced a median time to reaction of 7.5 minutes (range: 3–60 mins) and a median time to intervention of 27.5 minutes (range: 15–55 mins). Most reactions were resolved upon the intervention.
CONCLUSIONS: The initiation of the hypersensitivity management protocol, upon the event, minimizes exposure to the offending agent and implements appropriate therapeutic and supportive measures according to the predefined grade of severity. Our data supports the use of the protocol.

182E. A randomized open-label study of darbepoetin alfa administered every 3 weeks with or without parenteral iron in anemic subjects receiving chemotherapy. An Vandebroek, M.D.[1], Bernd Gaede, M.D.[2], Sevilay Altintas, M.D.[3], Kay Smith, B.sc., (Hons)[4], Bin Yao, M.S.[4], *Marco Schupp, M.D.*[5], Laurent Bastit, M.D.[6]; (1)Ziekenhuisnetwerk Antwerpen, Antwerpen, Belgium; (2)Schwerpunktpraxis Hamatologie/Onkologie (MediProjekt), Hannover, Germany; (3)Universitair Ziekenhuis Antwerpen, Oncologie, Edegem, Belgium; (4)Amgen Ltd, Cambridge, United Kingdom; (5)Amgen (Europe) GmbH, Zug, Switzerland; (6)Centre Frederic Joliot, Rouen, France.

Presented at the Annual Meeting of the Americal Society of Clinical Oncology, Atlanta, GA, June 2-6, 2006.

183. Assessment of the effect of aprepitant on cytochrome P450-mediated metabolism of taxane agents. *Judith A. Smith, Pharm.D., BCOP*[1], Larry C. Coffer, B.S.[1], Jiang Yu, M.D.[1], Jade M. Hatley, B.S., M.S.[2], Robert Coleman, MD[1]; (1)The University of Texas, M.D. Anderson Cancer Center, Houston, TX; (2)University of Texas Health Sciences at Houston Graduate School of Biomedical Sciences, Houston, TX.

PURPOSE: To investigate the effect(s) of aprepitant on in vitro cytochrome P450 (CYP450)-mediated taxane metabolism and evaluate the potential for drug-drug interaction.
METHODS: A high-throughput assay employing individual CYP450 isoenzymes was utilized to assess the potential for inhibition of CYP450 substrate metabolism. Enzyme microsomes were exposed to varying concentrations of aprepitant to determine IC50 values corresponding to each isoenzyme. Analysis of potential induction of CYP450-mediated paclitaxel and docetaxel metabolism was evaluated by a primary human hepatocyte ex vivo model in the presence or absence of pre-treatment with aprepitant. Appropriate controls were used in all metabolism experiements. The potential for alteration of steroid xenobiotic receptor (SXR) expression was assessed via RT-PCR utilizing mRNA isolated from hepatocytes exposed to paclitaxel, docetaxel, compared with each in combination with aprepitant.
RESULTS: At clinically relevant concentrations aprepitant demonstrated moderate inhibition of CYP450 3A4-mediated metabolism, but minimal inhibition of CYP450 2C8/9 isoenzymes. In the human hepatocyte experiments aprepitant significantly induced CYP450-mediated metabolism of paclitaxel with mean of 77% ± 17%, which was similar to induction by rifampin with mean of 70.1% ± 27%. SXR expression was also up-regulated in those cultures treated concomitantly with taxane and aprepitant.
CONCLUSIONS: Aprepitant-induced paclitaxel metabolism in the ex vivo human hepatocyte model suggesting in vivo aprepitant has the potential to alter paclitaxel pharmacokinetic profile and ultimately the efficacy of paclitaxel treatment. Additional concern about this drug-drug interaction arises from aprepitant's up-regulation of SXR expression, which is associated with modulation of MDR1/p-glycoprotein (PGP) expression could facilitate development of drug resistance to chemotherapy agents that are substrates of PGP. Confirmatory studies of the downstream effects of SXR up-regulation are needed.

184. Evaluation of palifermin to decrease mucositis during non-TBI stem cell transplant. *Marc Earl, Pharm.D.*, Kristi Lenz, Pharm.D., Kathy Hogan, Pharm.D.; Medical University of South Carolina, Charleston, SC.

PURPOSE: Patients undergoing hematopoietic stem cell transplant (HSCT) are at high risk of mucositis as a result of conditioning regimens. The FDA-approved indication to reduce intensity and severity of mucositis for palifermin is based on patients receiving total body irradiation (TBI). Data with conditioning regimens not containing TBI are lacking; however, these regimens cause 30% to 50% grade 3 or 4 mucositis. This study assessed the addition of palifermin to non-TBI conditioning regimens during HSCT to reduce the incidence and severity of mucositis.
METHODS: Autologous HSCT patients with non-Hodgkin's lymphoma or Hodgkin's disease treated between 2000 and 2006 were included. The primary outcome was the incidence of grade 3 or 4 mucositis. Secondary end points included use of total parenteral nutrition (TPN), patient-controlled analgesia (PCA), febrile neutropenia, and length of stay (LOS).
RESULTS: Sixty-three patients were included in the analysis (50 control patients, 13 patients receiving palifermin). The incidence of grade 3 or 4 mucositis was 60% for control patients and 0% for palifermin patients. There was no use of TPN or PCA in the palifermin group. Of control patients, 46% required PCA and 56% required TPN. There were no differences in time to neutrophil engraftment (median 11 days) or LOS (median, control – 21 days, palifermin – 20 days). For the control and palifermin groups, the incidence of febrile neutropenia (78% vs. 77%) and documented infection (12% vs. 15%) were similar. Three patients in the palifermin group developed grade 3 rash.
CONCLUSIONS: In autologous HSCT patients, palifermin use did not appear to affect the rate of neutrophil engraftment, LOS, or febrile neutropenia. However, it may decrease the incidence of grade 3 or 4 mucositis, TPN use, and PCA use. These are not only important for quality of life during HSCT but also could offset the costs of palifermin during autologous HSCT.

185E. Hematopoietic response to epoetin alfa 60,000 units every 2 weeks in anemic patients with cancer not receiving chemotherapy or radiation therapy. Daniel Shasha, M.D.[1], John Xie, Ph.D.[2], Richard C. Woodman, M.D.[2],

Denise Williams, M.D.[3], *Francois Wilhelm, M.D.*[2]; (1)Beth Israel Medical Center, New York, NY; (2)Ortho Biotech Clinical Affairs, LLC, Bridgewater, NJ; (3)Johnson and Johnson Pharmaceutical Research and Development, Raritan, NJ.

Presented at the 18th International Symposium of the Multinational Association of Supportive Care in Cancer, Toronto, ON, Canada, June 22-24, 2006.

186. An evaluation of colony-stimulating factor use in pediatric cancer patients. Amy B. Gamlin, Pharm.D., John H. Rodman, Pharm.D., Scott C. Howard, M.D., M.S., Victor M. Santana, M.D., Mary V. Relling, Pharm.D., *James M. Hoffman, Pharm.D., M.S.*; St. Jude Children's Research Hospital, Memphis, TN.

PURPOSE: Colony-stimulating factors (CSFs; filgrastim, pegfilgrastim, and sargramostim) are used in oncology to reduce febrile neutropenia and speed neutrophil recovery. Although CSFs are widely used in pediatrics, published CSF guidelines contain limited information for this patient population. As an initial step to establish pediatric guidelines, we studied patterns of CSF use at a major pediatric oncology center.
METHODS: Demographic, dosing, and laboratory data were prospectively collected from all patients that received a CSF from October 17 to December 31, 2005. Allogeneic transplant donors and chronic neutropenia patients were excluded.
RESULTS: During the study period, 234 courses of CSF were administered to 107 patients. Acquisition costs for CSFs constitute approximately 10% of the pharmacy budget for our hospital. Filgrastim accounted for 87% of doses and 194 courses of therapy. Most CSF courses were administered to hematopoietic stem cell transplant patients (n=110, 47%) and solid tumor patients (n=103, 44%). Consistent with label recommendations, the median dose of filgrastim was 5 µg/kg. The median duration of therapy for filgrastim and sargramostim was 7 days (range 1–29 days). Absolute neutrophil count (ANC) at CSF stop ranged from 0 to 41,400 cells/uL (mean 6,971, median 4,212). In 112 courses ordered with an ANC target to stop therapy, the target ranged from 500 to 10,000 cells/uL. In 56% of filgrastim and sargramostim courses, CSFs were given after the nadir when the ANC was > 1000 cells/uL; for 36% of courses, > 3 doses were administered after the nadir when the ANC was > 1000 cells/uL.
CONCLUSIONS: Substantial variability exists in the duration of therapy and in the ANC at the time of CSF discontinuation. Doses were often administered to patients who were not neutropenic. These data will be used to develop guidelines for use of CSFs in pediatrics.

Pediatrics

187. Dyslipidemia differences among protease inhibitors (PIs) in children. *Renee M. St. Germain, Pharm.D.*[1], S. Elizabeth Lucini, Pharm.D.[2], Jennifer M. Ellis, Pharm.D., BCPS[1], Craig I. Coleman, Pharm.D.[3], Juan C. Salazar, MD, MPH[1]; (1)University of Connecticut / Conn Children's Med Center, Hartford, CT; (2)University of Connecticut, School of Pharmacy, Storrs, CT; (3)University of Connecticut/Hartford Hospital, Hartford, CT.

PURPOSE: Adult data suggest that PI use is associated with dyslipidemias and increased cardiovascular risk. Similar abnormalities in children have recently been described. As such, data evaluating which PIs are more likely to cause dyslipidemias in children are needed.
METHODS: A retrospective cohort review between 6/1996 and 11/2005 was conducted to determine whether differences exist in total cholesterol (TC) or triglycerides (TG) between PIs in children. After receiving expedited IRB approval and HIPAA waiver, PI exposures were identified via pediatric HIV clinic records and recorded using a standardized data collection tool. Lipid elevations were defined as: borderline TC (170–199 mg/dL), high TC (≥ 200 mg/dL), and high TG (> 200 mg/dL). Age, gender, individual and total PI exposure, as well as CD4% were evaluated. The association between PI exposure and dyslipidemias was explored using multiple logistic regression analysis.
RESULTS: 363 PI exposures with TC and TG values were identified. 92 patients were excluded for either CD4% not recorded (n=33) or PI exposure < 90 days at recorded TC/TG (n=59). PI exposures included: amprenanvir (n=49), atazanavir (n=17), fosamprenavir (n=5), lopinavir (n=97), nelfinavir (n=49), ritonavir (n=52) and saquinavir (n=2). High TC, borderline TC, and high TG were shown with 26, 49, and 27% of total exposures, respectively. Exposure to nelfinavir was independently associated with both a decreased risk of high TC (p=0.01) and high TG (p<0.01). For high TG, total PI exposure > 5 years also demonstrated a decreased risk (p=0.02). For borderline TC, atazanavir (p<0.01) was independently associated with a decreased risk.
CONCLUSIONS: This small retrospective evaluation suggests that exposure to atazanavir and nelfinavir may be less likely to cause dyslipidemias in children. Although total PI exposure > 5 years appeared to decrease risk, it is likely that high TGs were not duration-related and if present, children were switched to non-PI containing regimens earlier in therapy.

188. Dexmedetomidine use in the pediatric intensive care unit. *Marcia L. Buck, Pharm.D.*, Douglas F. Willson, M.D.; University of Virginia Children's Hospital, Charlottesville, VA.

PURPOSE: Dexmedetomidine is a useful sedative for patients on mechanical ventilation, but little information is available on its use in children. Our initial experience with dexmedetomidine in the pediatric intensive care unit was assessed to evaluate efficacy, dosing requirements, and adverse effects.
METHODS: A prospective evaluation was conducted in children receiving dexmedetomidine between 5/05 and 5/06. Patient demographics, rationale for use, dose, duration, concomitant sedatives, and adverse effects were evaluated. Blood pressure and heart rate were assessed 1 hour before and following initiation, and again 1 hour before and after discontinuation. Results were compared with a two-tailed T-test for paired data.
RESULTS: Twenty treatment courses in 17 children were evaluated. Median age was 5 months (range 1 month-17 years). Thirteen patients had undergone cardiac surgery, two had respiratory failure, one had endocarditis, and one had orthopedic surgery. Ten patients had neurologic impairment, including nine with Down syndrome. Loading doses were not used. The mean starting dose was 0.2 ± 0.1 µg/kg/hr. The mean maximum dose was 0.5 ± 0.2 µg/kg/hr. Mean duration was 32 ± 21 hours (range 2–75 hours). In 15 cases, dexmedetomidine was initiated to reduce the dose of other sedatives prior to extubation. In the remaining cases, it was used with other agents during prolonged intubation. In 12 of the 13 patients given midazolam, dexmedetomidine use permitted discontinuation of midazolam within 24 hours. Mean arterial pressure and heart rate before and after starting therapy were not significantly different (60 ± 10 vs 60 ± 9 mm Hg; p=0.76 and 127 ± 26 vs 122 ± 28 bpm; p=0.09), nor were values taken at discontinuation (61 ± 11 vs 63 ± 12 mm Hg; p=0.31 and 114 ± 20 vs 121 ± 27 bpm; p=0.06).
CONCLUSIONS: Our experience with dexmedetomidine in children was favorable. It allowed for reduction or elimination of other sedatives, and was particularly useful in children with neurologic impairment. It was well tolerated, with minimal cardiovascular adverse effects.

189. Differences between pediatric asthma patients and their caregivers' perceived responsibilities for management tasks. *Paul J. Munzenberger, M.S., Pharm.D.*[1], Abdul Bahrainwala, M.D.[2]; (1)Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University, Detroit, MI; (2)Wayne State University, School of Medicine, Detroit, MI.

PURPOSE: The purpose was to explore the differences between pediatric asthma patients and their caregivers' perceived responsibilites for asthma management tasks.
METHODS: Within a pediatric allergy clinic, demographic data and patient asthma characteristics were collected via interview and patient record. The asthma responsibility survey was completed separately by the patient and caregiver. It contained 10 asthma management tasks, including recognition of an attack and starting treatment, use of controller and preventive medication, need for refills and used to take along with child when traveling, avoiding triggers, informing teachers, adjusting activity during episodes, and using peak flow meters. Each task was scored from 1, indicating caregiver responsible all of the time, through 5 indicating child responsible all of the time.
RESULTS: Eighty-eight children and their caregivers completed the survey. Patients had primarily moderate (57) to severe (27) asthma. Mean patient age, years with asthma and number of controller drugs were 11.1, 8.9, and 1.7, respectively. For all tasks, the caregive assumed responsibility (score < 3). Children assumed responsibility (score > 3) for treating an episode, avoiding triggers, and taking drugs along when traveling. The overall difference between child and caregiver perceived responsibility was 1.47. The greatest differences occurred with taking drugs along when traveling (1.8) and avoiding triggers (1.74). The least difference occurred with need for refills (1.18).
CONCLUSIONS: This study suggests there are differences in perceived responsibilities for asthma management tasks between children and their caregivers. This may influence adherence, and tasks should be reviewed, when appropriate, by the pharmacist with caregivers and children.

190E. Attention and deportment ratings of transdermal methylphenidate in ADHD. *Hilary Mandler, Pharm.D.*; Shire Pharmaceuticals, Wayne, PA.

Presented at the 2006 Annual Meeting of the American Psychiatric Association, Toronto, ON, Canada, May 24, 2006.

191E. Effects of variable wear times on transdermal methylphenidate in ADHD. *Hilary Mandler, Pharm.D.*; Shire Pharmaceuticals, Wayne, PA.

Presented at the Annual Meeting of the American Psychiatric Association, Toronto, ON, Canada, May 23, 2006.

192E. Clinician-rated effects of MTS and OROS methylphenidate in pediatric ADHD. *Nicole Griswold, Pharm.D.*; Shire Pharmaceuticals, Wayne, PA.

Presented at the Annual Meeting of the American Psychiatric Association, Toronto, ON, Canada, May 24, 2006.

193E. Abrupt conversion from oral methylphenidate to a transdermal patch. *Nicole Griswold, Pharm.D.*; Shire Pharmaceuticals, Wayne, PA.

Presented at the Annual Meeting of the American Psychiatric Association, Toronto, ON, Canada, May 24, 2006.

194. A study utilizing a survey and a mock scenario to evaluate community pharmacists' recommendations for treatment of fever in children. Allison M. Chung, Pharm.D., BCPS[1], *Elizabeth A. Cobb, Pharm.D.*[2]; (1)Auburn University, Department of Pharmacy Practice; University of South Alabama, Department of Pediatrics, Mobile, AL; (2)CVS Pharmacy, Milton, FL.

PURPOSE: To assess community-based pharmacists recommendations for treatment of fever in children. More specifically, our study focused on how often alternating doses of acetaminophen (APAP) and ibuprofen (IBU) was recommended.
METHODS: This was a prospective, non-controlled descriptive evaluation. The project used both a survey and a mock case scenario to assess the responses of community-based pharmacists in the Gulf Coast region of Alabama and Florida. 125 surveys were mailed to all pharmacies identified in the region. Forty pharmacies were randomly selected for mock scenario interventions. Mock scenarios were conducted over the phone using an objective nonmedical person.
RESULTS: We achieved a 45% response rate from the survey. The majority of pharmacists who responded to the survey were male (61%) and worked in chain pharmacies (71%). For the majority surveyed, the agent of choice for fever was APAP (59%). Alternating APAP and IBU was recommended by 82%. Of the pharmacists that recommended alternating therapy, the alternating schedules varied: q4h (28%), q3h (21%), q2h (21%) and q6h (16%). Regression analysis noted that a longer amount of time in pharmacy practice (p=0.016) and an older age (p=0.026) correlated with an increased likelihood to recommend alternating APAP and IBU. Thirty-five pharmacies were included for analysis of the mock scenario. Results from the mock scenario demonstrated that pharmacists would initially recommend either APAP (31%) or IBU (34%). Alternating was recommended by 51% of pharmacists. Of the pharmacists who recommended alternating therapy, 72% recommended an alternation schedule: q3h (38%), q4h (31%), q2h (23%) and q6h (8%). Pharmacists who recommended limiting APAP to 5 doses per day were less likely to recommend alternating APAP (p=0.017).
CONCLUSIONS: Pharmacists recommend either APAP or IBU as first-line therapy of fever. However, a majority do recommend alternating APAP and IBU with highly variable dose regimens to reduce fever in children.

195. Acanthosis nigricans in Mexican-American adolescents. *Sandra Benavides, Pharm.D.*[1], Anthony Romo, Pharm.D., student[2], Joshua Caballero, Pharm.D.[1], Unnyampath Sugunan, M.D.[3]; (1)Nova Southeastern University, Ft. Lauderdale, FL; (2)University of Texas, Austin College of Pharmacy, Austin, TX; (3)Su Clinica Familiar, Harlingen, TX.

PURPOSE: Acanthosis nigricans (AN) is a dermatological skin disorder characterized by thickened, velvety, hyperpigmented patches on the sides of the neck and flexural surfaces. Several types of AN are recognized; however, a benign form referred to as insulin resistance/obesity related acanthosis nigricans (IRORAN) has been increasing in Mexican-American (M-A) adolescents. There is debate regarding the use of AN for screening of insulin resistance. In addition, the perception and attitudes of AN are unknown in any population. The efficacy of metformin on the treatment for AN has not been systematically evaluated.
METHODS: We enrolled 22 children with AN in this prospective cross-sectional study from the Rio Grande Valley in south Texas. Each child underwent a physical exam (including anthropometric measurements) and a laboratory analysis, and completed a Beck Depression/Anxiety Inventory, and an AN perception questionnaire. Children diagnosed with IRORAN were to be enrolled in a separate arm of the trial to determine the efficacy of metformin for IRORAN. The study was approved by both UTPA and Su Clinica Familiar Institutional Review Board.
RESULTS: A total of 22 (14 male, 8 female) Mexican-American patients were enrolled over the 1-year period. The mean age was 12.1 ± 3.7 years. The average BMI was 24.3 kg/m^2. The average fasting serum glucose was 86.2 ± 4.7 mg/dL. The average glycosylated hemoglobin was 5.4 ± 0.2%. The average insulin concentrations were 8.5 ± 5.2. Minimal/mild symptoms of depression and anxiety were noted. Results of the perception survey revealed that the children were familiar with AN and were not bothered by it. They also rated the need for treatment as low.
CONCLUSIONS: AN may not be a good marker for IR. Additonally, M-A adolesccents in this population did not seem bothered by the AN. Therapy with metformin was not conducted due to the risks outweighing the benefits of treatment.

196. Systemic exposure of HFA fluticasone propionate administered by valved holding chambers with face-masks in preschool children. *Kathryn Blake, Pharm.D.*[1], Leslie Hendeles, Pharm.D.[2], Terry Spencer, M.D.[2], Rashmi Mehta, Ph.D.[3], Misba Beerahee, Ph.D.[4], Peter Daley-Yates, Ph.D.[4], Robert Kunka, Ph.D.[3]; (1)Nemours Children's Clinic, Jacksonville, FL; (2)University of Florida, Gainesville, FL; (3)GlaxoSmithKline, Research Triangle Park, NC; (4)GlaxoSmithKline, Greenford, United Kingdom.

PURPOSE: Valved holding chambers with masks are often used with metered-dose inhalers in children with asthma to deliver drug to the lungs. Differences in holding chamber design can influence the amount of drug delivered. Lung deposition of fluticasone propionate (FP) using hydrofluoroalkane (HFA) propellant was examined using the Aerochamber Plus and Babyhaler valved holding chambers.
METHODS: Children 1 to < 4 years old were randomized in an open-label, 2-way crossover design (no washout between treatments) to receive 88 µg (44 µg/actuation) twice daily (every 12 hours) for 7.5 days (15 doses) using the Aerochamber Plus and Babyhaler with face-masks (FAS10002). The first and last 4 doses were directly observed by study staff. To limit the amount of blood collected from any one patient, children were randomized to one of three groups for blood sampling: Group 1: pre-dose, and 0.5–1, 1.5–2, 2.5–3, 3.5–4 hrs post-dose; Group 2: 2.5–3, 3.5–4, 4.5–5, 6.5–7, 7.5–8 hrs post-dose; Group 3: 7.5–8, 8.5–9, 9.5–10, 11.5–12, post-dose, 12.5–13 hrs (0.5–1 hour post dose #16). FP systemic exposure as described by area under the curve (AUC) was determined by population pharmacokinetics.
RESULTS: Seventeen and 18 children completed Aerochamber and Babyhaler treatments, respectively; one child completed only the Babyhaler treatment. Population mean (95% confidence interval) for FP exposure following dosing with the Aerochamber Plus was 97pg*h/ml (85, 113) and with the Babyhaler was 52pg*h/ml (34, 64).
CONCLUSIONS: Lung deposition of FP through the Aerochamber Plus was higher compared with the Babyhaler. However, systemic exposure for both devices was well below the threshold observed for decreases in cortisol production (1000 pg*h/mL). Thus, both devices provide safe delivery of FP HFA to young children.

Pharmacoeconomics/Outcomes

197. Impact of hyponatremia on length of stay and total costs in hospitalized patients. Mark A. Callahan, M.D.[1], Huong T. Do, M.A.[1], David W. Caplan, B.A.[2], Kahyun Yoon-Flannery, M.P.H.[1], *Raafat Seifeldin, Ph.D.*[3]; (1)Weill Medical College of Cornell University, New York, NY; (2)New York Presbyterian Hospital, New York, NY; (3)Astellas Pharma US, Inc., Deerfield, IL.

PURPOSE: To evaluate the impact of hyponatremia, the most common electrolyte abnormality in hospitalized patients, on the length of hospital stay (LOS) and cost of care in a large academic hospital.
METHODS: In a retrospective case-controlled study, the laboratory and cost-accounting data from adult patients admitted to the hospital between January 2004 and May 2005 with a serum sodium concentration (Na^+) ≤ 134 mEq/L and a principal diagnosis of neoplasm, hepatic failure, or congestive heart failure were compared with those of control subjects whose serum (Na^+) was 135 to 145 mEq/L. Hyponatremia was classified as either moderate to severe (serum [Na^+] <130 mEq/L) or mild to moderate (130–134 mEq/L). Control subjects were matched according to their principal ICD-9 codes during the same admission period.
RESULTS: Hyponatremia was confirmed in 2.7% of all patients admitted to the hospital. Patients with moderate-to-severe hyponatremia (n=576) or mild-to-moderate hyponatremia (n=1555) had a significantly longer LOS than did control subjects (p<0.001) and were more likely to be admitted to the ICU during the admission (p<0.001) (Table). Patients with hyponatremia also incurred higher total costs (p<0.001). The results were similar after adjustments were made for clinical and demographic variables or when serum (Na^+) was evaluated as a continuous, rather than a categorical, independent variable.The table shows outcomes by hyponatremia status at hospital admission.

	Controls	Hyponatremia Mild-to-moderate	Moderate-to-severe
Median LOS, days	5	7	8
% admitted to ICU	19	23	30
Median total cost per patient	$12,439	$13,353	$15,249

CONCLUSIONS: Hyponatremia is associated with a longer LOS and higher ICU admission rate and total medical costs. Therapies that can promptly and safely correct hyponatremia may lead to a shorter LOS and lower overall cost of healthcare.

198. Racial comparison of outcomes and cost of hospitalized cancer patients. *Susannah E. Motl, Pharm.D.*[1], Katie J. Suda, Pharm.D.[2]; (1)University of Illinois, College of Pharmacy, Chicago, IL; (2)University of Tennessee, College of Pharmacy, Memphis, TN.

PURPOSE: Racial disparities have been reported in the care and outcome of cancer patients. We evaluated whether race would influence the treatment of cancer patients in a private MidSouth hospital.
METHODS: Health and economic outcomes were extracted from a health claims database from 10/01/02 to 09/30/03. Patients with a diagnosis code for malignant neoplasms (ICD-9 code: 140-208, 230-239; Medicode, DRG Expert) were selected and divided into two groups based on reported race. Student's t-test, Mann Whitney U and contingency tables were used to evaluate differences between groups. A p-value < 0.05 was considered significant.
RESULTS: Eight hundred and ninety two patients (3.3% of all admits) had a diagnosis of cancer; 689 (77%) were Caucasian (C) and 23% were African American (AA). Cancer diagnoses, insurance status, and case mix index was not statistically different between the two groups, although AA patients were more likely to be younger than C (62.3 years vs. 66.1, p<0.001). Length of stay (LOS), ICU LOS, and discharge status were not statistically different with a similar proportion of patients discharged home, to hospice, expiring, or receiving additional care. Total hospital costs ($6936 vs. $7024), medication costs ($485 vs. $467), nursing, radiology, PT/OT, and respiratory care were all similar for AA vs. C patients, respectively (p=not significant). Laboratory ($202 vs. $108) and surgery costs ($632 vs. $763), although statistically significant, were unlikely to be clinically significant for AA vs. C, respectively.
CONCLUSIONS: Only minor differences were seen in the health and economic outcomes of C and AA cancer patients at this hospital. These results are encouraging.

199. Health economic evaluation of the Val-Syst trial. *Daniel Hilleman, Pharm.D.*[1], Stephanie Maciejewski, Pharm.D.[2]; (1)Creighton University Medical Center, Omaha, NE; (2)Creighton Cardiac Center, Omaha, NE.

PURPOSE: The economic burden related to hypertension and its complications is expected to increase as the United States population ages. Hence, studies focusing on elderly patients with isolated systolic hypertension are important. The present study is a health economic evaluation of the Val-Syst trial.
METHODS: Val-Syst was a randomized, active-controlled, double-blind comparison of amlodipine to valsartan in elderly (mean age 69, range 60–89 yrs) patients with ISH. Non-responders to monotherapy had HCTZ added. A health-care resource utilization analysis was developed to assess the relevant costs associated with these two treatment approaches in clinical practice. Costs (U.S.$ 2006) of the antihypertensive drugs, clinic visits for BP evaluation, and clinic visits incurred secondary to the development of treatment related adverse events were included. Mean costs in the two treatment groups were compared using the Mann Whitney U test.
RESULTS: A total of 421 elderly hypertensive patients were randomized to amlodipine (n=213) or valsartan (n=208). Rates of BP control with monotherapy and need to add HCTZ were not different between the treatment groups. Adverse events occurred in 68 (32%) of amlodipine patients and 42 (20%) of valsartan patients (p<0.003). Patients discontinuing treatment for adverse events occurred in 14 (7%) of amlodipine patients and 11 (5%) of valsartan patients. Drug acquisition costs in the amlodipine and valsartan treatment groups were $592 per patient per year and $536 per patient per year, respectively. Total per patient clinic visit costs were $147 for amlodipine and $135 for valsartan. Total prescription and clinic visit costs were $739 per patient for amlodipine and $672 per patient for valsartan.
CONCLUSIONS: Total treatment costs are slightly (but not significantly) lower with valsartan compared with amlodipine. The lower cost occurs primarily due to a lower frequency of adverse drug reactions in the valsartan treatment group.

200. Prevalence of anemia in heart failure patients and cost analysis of epoetin treatment. *Christine K. Choy, Pharm.D.*, Anne P. Spencer, Pharm.D., Jean M. Nappi, Pharm.D.; Medical University of South Carolina, Charleston, SC.

PURPOSE: To determine the prevalence of anemia in an outpatient heart failure (HF) clinic and evaluate potential costs associated with epoetin therapy in HF patients with comorbid anemia.
METHODS: We conducted a single-center, retrospective cohort analysis (part 1) and literature-based cost-offset analysis (part 2). In part 1 of the study, patients were included if they were at least 18 years of age, diagnosed with chronic HF, enrolled in a multidisciplinary outpatient HF clinic, and recipients of at least 1 complete blood count measurement between January 1, 2003, and April 15, 2006. The World Health Organization (WHO) and the National Kidney Foundation (NKF) definitions of anemia were employed in the prevalence assessment. In part 2 of the analysis, a hypothetical cohort, including 100 patients with HF and anemia, was created for the cost evaluation. Hospitalization and medication utilization costs per 100 patients treated with epoetin and parenteral iron were compared with analogous costs per 100 patients not treated with epoetin and parenteral iron.
RESULTS: In part 1 of the study, the overall prevalence of anemia within the cohort (n=170) was 47.6% and 47.1%, based on the WHO and NKF definitions, respectively. Seventy-five percent of patients with anemia were characterized with a normocytic, normochromic type. In part 2 of the analysis, calculated costs of acquiring and administering epoetin and parenteral iron in the hypothetical cohort exceeded hospitalization cost savings by $83,070. If applied to the cohort studied in part 1, epoetin and parenteral iron therapy would be associated with a $66,456 increase in overall healthcare expenditure.
CONCLUSIONS: This study suggests that anemia is a common comorbidity in chronic HF clinic patients. For patients with HF and anemia, the analysis also suggests that the cost of epoetin and parenteral iron therapy would not be offset by a reduction in HF-related hospitalization costs.

201. Cost analysis of aprepitant and ondansetron for the prevention of postoperative vomiting. Ya-Ting Chen, Ph.D.[1], James Pellissier, Ph.D.[2], Ritesh Kumar, Ph.D.[3], *X. Henry Hu, M.D., Ph.D.*[1]; (1)Merck & Co., Inc., West Point, PA; (2)Merck & Co., Inc., Upper Gwynedd, PA; (3)Merck & Co., Inc., Whitehouse Station, NJ.

PURPOSE: Aprepitant, a potent and highly selective NK-1 receptor antagonist, has been shown in clinical trials to be efficacious in preventing postoperative nausea and vomiting. This study explores the potential cost impact from the hospital's perspective of using aprepitant versus ondansetron to prevent post-operative vomiting.
METHODS: A cost analysis was conducted for a hypothetical cohort of 1,000 patients receiving general anesthesia for open abdominal surgery. Efficacy data were obtained from a randomized double-blind trial comparing oral aprepitant 40 mg to intravenous ondansetron 4 mg for the primary end point of no vomiting in 24 hours following the end of surgery. 84.0% and 71.4% of the patients had no vomiting in the aprepitant and ondansetron group, respectively. Average costs of managing postoperative vomiting per patient ($304.60) were obtained from published literature. Wholesale acquisition cost (WAC), or manufacturer's published price to wholesalers, was used for ondansetron (4 mg IV, $21.37) while costs for aprepitant 40 mg were explored across a range of prices from approximately 1.5 to 3 times the WAC of ondansetron ($32–$60). Total cost was calculated for each treatment by adding the cost for managing vomiting and drug cost. Sensitivity analyses were conducted to assess the impact of varying key model parameters on total cost.
RESULTS: In a cohort of 1,000 patients, 160 patients receiving aprepitant were expected to experience vomiting compared with 290 patients receiving ondansetron. Summarized cost results are shown in table below.

	Aprepitant	Ondansetron	
Drug unit cost	$32	$60	$21.37
Total drug cost per 1,000 patients	$32,000	$60,000	$21,370
Cost of managing vomiting	$48,736	$48,736	$88,334
Total cost per 1,000 patients	$80,736	$108,736	$109,704

CONCLUSIONS: Within the study range of prices, aprepitant is cost-saving compared with ondansetron for preventing postoperative vomiting in adult patients undergoing open abdominal surgery.

202. A systematic approach to blood transfusion cost: including labor and material costs. *Aryeh Shander, M.D., FCCM, FCCP*[1], Axel Hofmann, M.E.[2], Sherri Ozawa, R.N.[1]; (1)Englewood Hospital and Medical Center, Englewood, NJ; (2)Medizinische Gesellschaft fur Blutmanagement, Laxenburg, Austria.

PURPOSE: Current assessments of costs associated with blood transfusion often do not include cost of personnel and materials involved. A full accounting of the overall cost of transfusion is needed to provide a more complete basis for transfusion policy-making.
METHODS: A panel of experts convened a multidisciplinary consensus conference in 2003 and agreed upon activity-based costing (ABC) as a comprehensive approach to account for the total cost of transfusion. This study is a prospective ABC cost analysis of each process step involved with transfusion of a unit of blood. A software module inclusive of these steps was

then developed to perform an accurate cost analysis in hemotherapy.
RESULTS: More than 200 resource-consuming steps (labor, materials, equipment) across numerous cost centers have been identified in this phase. The entire process can be divided into 6 main process steps starting from recruiting donors to treatment of transfusion complications. Each of these 6 processes was further broken down to account for the different steps and personnel involved at each level. Main process steps are summarized in Table 1.

Transfusion steps	Main process step	# of total steps involved	Minimum # of personnel involved
1	Recruiting donors, issuing and delivering blood to sites	23	3
2	Receiving, controlling and storing in blood bank	11	2
3	Preparing transfusion	119	16
4	Administration and monitoring of transfusion	71	7
5	Treating short-term complication	39	9
6	Review by transfusion committee	23	19

CONCLUSIONS: Transfusion is complex and labor intense. These preliminary results show that including the labor and materials associated with blood transfusion and treatment of short-term and long-term complications would add considerably to its cost. When evaluating modalities for maintaining a patient's tissue oxygenation, the cost of the entire transfusion process should be compared with the full cost of other treatment options.

203. Cost-effectiveness of linezolid versus vancomycin in the treatment of surgical site infections. *Brian Erstad, Pharm.D.*, Asad E. Patanwala, Pharm.D., David E. Nix, Pharm.D.; University of Arizona College of Pharmacy, Tucson, AZ.

PURPOSE: To compare the cost-effectiveness (cost per cure) of linezolid versus vancomycin for treating surgical site infections (SSIs) caused by methicillin-resistant Staphyloccocus aureus (MRSA) from the perspective of a tertiary care academic medical center in the United States.
METHODS: Cure rate probabilities for MRSA SSIs were obtained from records at the medical center and from results of a randomized, multicenter trial. Healthcare costs for each scenario were obtained from the medical center, health care buying groups, and national databases. Three clinical scenarios were considered in the decision analysis: (1) treatment with intravenous (IV) vancomycin during hospitalization and after discharge with home care follow-up; (2) treatment with IV vancomycin during hospitalization, followed by oral linezolid after discharge; (3) treatment with oral linezolid during hospitalization and after discharge. Discounting was not performed since the costs and consequences of treating the MRSA SSIs were expected to occur within 1 year. The robustness of the baseline cost-effectiveness determination was evaluated using one-way and two-way sensitivity analyses, as well as threshold, analyses.
RESULTS: Treatment with oral linezolid was the most cost-effective approach at $10,292 per MRSA SSI cure. Treatment with IV vancomycin during hospitalization and linezolid after discharge was more cost-effective than IV vancomycin during both hospitalization and after discharge, $14,586 per cure vs. $17,653 per cure, respectively. Treatment with oral linezolid during hospitalization and after discharge dominated (i.e., superior effectiveness and lower costs) the other two scenarios in the incremental cost-effectiveness analysis.
CONCLUSIONS: Treatment with oral linezolid during hospitalization and after discharge is the most cost-effective approach for treating SSIs caused by MRSA.

204. Real-world dosing and cost considerations of epoetin alfa and darbepoetin alfa in the inpatient hospital setting. Mei-Sheng Duh, M.P.H., Sc.D.[1], Francis Vekeman, M.A.[2], *R. Scott McKenzie, M.D.*[3], Patrick Lefebvre, M.A.[2], Sue Watson, Pharm.D.[3], Samir H. Mody, Pharm.D., M.B.A.[3], Catherine Tak Piech, M.B.A.[3]; (1)Analysis Group, Inc, Boston, MA; (2)Groupe d'Analyse, Ltée., Montréal, QC, Canada; (3)Ortho Biotech Clinical Affairs, LLC, Bridgewater, NJ.

PURPOSE: To examine inpatient dosing patterns and erythropoietic treatment costs in cancer or pre-dialysis chronic kidney disease (pCKD) inpatients treated with erythropoietic agents from a hospital pharmacy perspective.
METHODS: An analysis of electronic inpatient records from the Premier Perspective Comparative Hospital Database was conducted. Study subjects were identified through hospitalizations recorded between July 2002 and March 2005 from more than 500 hospitals nationwide. Adult patients (≥ 18 years of age) with an admitting diagnosis of cancer or CKD and receipt of epoetin alfa (EPO) or darbepoetin alfa (DARB) during hospitalization were included. Patients who had received dialysis or both agents were excluded. For both cancer and CKD indications, baseline demographics, severity of illness, inpatient length of stay, cumulative administered dose and drug costs were compared between EPO and DARB patients. March 2006 wholesale acquisition costs were used to calculate erythropoietic costs.
RESULTS: A total of 25,645 hospitalizations (EPO: 22,873; DARB: 2,772) for patients with cancer and 66,822 (EPO: 60,079; DARB: 6,743) for patients with pCKD were identified. For both indications, patient characteristics were generally comparable between the two groups. The mean cumulative administered dose per inpatient stay (cancer: EPO 62,060 Units, DARB 253.4 µg; pCKD EPO 39,385 Units, DARB 162.7 µg) resulted in a dose ratio between EPO and DARB of 245:1 and 242:1 (Units EPO: µg DARB) for cancer and pCKD patients, respectively. Based on the cumulative administered dose per hospitalization, the price premium associated with DARB drug cost was approximately 50% more than EPO for both the oncology and pCKD patients (oncology: EPO $755 vs. DARB $1,127, p<0.0001; pCKD: EPO $479 vs. DARB $723, p<0.0001).
CONCLUSIONS: Based on the evidence from this large retrospective study, EPO was significantly less costly compared with DARB in the inpatient hospital setting, and these findings correspond to those observed in the outpatient setting.

205. Hematologic outcomes and costs in epoetin alfa (EPO)-treated and darbepoetin alfa (DARB)-treated cancer patients: results of the dosing and outcomes study of erythropoiesis-stimulating therapies (D.O.S.E. registry). Cyrus Peake, M.S.[1], Qin Wang[1], Er Chen[1], *R. Scott McKenzie, M.D.*[2], Jamie Forlenza, Pharm.D., M.S.[2], Catherine Tak Piech, M.B.A.[2]; (1)Abt Associates - HERQuLES, Lexington, MA; (2)Ortho Biotech Clinical Affairs, LLC, Bridgewater, NJ.

PURPOSE: National Comprehensive Cancer Network anemia treatment guidelines recommend maintenance of hemoglobin (Hb) levels between 11 g/dL and 12 g/dL. To investigate hematologic outcomes and costs of erythropoiesis-stimulating therapies (ESTs), data were analyzed from the D.O.S.E. Registry, an ongoing, prospective registry collecting data on real-world practice patterns and outcomes in cancer patients treated with ESTs.
METHODS: Data come from U.S. hospital and community-based outpatient practices assessed from 1/04 to 5/06. Adult patients with a non-myeloid malignancy and receipt of at least 2 doses of either EPO or DARB were included in analyses. Outcomes assessed included mean treatment duration; mean cumulative dose; mean Hb level at Weeks 4, 8, 12, and 16; and proportion of patients receiving blood transfusions. Costs were based on May 2006 wholesale acquisition costs.
RESULTS: 783 patients (276 EPO, 507 DARB) from 40 sites were identified. Mean baseline characteristics were similar between groups (entire cohort: age 62.2 years, weight 75.8 kg, and Hb 10.4 g/dL) with the exception of proportion of patients receiving iron supplementation (29.1% DARB, 17.4% EPO, p<0.01). Both groups had similar mean treatment duration (~8 weeks), number of Hb assessments (8) and proportion of patients requiring blood transfusion (19%). The mean cumulative doses for EPO 365,181 Units and DARB 1,163 µg were associated with EST drug costs of $4,444 for EPO and $5,171 for DARB, (p<0.0001). Mean Hb level was ≥ 11 g/dL at all post-baseline time points in the EPO-treated group; however, it was < 11 g/dL in the DARB-treated group at Weeks 12 and 16. Mean Hb level was significantly higher in the EPO-treated group at Week 12 (EPO 11.4 g/dL, DARB 10.8 g/dL, p=0.02).
CONCLUSIONS: This prospective observational study reported that the EPO-treated patients achieved and maintained NCCN target Hb levels at all timepoints. EST cost in the DARB-treated group was 16% higher than in the EPO-treated group.

206. Major bleed and all-cause inpatient mortality between anticoagulants used post-orthopedic surgery in a clinical setting. *Richard Stanford, Pharm.D., M.S.*[1], Nikita Mody-Patel, Pharm.D.[1], Laura Happe, Pharm.D., M.P.H.[2], Eileen Farrelly, M.S.[2], Matthew W. Sarnes, Pharm.D.[2]; (1)GlaxoSmithKline, Research Triangle Park, NC; (2)Applied Health Outcomes, Havertown, PA.

PURPOSE: Clinical trials have reported variable rates of major bleeding and associated fatalities with anticoagulant use post-orthopedic surgery. This retrospective, observational study examined major bleed and all-cause inpatient mortality among users of anticoagulants post-surgery in clinical practice.
METHODS: Inpatient data from more than 500 hospitals in the U.S. between January 2003 and March 2005 was used to identify patients undergoing hip/knee replacement or hip fracture surgery who received dalteparin, enoxaparin, fondaparinux, or unfractionated heparin (UFH) post-surgery. The primary outcome was major bleed defined as: hemoperitoneum, intracranial hemorrhage/hemorrhagic stroke, hemorrhage complicating a procedure, or other bleeding accompanied by ≥ 2 units of blood transfused, and all-cause inpatient death during initial hospitalization or a re-hospitalization within 60 days post-discharge. Logistic regression adjusting for patient and hospital demographics was conducted to assess differences between anticoagulants. Sensitivity analyses were conducted with transfusions removed and on all-cause mortality alone.
RESULTS: 144,806 subjects were identified, dalteparin=16,109;

enoxaparin=97,827; fondaparinux=12,532; and UFH=18,338. After adjusting for differences in demographics, the use of dalteparin (OR=0.53, 95% CI 0.46, 0.61), enoxaparin (OR=0.69, 95% CI 0.63, 0.75) and fondaparinux (OR=0.71, 95% CI 0.61, 0.82) were associated with lower risks of major bleed or inpatient mortality compared with UFH. Similar results were observed when transfusions were excluded. In addition, dalteparin (OR=0.43, 95% CI 0.35, 0.54), enoxaparin (OR=0.56, 95% CI 0.50, 0.64), and fondaparinux (OR=0.47, 95% CI 0.37, 0.61) were associated with lower risks of all-cause inpatient deaths.
CONCLUSIONS: In this observational study, the risk of a major bleed or inpatient all-cause mortality was significantly lower in patients receiving dalteparin, enoxaparin, and fondaparinux, compared with UFH. Risk of all-cause inpatient mortality was also reduced with the use of fondaparinux and dalteparin. These results are important as data outside of clinical trials are limited, and information regarding these bleeding events is essential to clinical practice.

207. A decision analytic model comparing urokinase versus recombinant tissue plasminogen activator in the treatment of acute peripheral arterial occlusions. *Eleanor L. Olvey, Pharm.D.*, Grant H. Skrepnek, Ph.D., Paul Nolan, Pharm.D.; The University of Arizona College of Pharmacy, Tucson, AZ.

PURPOSE: To determine the cost-effectiveness of urokinase (UK) and recombinant tissue plasminogen activator (alteplase, rt-PA) when used intra-arterially for the treatment of acute peripheral arterial occlusions.
METHODS: A decision-analytic methodology was employed with a base case defined as a 65-year-old male diagnosed with an acute peripheral arterial occlusion. Data for probabilities were collected from published clinical trials, and direct medical costs were measured from the perspective of the healthcare institution. The primary outcome assessed was 30-day survival. Average and incremental cost-effectiveness ratios (ICER) were calculated and included 95th % confidence intervals. A two-dimensional (sampling plus trials) Monte Carlo simulation with 5,000 patients was performed, and sensitivity analyses were conducted on both costs and probabilities.
RESULTS: The Monte Carlo simulation indicated that average cost-effectiveness (C/E) ratio for rt-PA was $54,141 (95% CI=44,647–62,832) per successful treatment, whereas the average C/E ratio for UK was $65,515 (95% CI=56,286–76,135). The ICER for rt-PA versus UK as the baseline was calculated to be $284,170 per additional survival over 30 days (95% CI= 186,097–418,443). Neither treatment strategy appeared to be dominant, and the model was most sensitive to variations in the cost of treatment.
CONCLUSIONS: This study found rt-PA to be less costly but also slightly less efficacious than UK for patients treated for acute arterial occlusions. Neither therapy was observed to be dominant for the outcome of 30-day survival. Additional long-term outcome data are necessary to assess more extensively assess the benefits of each therapy.

Pharmacoepidemiology

208. Relationship between proton pump inhibitor use and renal disease. *Donald G. Klepser, Ph.D., M.B.A.*, Dean S. Collier, Pharm.D., Gary L. Cochran, Pharm.D., Gerald Groggel, M.D.; University of Nebraska Medical Center, Omaha, NE.

PURPOSE: Proton pump inhibitors (PPI) are widely prescribed for treatment of peptic acid-related disorders. Although PPIs are generally well tolerated, some case reports suggest an association with acute interstitial nephritis (AIN). The objective of this study was to evaluate the relationship between PPI use and renal disease in a privately insured population.
METHODS: We used a retrospective nested case-control study design. Demographic and clinical data were analyzed from an administrative database of over 400,000 individuals from 2002-2005. All patients ages 18–64, continuously enrolled in a plan for at least 24 months, and with no renal disease diagnosis within the first 12 months of enrollment, were eligible for study. Cases were defined as patients with selected renal disease diagnoses, based on ICD-9 codes. Each case was matched with up to 4 randomly selected controls based on age, gender, county of residence, and date of entry into the cohort. PPI exposure was obtained through prescription drug claims. The association between PPI use and renal disease was analyzed with a conditional logistic regression model that controlled for potential confounders such as diabetes, hypertension, high cholesterol, NSAID use, and patient comorbidities. A secondary model examined the association in healthier patients by excluding cases and controls with comorbidities.
RESULTS: In the primary model, 854 cases of renal disease were matched to 3289 controls. The relationship between PPI use and renal disease was statistically significant (OR=2.04; CI 1.53, 2.71). In the secondary model the number of cases (n=200) and controls (n=648) was lower, but the relationship between PPI use and renal disease remained consistent (OR=2.30; CI 1.19, 3.75).
CONCLUSIONS: The results of our nested case-controlled study suggest that PPI use is significantly associated with renal disease. Further studies are needed to establish a causal relationship between PPI use and renal disease.

209E. Evaluation of venous thromboembolism prophylaxis in surgical patients. *Melvin J. Rivera, Pharm.D.*, Fahd Forsa, Pharm.D., Keith Thomasset, Pharm.D., BCPS, Ishaq Lat, Pharm.D., BCPS, Toby Trujillo, Pharm.D., BCPS; Boston Medical Center, Boston, MA.

Presented at the Eastern States Pharmacy Residency Conference, Baltimore, MD, May 10-13, 2006.

210. Factors associated with treatment initiation of atomoxetine vs. long-acting stimulants in adults with ADHD. *Wenyu Ye, Ph.D.*[1], David Van Brunt, Ph.D.[1], Gerhardt M Pohl, Ph.D.[1], Joseph A. Johnston, M.D., MSc[1], Scott C. Henderson, M.S.[2]; (1)Eli Lilly and Company, Indianapolis, IN; (2)IMS, Plymouth Meeting, PA.

PURPOSE: To investigate factors associated with initiation of atomoxetine (ATX) compared with long-acting stimulants (LA-STIM) in adults with ADHD.
METHODS: Data were from the IMS Health LRx Database. Patients ≥ 18 years old were selected if they initiated treatment with an ADHD medication categorized as ATX, long-acting methylphenidate (LA-MPA), or long-acting amphetamine (LA-AMP) between April 2004 and March 2005. Initiation was defined as the first use of a medication preceded by 3 months without a prescription in the same category. For each patient, the most recent initiation of ATX vs. LA-MPA or ATX vs. LA-AMP, was modeled via stepwise logistic regression. Factors considered were age (18–25 vs. 26+), gender, prior ADHD medication types, initiation type (treatment naïve, switch, add-on, reintroduction), concomitant medications, provider specialty (neurologist, nurse practitioner, primary care physician, or psychiatrist), payment type (cash, Medicaid, or third party), and historical compliance with ADHD medications.
RESULTS: Of 356,511 patients (51.1% female), 29.1% most recently initiated ATX, 31.6% LA-MPA, and 39.3% LA-AMP. Patients identified as add-on, naïve, or switch patients, having prescriptions from primary care physicians or nurse practitioners, paying by cash or Medicaid, with previous use of ATX, or with concomitant use of other psychiatric medications, were more likely to initiate ATX than LA-MPA (lower confidence bound of adjusted odds ratios > 1). Conversely, LA-MPA initiation was more likely for women, younger adults, patients with prior use of stimulant, and patients with better compliance with ADHD medications. The model factors selected for initiation of ATX vs. LA-AMP were consistent with those for the comparison with LA-MPA.
CONCLUSIONS: The factors significantly associated with initiation of ATX vs. LA-MPA or vs. LA-AMP suggest that therapy with ATX and LA-STIM may be addressing different patient treatment needs. The findings suggest that ATX is being preferentially prescribed for patients with psychiatric comorbidities.

211. Human albumin solutions utilization pattern in Riyadh Central Hospital, Riyadh, Saudi Arabia. *Yousef Ahmed Alomi, Bsc., Msc., BCPS*, Idena Bacalia, Bsc., Amel Alnajar, Bsc., Layla Laiga, Bsc.; Riyadh Medical Complex, Riyadh, Saudi Arabia.

PURPOSE: To describe the proper usage of albumin solutions in such clinical situations as Riyadh Central Hospital.
METHODS: An observational study conducted in Riyadh Central Hospital from 6/31/2000 through 6/22/2001, a 12-month period. Human Albumin Solutions case report forms were prepared to collect data, including patient and prescriber demographics, total serum protein, serum albumin level, and indication for use.
RESULTS: A total of 1197 case reports forms were reviewed. One hundred forty three forms were excluded because of missing information. The remaining 1054 (88.1%) case report forms provided data from 587 patients. Of those 912 (86.6%) forms were albumin, 141 (13.4%), plasma protein fraction (PPF), and one form (0.1%) was both. In 830 (78.7%) of cases, albumin or PPF were prescribed for hypoalbuminemia 415 (50%), liver cirrhosis 85 (10.2%), Burn 75 (9%), Hypotension 57 (6.8%), and Nutrition 52 (6.2%). The most common prescribers of these products were intensive care 233 (22.1%), general surgery 231 (21.9%), and plastic surgery 197 (18.7%). Approximately $179,000 was spent on Albumin and PPF therapy for 1000 cases.
CONCLUSIONS: This study reveals that more than 50% of using albumin was inappropriate. Targeting of development of Albumin clinical guidelines and education program will improve patient outcomes and reduce care costs in Riyadh Central Hospital.

212E. Documentation pattern of clinical pharmacists' activities in Riyadh, Saudi Arabia. *Yousef Ahmed Alomi, Bsc., Msc., BCPS*, Naif Bakarman, Bsc., Samy Al-Medlej, Pharm D.; Riyadh Medical Complex, Riyadh, Saudi Arabia.

Presented at the 9th International Pharmaceutical Science Conference, Riyadh, Saudi Arabia, December 18-21, 2005.

213E. Satellite pharmacist intervention at Security Forces Hospital, Riyadh, Saudi Arabia. *Yousef Ahmed Alomi, Bsc., Msc., BCPS*, Waleed Alsheri, Bsc., Manal Bashihab, Bsc., Maher Bahisi, Bsc., Badiria Alahmari, Bsc.; Riyadh Medical Complex, Riyadh, Saudi Arabia.

Presented at the 9th International Pharmaceutical Science Conference, Riyadh, Saudi Arabia, December 18-21, 2005.

214E. Computerized documentation of clinical pharmacists' activities in Saudi Arabia. *Yousef Ahmed Alomi, Bsc., Msc., BCPS*, Noura Albinyan, Bsc., Naif Bakarman, Bsc., Areej Melhani, Bsc.; Riyadh Medical Complex, Riyadh, Saudi Arabia.

Presented at the 9th International Pharmaceutical Science Conference, Riyadh, Saudi Arabia, December 18-21, 2005.

215. Antimicrobial resistance among hospitals in Puerto Rico: results of the Antimicrobial Resistance Management (ARM) Program. *John G. Gums, Pharm.D.*[1], D. Wesston Boatwright, Pharm.D.[2], Noel Totti, M.D.[3], Martty Martinez, Pharm.D.[4]; (1)University of Florida, Gainesville, FL; (2)Roche Laboratories, Jacksonville, FL; (3)Hospital Espano Auxilio Mutuo, San Juan, PR; (4)Urb. Estancia, Bayamon, PR.

PURPOSE: The Antimicrobial Resistance Management Program was established in 1997 as an ongoing project to document trends in antimicrobial susceptibility patterns in inpatient/outpatient isolates and track resistance that may occur with specific antibiotic use.
METHODS: Institutions provide at least 3 years of antibiogram data. Between 1996 and 2003, data on 328,837 isolates were collected from 11 hospitals throughout Puerto Rico (PR), as were aggregate data on 5,388,897 isolates from 46 institutions in Florida (FL) and 24,951,098 isolates from 358 U.S. institutions for comparative purposes. Organisms reviewed for antibiotic susceptibility (no. of antibiotics tested against) were *Enterococcus faecalis* (7), *Enterococcus faecium* (5), *Enterococcus* spp (4), *Escherichia coli* (24), *Klebsiella pneumoniae* (24), *Proteus mirabilis* (22), *Pseudomonas aeruginosa* (14), *Serratia marcescens* (22), *Staphylococcus aureus* (23), and *Streptococcus pneumoniae* (9).
RESULTS: Vancomycin-resistant Enterococci levels were significantly less in PR (23.2%) vs FL (50.7%) or U.S. (56%). For *E. coli*, ampicillin resistance was 48% in PR, higher than FL (42%) or U.S. (38%). *E. coli* isolates were also more resistant to fluoroquinolones (e.g., ciprofloxacin 16.9% in PR, 9% FL, 6.7% U.S.). Similar resistance rates were observed for *K. pneumoniae* for the fluoroquinolones. *P. mirabilis* resistance to a wide spectrum of antibiotics was significantly less in PR than in FL/U.S. *P. aeruginosa* susceptibilities to gentamicin are suppressed compared with tobramycin or amikacin, consistent with FL/U.S. Activity from *S. marcescens* was suppressed against all antibiotics tested compared with FL/U.S. Higher MRSA levels and *S. aureus* vancomycin resistance was observed in PR. Differences in *S. pneumoniae* susceptibility to cefotaxime (71.4%) vs. ceftriaxone (100%) were consistent with that previously reported in FL/U.S.
CONCLUSIONS: This broad analysis represents the first summary of antimicrobial resistance among hospitals in Puerto Rico from 1996 to 2003. The analysis provides important baseline data for sentinel surveillance programs and in determining strategies for intervention.

216. Comparison of IV acid suppressive therapy pre- and post-availability of IV pantoprazole in gastrointestinal bleeding. *Nancy Yunker, Pharm.D.*[1], William R. Garnett, Pharm.D.[1], Carol B. Pugh, Pharm.D., MS[2]; (1)VCU/MCV School of Pharmacy, Richmond, VA; (2)Virginia Association of Free Clinics, Glen Allen, VA.

PURPOSE: Intravenous (IV) proton pump inhibitors (PPI) are felt to be more effective in gastrointestional bleeding (GIB) than IV histamine 2 receptor antagonists (H2RAs). No studies using a large database have evaluated the outcomes of IV H2RAs versus IV pantoprazole therapy. The objectives of this study were to compare the past and present patterns of IV acid suppressive therapy (AST) in the treatment of GIB and ulceration, the rate of blood transfusions, and mortality rates.
METHODS: A retrospective review of records from UHC clinical database participating hospitals was conducted. Inpatient records from patients 18 years and older receiving at least one dose of IV AST and also carrying a diagnosis of GIB or ulceration were evaluated. Data from the last 6 months prior to the availability of IV pantoprazole were compared with that from the same time of year 3 years later, just prior to the release of another IV PPI.
RESULTS: In periods one and two, 1319 and 1615 patients experienced a GIB and received AST respectively. There were no significant differences between the groups for age, sex, severity of illness or percentage of overall NSAID use. More patients in the second group had a *H. Pylori* diagnosis and received a blood transfusion. There was no difference in duration of AST therapy as a percentage of length of stay or mortality between the two groups. H2RAs were used in group 2 patients with a lower severity index.
CONCLUSIONS: No significant mortality differences were seen, but pantoprazole may have been reserved for patients with a higher severity index in period two.

217. Polypharmacy, polyherbacy and potential interactions among senior citizens in the Paso del Norte region. *Amanda M. Loya, Pharm.D.*, Jose O. Rivera, Pharm.D., Armando Gonzalez-Stuart, Ph.D.; UTEP/UT-Austin Cooperative Pharmacy Program, El Paso, TX.

PURPOSE: Polypharmacy refers to the use of several medications whereas polyherbacy describes the ingestion of multiple herbal products. Significant consequences are associated with the concomitant use of several medications and herbs, particularly among older adults. The purpose of this project is to estimate the prevalence of polypharmacy and polyherbacy among seniors in the Paso del Norte region (El Paso, Texas, Southeastern New Mexico and Ciudad Juárez, México). This study also evaluates the presence of potential interactions between drugs and herbal products.
METHODS: A bilingual (English/Spanish) questionnaire was administered to 130 adults ≥ 60 years of age attending senior centers in the Paso del Norte region. This survey assessed their use of prescription and over-the-counter medications, herbal products, and nutritional supplements. A drug interaction software program was also used to evaluate potential drug/drug, drug/herbal product/supplement, and herbal product/supplement interactions.
RESULTS: The prevalence of polypharmacy among seniors taking ≥ 2 concomitant prescription medications was 66.9% (n=87). The prevalence of minor polypharmacy (2–4 prescription medications) was 41.5% (n=54), and major polypharmacy (5 or more prescription medications) was 25.4% (n= 33). The prevalence of polyherbacy among seniors taking ≥ 2 herbal products or supplements was 38.5% (n=50). In addition, 38.5% (n=50) of seniors were identified as having at least one potential drug/drug interaction, while 11.5% (n=15) of seniors had at least one potential major drug/drug interaction. Drug/herbal product interactions were identified in 24.6% (n=32) of seniors.
CONCLUSIONS: Polypharmacy and polyherbacy are a concern among the senior population in the Paso del Norte region, and the potential for interactions in this study population is substantial. Information obtained from this survey was used to develop an educational program designed to inform seniors about the risks associated with polypharmacy and polyherbacy and to provide them with strategies and tools to safely manage their drug therapy.

218. Prevalence of delirium in surgical intensive care unit patients. *Wesley D. McMillian, Pharm.D.*[1], Ishaq Lat, Pharm.D., BCPS[2], Suresh Agarwal, M.D.[2], Peter Burke, M.D.[2], Ruben Azocar, M.D.[2], Haejin In, M.D.[2]; (1)Fletcher Allen Health Care, Burlington, VT; (2)Boston Medical Center, Boston, MA.

PURPOSE: Previous literature has detailed the prevalence of delirium in the medical population. At initiation of this study, there were no reports on the prevalence of delirium in the surgical ICU patient population. The purpose of this prospective observational study is to determine the prevalence of delirium in the surgical ICU population and to identify an association between psychotropic medication utilization and transition to delirium.
METHODS: Fifty consecutive, mechanically ventilated surgical ICU patients were assessed daily for delirium using the Confusion Assessment Method for the ICU (CAM-ICU) and were followed until hospital discharge or death. Medication administration was assessed by review of bedside flow sheet for infusions, and electronic medication administration records for PRN orders and oral dosage forms.
RESULTS: Twenty surgical and 30 trauma patients were included with 70% male, mean age of 50 ± 22.5 years, mean APACHE II score of 19.5 ± 7.9, and mean SOFA score of 6.8 ± 3.4. The prevalence of delirium in surgical ICU patients was 69%. Patients with delirium had increased ICU length of stay, 13.7 ± 11 days vs. 5.8 ± 4 days and had fewer ventilator-free days, 16.4 ± 9.5 days vs.24.9 ± 2.3 days. Delirious patients were administered greater daily and cumulative lorazepam equivalents, 25.9 mg/day vs. 9.5 mg/day and 227.3 mg vs. 52.1 mg, respectively, and required more cumulative fentanyl equivalents 24.3 mg ± 30.2 mg vs. 5.8 mg ± 6.3 mg.
CONCLUSIONS: Delirium was diagnosed in 69% of surgical ICU patients. The presence of delirium was associated with longer ICU lengths of stay, fewer ventilator-free days, and greater utilization of psychotropic medications. A potential for future study could be to determine if the incidence of delirium is an independent risk factor for mortality in the surgical ICU population.

Pharmacogenomics

219E. CXCL5 gene polymorphism and major cardiovascular events in the International Verapamil SR-Trandolapril Study (INVEST). *Issam Zineh, Pharm.D.*[1], Amber L. Beitelshees, Pharm.D., M.P.H.[2], Taimour Y. Langaee, Ph.D., M.S.P.H.[1], Rhonda M. Cooper-DeHoff, Pharm.D.[3], Carl J. Pepine, M.D.[3], Julie A. Johnson, Pharm.D.[1]; (1)Department of Pharmacy Practice, University of Florida College of Pharmacy, Gainesville, FL; (2)Washington

University School of Medicine, St. Louis, MO; (3)University of Florida College of Medicine, Division of Cardiovascular Medicine, Gainesville, FL.

Presented at the XIV International Symposium on Atherosclerosis, Rome, Italy, June 18-22, 2006.

220E. The dopamine-2 receptor (DRD2) TaqAI polymorphism, prolactin elevation, and bone mineral density in persons with schizophrenia. *Jeffrey R. Bishop, Pharm.D., M.S.*[1], Vicki L. Ellingrod, Pharm.D.[2], Jessica Moline, B.S.[2]; (1)University of Illinois at Chicago College of Pharmacy, Chicago, IL; (2)University of Iowa College of Pharmacy, Iowa City, IA.

eurologic Pharmacists, Baltimore, MD, April 24, 2006.

221E. The serotonin transporter promoter insertion/deletion in patients with depression and selective serotonin reuptake inhibitor (SSRI) associated sexual side-effects. *Jeffrey R. Bishop, Pharm.D., M.S.*[1], Jessica Moline, B.S.[2], Vicki L. Ellingrod, Pharm.D.[2], Susan K. Schultz, M.D.[2], Anita Clayton, M.D.[3]; (1)University of Illinois at Chicago College of Pharmacy, Chicago, IL; (2)University of Iowa College of Pharmacy, Iowa City, IA; (3)University of Virginia Health System, Charlottesville, VA.

Presented at the Annual Meeting of the Pharmacogenetics in Psychiatry, New York, NY, April 6-8, 2006.

222. Influence of CYP3A5 genotype of the recipient on tacrolimus concentration/dose ratio at early stage after liver transplantation. *Eunhee Ji, M.S.*[1], Kyung Suk Suh, M.D., Ph.D.[2], Jung Mi Oh, Pharm.D.[1]; (1)College of Pharmacy, Seoul National University, Seoul, South Korea; (2)Department of Surgery, Seoul National University Hospital, College of Medicine, Seoul National University, Seoul, South Korea.

PURPOSE: As tacrolimus is a substrate for cytochrome P450 3A and p-glycoprotein, its marked interindividual variability has been studied in relation to the genetic polymorphisms of CYP3A5 and ABCB1, which encode cytochrome P450 3A and p-glycoprotein, respectively. This retrospective study aimed to investigate 1) the association between genotype of CYP3A5 and ABCB1 in donor or recipient and tacrolimus concentration/dose ratio (C/D), and 2) the influence of polymorphism on the time to reach steady state after liver transplantation.
METHODS: ABCB1 C1236T, G2677(T/A), C3435T, and CYP3A5 A6986G in both recipient and donor were genotyped from peripheral blood by polymerase chain reaction followed by restriction fragment length polymorphism analysis in 43 Korean liver transplant patients receiving tacrolimus. Dose-adjusted trough concentration was calculated by half of daily dosage(ng/mL per mg), as tacrolimus was administered twice daily.
RESULTS: Recipient's CYP3A5 correlated with the tacrolimus C/D. 58.1% of patients were CYP3A5*3/*3 carriers. The dose-adjusted trough level was significantly lower in CYP3A5*1 carriers than CYP*3/*3 carriers(3.02, SD:1.52 vs 5.76, SD:3.76 ng/mL/mg, p=0.0057). The dose requirement was significantly higher in CYP3A5*1 carriers than in CYP*3/*3 carriers(3.39, SD: 1.18 vs 2.19, SD: 0.94 ng/mL/mg, p=0.0012) for drug level of 9.40 ng/mL(SD 2.28).The ABCB1 as well as donor's CYP3A5 polymorphisms were not associated with any pharmacokinetic parameter. There was no significant difference in time to reach steady state(23.86, SD 8.86days).
CONCLUSIONS: Recipient's, not donor's, CYP3A5 polymorphism is associated with tacrolimus concentration/dose ratio and dose requirements in early stage after liver transplantation. Further sequential analysis may explain the role of donor's CYP3A5 genotype.

223. *MDR1* polymorphism significantly affects the pharmacokinetics of losartan. *Jung-Woo Bae, M.S.*, Nam-Tae Kim, B.S., Jin-Hee Lee, B.S., Whan-Joo Lee, B.S., Dong-Won Jung, B.S., Choon-Gon Jang, Ph.D., Seok-Yong Lee, Ph.D.; College of Pharmacy, Sungkyunkwan University, Suwon, South Korea.

PURPOSE: Losartan is a selective angiotensin receptor antagonist that is used to treat hypertension and heart failure. The frequency of the *MDR1* variant allele in the Korean population was identified, and the effects of the major polymorphisms of the *MDR1* gene on the pharmacokinetics of losartan as well as its active metabolite E-3174 were investigated.
METHODS: Three hundred and fifty eight healthy Korean subjects were recruited and genotyped for the variant alleles of the *MDR1* genes. The genotypes of the *MDR1* gene were determined using a polymerase chain reaction-restriction fragment length polymorphism method. A 50 mg oral dose of losartan potassium was given to 13 healthy Korean male volunteers with the different *MDR1* genotypes for the G2677T SNP in exon 21 and the C3435T SNP in exon 26. Losartan and E-3174 were analyzed by HPLC in the plasma samples collected up to 24 hours after ingesting the drug.
RESULTS: G2677T genotyping revealed GG in 39.7%, GT in 50.3%, and TT in 10.0%, and the frequencies of the CC, CT, and TT genotypes in the C3435T SNP were 44.7, 45.8, and 9.5%, respectively. Significant differences were observed in the area under the plasma concentration-time curve from time zero to 3 hr [$AUC_{0\text{-}3}$] and the C_{max} of losartan and in the $AUC_{0\text{-}3}$ and the t_{max} of E-3174 among the genotype groups (GG/CC, GT/CT and TT/TT; G2677T/C3435T) ($p<0.05$).
CONCLUSIONS: Polymorphisms of *MDR1* may significantly affect the pharmacokinetics of losartan and its active metabolite, E-3174.

224. CYP2C9*3 and CYP2C9*13 allele were associated with the decreased metabolism of losartan. *Jung-Woo Bae, M.S.*, Whan-Joo Lee, B.S., Dong-Won Jung, B.S., Jin-Hee Lee, B.S., Nam-Tae Kim, B.S., Choon-Gon Jang, Ph.D., Seok-Yong Lee, Ph.D.; College of Pharmacy, Sungkyunkwan University, Suwon, South Korea.

PURPOSE: Losartan is metabolized by polymorphic CYP2C9 to E-3174. In this study, the effects of major polymorphisms of the CYP2C9 on pharmacokinetics of losartan and E-3174 were investigated.
METHODS: 498 healthy Korean subjects were recruited and genotyped for the variant alleles of the CYP2C9 genes. A 50 mg oral dose of losartan was given to 27 Korean volunteers with different CYP2C9 genotypes (13, 11 and 3 carriers of CYP2C9*1/*1, *1/*3 and *1/*13 genotypes, respectively). Losartan and E-3174 were analyzed by HPLC in plasma and urine samples collected up to 24 hours after drug intake.
RESULTS: In subjects heterozygous for the CYP2C9*3 and CYP2C9*13 allele, C_{max} and $AUC_{0\text{-}inf}$ of losartan were significantly greater, the half-life of losartan significantly longer, and oral clearance significantly lower than those in homozygous CYP2C9*1 subjects. The increase in C_{max}, $AUC_{0\text{-}inf}$, and half-life, and decrease in oral clearance observed in the CYP2C9*1/*13 individuals were also significantly greater than those expressing the CYP2C9*1/*3 genotypes. The ratio of the total losartan area under the plasma concentration-time curve ($AUC_{0\text{-}inf}$) to the total E-3174 AUC ($AUC_{losartan}/AUC_{E\text{-}3174}$) was higher in the subject with the CYP2C9*1/*3 (approximately 2-fold) and CYP2C9*1/*13 (approximately 3.4-fold) groups compared with the CYP2C9*1/*1 group. The urinary ratio was significantly higher in subjects with the CYP2C9*1 heterozygous genotype than in those with the CYP2C9*1/*1 genotype ($p<0.001$).
CONCLUSIONS: Losartan pharmacokinetics differed significantly between subgroups with different CYP2C9 genotypes. The CYP2C9*3 and CYP2C9*13 allele was shown to be associated with decreased formation of E-3174 from losartan.

225. Liver X receptor-α; (LXRA) genotype and response to intensive lipid-lowering therapy with statins. *Elvin T. Price, Pharm.D.*[1], Christopher B. Arant, M.D.[2], Timothy R. Wessel, M.D.[2], Richard S. Schofield, M.D.[2], Issam Zineh, Pharm.D.[1]; (1)University of Florida College of Pharmacy Department of Pharmacy Practice and Center for Pharmacogenomics, Gainesville, FL; (2)Division of Cardiovascular Medicine, University of Florida College of Medicine, Gainesville, FL.

PURPOSE: Intensive lipid lowering with statins is a preferred treatment strategy in certain patient populations. The benefit of high-dose treatment is thought to be due to both greater low-density lipoprotein (LDL) and C-reactive protein (CRP) reduction. However, variability in LDL and CRP responses exist, and genetic factors may contribute. We investigated whether a single nucleotide polymorphism (SNP) in the LXRA gene, a potential nuclear site of statin action, is associated with either LDL or CRP responses to atorvastatin 80 mg.
METHODS: Subjects were eligible if they were at least 18 years old without CHD, CHD risk equivalents, or contraindications to statins. Subjects received atorvastatin 80 mg daily for 8 weeks. Baseline and 8-week lipids and CRP were obtained from the university hospital clinical laboratory. Genotype determination of the LXRA rs12221497 G/A SNP was performed by pyrosequencing. Biomarker changes were tested by t-test and multivariate analysis.
RESULTS: A total of 61 subjects (59% women; 79% white) were analyzed. Baseline age, total cholesterol, LDL, HDL, triglycerides, and CRP were 32 ± 13 years, 178 ± 38 mg/dl, 98 ± 31 mg/dl, 62 ± 18 mg/dl, 97 ± 54 mg/dl, and 1.8 ± 2.9 mg/L, respectively. The variant A allele frequency was 16%. There were no differences in lipid changes by genotype (not shown). However, wild-type homozygotes (G/G) had an 11% reduction in CRP compared with a 25% increase in variant carriers ($p=0.047$). In multivariate analysis, age ($p=0.01$), baseline CRP ($p=0.02$), and LXRA genotype ($p=0.04$) were significant predictors of CRP response (model $p=0.002$; $r^2=0.23$).
CONCLUSIONS: LXRA genotype did not affect LDL response to 8 weeks of high-dose atorvastatin. However, LXRA genotype was associated with atorvastatin-mediated CRP changes. This is the first study to demonstrate a genetic association with the CRP statin response and should be further evaluated.

226. SLCO1B1 gene variation and apolipoprotein response to atorvastatin. *Gregory J. Welder, A.A.*[1], Christopher B. Arant, M.D.[2], Timothy R. Wessel,

M.D.[2], Richard S. Schofield, M.D.[3], Taimour Y. Langaee, Ph.D., M.S.P.H.[1], Issam Zineh, Pharm.D.[1]; (1)Department of Pharmacy Practice and Center for Pharmacogenomics, University of Florida College of Pharmacy, Gainesville, FL; (2)Division of Cardiovascular Medicine, University of Florida College of Medicine, Gainesville, FL; (3)Division of Cardiovascular Medicine, University of Florida College of Medicine, and Department of Veterans Affairs Medical Center, Gainesville, FL.

PURPOSE: Studies suggest that apolipoprotein (apo) B, apoA1, and apoB/apoA1 ratio may be superior predictors of cardiovascular disease (CVD) risk over low-density lipoprotein (LDL) cholesterol. There are no pharmacogenetic studies evaluating variable statin effects on apos. The SLCO1B1 gene encodes a hepatic transporter responsible for statin uptake into their site of action. We investigated whether genetic variants in SLCO1B1 affect the apo response to atorvastatin.
METHODS: Forty-five subjects (64% women) without CVD or risk equivalents were analyzed. Fasting apos were measured at baseline and after 8 weeks of atorvastatin 80 mg daily. SLCO1B1 genotypes and haplotypes were determined by PCR and pyrosequencing. T-tests were used to test the hypothesis that 174Ala variant carriers and/or subjects with the *5 haplotype had diminished apo responses when compared with wildtype homozygotes (*1a/*1a), because it has been shown that these variants have diminished transporter activity.
RESULTS: Baseline age, apoB, and apoA1 were: 34 ± 15 years, 81 ± 23 mg/dl, and 144 ± 31 mg/dl respectively. There were no differences in baseline characteristics between genotype groups. 174Ala carriers (n=18) had an apoB reduction of 33% compared with 41% in *1a/*1a subjects (p=0.10) and a 12% greater increase in apoA1 (p=0.08). Those with the SLCO1B1*5 haplotype (n=6) had an apoB reduction of 34% compared with *1a/*1a subjects (p=0.07). An apoB/apoA1 reduction of 32% was seen in this haplotype group compared with 41% in wild-type homozygotes (p=0.07).
CONCLUSIONS: SLCO1B1 polymorphisms were associated with differences in the apo response to atorvastatin 80 mg daily. Further investigations into SLCO1B1 variations are warranted to confirm differences in the therapeutic effects of statin treatment.

227. The G-765C promoter polymorphism in cyclooxygenase-2 (PTGS2), aspirin utilization and cardiovascular disease risk: the 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-2 derived prostaglandins modulate cardiovascular disease risk. We sought to determine whether the reduced function G-765C promoter polymorphism in PTGS2 was associated with incident coronary heart disease (CHD) or ischemic stroke risk, and whether this was modified by aspirin utilization.
METHODS: Using a case-cohort design, 2275 participants (73% Caucasian) of the biethnic, multicenter ARIC study [all incident CHD (n=1085) and ischemic stroke (n=300) cases occurring from 1987 to 1998; 958 noncases from a cohort representative sample] were genotyped for the *G-765C* polymorphism. Associations between genotype and risk of incident CHD and ischemic stroke events were evaluated by proportional hazards regression with covariate adjustment. All analyses were race stratified. The putative interaction between baseline aspirin utilization (yes/no) and genotype was assessed in Caucasians, but not African Americans due to sample size limitations.
RESULTS: In African Americans, presence of at least one variant -765C allele was significantly more common in stroke cases vs. noncases (61.4% vs. 49.4%, p=0.032), and associated with higher incident stroke risk relative to two -765G alleles (adjusted hazard rate ratio (aHRR) 1.76, 95% CI=1.05–2.94, p=0.031). No significant association with incident CHD was observed (aHRR 1.03, 95% CI=0.69–1.52, p=0.894). In Caucasians, no significant association with incident stroke was observed (aHRR 0.79, 95% CI=0.50–1.25, p=0.314). This relationship was not modified by aspirin utilization (p=0.630). No significant association between the -765C allele and CHD risk was observed. This relationship appeared to be modified by aspirin utilization (Table); however, the interaction did not attain statistical significance.

	aHRR	95% CI	p-value
All	1.08	0.83-1.42	0.567
No aspirin	1.37	0.98-1.92	0.064
Aspirin	0.60	0.36-1.02	0.058
Interaction			0.065

CONCLUSIONS: The variant -765C allele in PTGS2 was associated with significantly higher ischemic stroke risk in African Americans. Association between the -765C allele and CHD risk may be modified by aspirin utilization in Caucasians. Confirmatory studies are necessary.

228. Genetic variation in UDP-glucuronosyltransferases and metabolism of mycophenolic acid in thoracic (heart or lung) transplant recipients. *Lillian S. L. Ting, B.Sc., M.Sc.(Pharm), Ph.D.-student*[1], Olivier Bernard, B.Sc.(Pharm), M.Sc.[2], Chantal Guillemette, Ph.D.[2], Mary H. H. Ensom, B.S.(Pharm), Pharm.D., FCCP[3]; (1)University of British Columbia, Vancouver, BC; (2)CHUL Research Center, Laval University, Quebec City, QC; (3)University of British Columbia and Children's and 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) in thoracic (heart or lung) transplant recipients, the purpose of this study was to assess associations between polymorphisms in UDP-glucuronosyltransferase (UGT) genes with the metabolic ratios of MPA glucuronide (MPAG) /MPA and acyl MPAG (AcMPAG)/MPA.
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 heart (n=10) or lung (n=21) transplant recipients. Concentrations of MPA, MPAG and AcMPAG were determined by a validated high-performance liquid chromatography method with ultraviolet detection. Pharmacokinetic parameters were calculated by non-compartmental analysis of serum concentration-time curve data using WinNonlin software (Pharsight Corporation, CA, USA) and metabolic ratios (MPAG/MPA and AcMPAG/MPA) were log-transformed. Patients were genotyped for UGT1A8 and UGT1A9 known polymorphisms by direct sequencing of polymerase chain reactions. In the one-way analysis of variance analysis of the relationship of polymorphisms with PK metabolic ratios, heterogeneous and homogeneous carriers were combined.
RESULTS: Polymorphisms were investigated for the UGT1A8 (variants $A^{173}G$ and $C^{277}Y$) and 1A9 (variants -275/-2152, -118T repeat, $G^{3}A$, $T^{33}C$) genes, respectively. No genotypes were observed to be significantly associated with steady-state MPA pharmacokinetics. A trend was observed with higher AcMPAG/MPA ratios for the UGT1A8 variant $A^{173}G$ (p=0.055).
CONCLUSIONS: This pilot study prompts a larger study to identify the UGT genes that could influence MPA metabolism in order to individualize immunosuppressive therapy in this patient population.

Pharmacokinetics/Pharmacodynamics/Drug Metabolism/Drug Delivery

229. Pharmacokinetics of mycophenolic acid and its phenolic-glucuronide and acyl-glucuronide metabolites in stable heart transplant recipients. *Lillian S. L. Ting, B.Sc., M.Sc.(Pharm), Ph.D., student*[1], Nilufar Partovi, B.Sc.(Pharm), Pharm.D.[2], Andrew P. Ignaszewski, M.D., FRCPC[3], Robert D. Levy, M.D., FRCPC[4], K. Wayne Riggs, B.Sc.(Pharm), Ph.D.[1], Mary H. H. Ensom, B.S.(Pharm), Pharm.D., FCCP[5]; (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; (4)University of British Columbia, St. Paul's Hospital and BC Transplant Society, Vancouver, BC, Canada; (5)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 heart transplant recipients.
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: 16 males and 3 females, mean(± SD) 4.8 ± 3.2 years post-transplant, age 60.2 ± 13.1yr and weight 78.8 ± 13.4kg. In addition to MMF, 9 subjects were on cyclosporine, 8 on tacrolimus, and 2 on sirolimus. One subject was also on prednisone (and tacrolimus). Albumin concentration was 4.5 ± 1.2g/dL and serum creatinine 1.5 ± 0.4 mg%. MMF dosage ranged from 0.5 to 3 grams daily. Mean(± SD) MPA PK parameters in cyclosporine, tacrolimus, and sirolimus groups were: area-under-the-curve0-12h (AUC) 62.31 ± 55.32, 50.73 ± 18.58, and 30.56 ± 11.70 µg*hr/mL; dose-normalized AUC 76.99 ± 75.07, 101.42 ± 52.41, and 83.42 ± 8.13 µg*hr/mL/g; maximal concentration 15.87 ± 13.48, 11.18 ± 3.49, and 4.68 ± 2.35 µg/mL; time to Cmax 2.9 ± 3.8, 2.4 ± 3.9, and 4.2 ± 5.4 h; and minimum concentration 1.01 ± 0.67, 1.79 ± 0.74, and 0.89 ± 1.12 µg/mL, respectively. Mean(± SD) AUC ratios of MPAG/MPA were 9.71 ± 7.07, 6.31 ± 3.18, and 8.90 ± 7.16; and AcMPAG/MPA were 0.18 ± 0.10, 0.42 ± 0.35, and 2.00 ± 2.46, respectively. Mean fMPA was 4.3 ± 4.3%.
CONCLUSIONS: Large inter-patient variability was observed in MPA PK parameters and metabolic ratios in heart transplant recipients. Concomitant medications alone cannot explain the variability observed. Population PK and

pharmacogenetic studies are under way to identify other factors that contribute to the variability. These results will help optimize treatment strategies for the heart transplant population.

230E. Nephrotoxicity associated with aggressive vancomycin therapy. *Sun C. Lee-Such, Pharm.D., BCPS*[1], Brian R. Overholser, Pharm.D.[2], L. Silvia Munoz-Price, M.D.[3]; (1)St. Margaret Mercy/Cardinal Health, Hammond, IN; (2)Department of Pharmacy Practice, Purdue University School of Pharmacy and Pharmaceutical Sciences, Indianapolis, IN; (3)St. Margaret Mercy, Hammond, IN.

Presented at the 46th Interscience Conference on Antimicrobial Agents and Chemotherapy, San Francisco, CA, September 27-30, 2006.

231. Alvimopan is effective when administered 0.5 to 5 hours preoperatively followed by twice-daily postoperatively in patients undergoing laparotomy. *Eugene R. Viscusi, M.D.*[1], Eric T. Wittbrodt, Pharm.D.[2], John G. Fort, M.D.[3], Wei Du, Ph.D.[3], Lee Techner, D.P.M.[3]; (1)Jefferson Medical College, Philadelphia, PA; (2)University of the Sciences in Philadelphia, Philadelphia, PA; (3)Adolor Corporation, Exton, PA.

PURPOSE: To analyze alvimopan preoperative dose-timing for the management of postoperative ileus. Data from a new phase III trial with 30-90-minute preoperative dosing were compared with a post-hoc analysis of 3 previous trials.
METHODS: The post-hoc analysis was completed using the pooled modified intent-to-treat (MITT) population from 3 US/Canadian, phase III, randomized trials of alvimopan 6 mg (n=502) and 12 mg (n=508) versus placebo (n=501) in patients undergoing bowel resection (BR) or total abdominal hysterectomy. The new trial included patients undergoing BR treated with alvimopan 12 mg (n=317, MITT) or placebo (n=312, MITT). The 3 trials specified ≥ 2-hour preoperative dosing, whereas the new trial specified 30–90-minute preoperative dosing. All trials included twice-daily postoperative dosing until hospital discharge for up to 7 postoperative days. For all trials, efficacy measures included time-to-first toleration of solid food and first bowel movement (BM) or flatus (GI-3 recovery) and first toleration of solid food and first BM (GI-2 recovery). Time-to-event data were calculated using Cox proportional hazard models; P-values were calculated using the Wald Chi-square test. For the post-hoc analysis of the pooled trials, covariate analysis was conducted to evaluate whether preoperative dose-timing (≤ or > 2 hours) influenced time to GI recovery. The upper limit of preoperative dosing for the majority of patients was 5 hours.
RESULTS: Pooled phase III studies demonstrated that alvimopan treatment significantly accelerated GI-2 (HR=1.28) and GI-3 (HR=1.39) recovery (both p<0.001). Post-hoc covariate analysis demonstrated that preoperative dose-timing did not influence time to GI recovery (GI-3,p=0.185; GI-2, p=0.154). In the new trial, alvimopan 12 mg administered 30–90 minutes preoperatively and twice-daily postoperatively significantly accelerated GI-3 (HR=1.45) and GI-2 (HR=1.53) recovery (both p<0.001).
CONCLUSIONS: Collectively, these data support a preoperative dosing window of 0.5–5 hours. This should allow for flexibility in time between alvimopan administration and surgery without loss of efficacy.

232E. Concentrations of radioactivity in ocular tissues following a single topical ocular dose of ^{14}C-bromfenac ophthalmic solution. George A. Baklayan, M.S., Hemant M. Deshmukh, Ph.D., Harold M. Patterson, B.S., James A. Gow, M.D., *Timothy R. McNamara, Pharm.D.*; ISTA Pharmaceuticals, Inc., Irvine, CA.

Presented at the Annual Meeting of the American Society of Cataract & Refractive Surgery, San Francisco, CA, March 17–22, 2006.

233E. Pharmacokinetic profile of topically applied bromfenac sodium ophthalmic solution 0.1% in subjects undergoing cataract surgery. Takahiro Ogawa, Ph.D.[1], Kensaku Miyake, M.D.[2], *Timothy R. McNamara, Pharm.D.*[3], James A. Gow, M.D.[3]; (1)Senju Pharmaceutical Co., LTD, Los Angeles, CA; (2)Shozankai Medical Foundation of the Miyake Eye Clinic, Nagoya, Japan; (3)ISTA Pharmaceuticals, Inc., Irvine, CA.

Presented at the Annual Meeting of the Association for Research in Vision and Ophthalmology, Fort Lauderdale, FL, April 30-May 4, 2006.

234E. The compatibility of Vitrase® combined with Avastin®. Bruce A. Aird, Ph.D., *Timothy R. McNamara, Pharm.D.*, Clara K. Song, Pharm.D., James A. Gow, M.D., Terence W. Joe, M.S., George A. Baklayan, M.S.; ISTA Pharmaceuticals, Inc., Irvine, CA.

Presented at the Annual Meeting of the Association for Research in Vision and Ophthalmology, Fort Lauderdale, FL, April 30-May 4, 2006.

235E. Pharmacokinetics of extended-release guanfacine in children and adolescents with ADHD. Samuel W. Boellner, M.D.[1], Michael Pennick, B.Sc.[2], *Amir Shojaei, Ph.D.*[3], Kimberly Fiske, B.S.[3]; (1)Clinical Study Centers, Little Rock, AR; (2)Shire Pharmaceuticals Group, Chineham, United Kingdom; (3)Shire Development Inc, Wayne, PA.

Presented at the Annual Meeting of the New Clinical Drug Evaluation Unit, Boca Raton, FL, June 12-15, 2006.

236. Pharmacokinetic analysis of guanfacine extended release in healthy adult. *Dennis Swearingen, M.D.*[1], Michael Pennick, B.Sc.[2], Amir Shojaei, Ph.D.[3], Kimberly Fiske, B.S.[3], Brian Scheckner, Pharm.D.[3]; (1)MDS Pharma Services, Phoenix, AZ; (2)Shire Pharmaceuticals Group, Chineham, United Kingdom; (3)Shire Development Inc, Wayne, PA.

PURPOSE: Guanfacine immediate-release is a nonstimulant alpha 2A-adrenoceptor agonist used "off-label" for ADHD. Guanfacine extended-release (GXR) is a novel formulation of guanfacine for ADHD. This study assessed dose proportionality of 1, 2, and 4 mg GXR tablets.
METHODS: Randomized, open-label, single-dose, crossover study was conducted in healthy adults aged 18-55. Vital signs, ECGs, and plasma samples were taken at predose and at regular intervals over 96 hours. Subjects initially administered a single 1 mg dose and then randomized to receive single 2 mg and 4 mg doses at 4 separate weekly visits. Dose proportionality was assessed using AUC and C_{max}. Safety was assessed at each visit.
RESULTS: Mean guanfacine plasma concentrations increased in a dose-proportional manner following 1, 2, and 4 mg doses of GXR. C_{max} for the 1 mg, 2 mg, and 4 mg doses were 0.98 ± 0.26 ng/mL, 1.57 ± 0.51 ng/mL, and 3.58 ± 1.39 ng/mL, respectively. $AUC_{0\text{-}t}$ values were 29.3 ± 8.84 h•ng/mL, 54.5 ± 17.7 h•ng/mL, and 119.1 ± 42.3h•ng/mL respectively. $AUC_{0\text{-}\infty;}$ were 32.4 ± 8.78 h•ng/mL, 58.0 ± 18.9 h•ng/mL, and 124.1 ± 45.1 h•ng/mL, respectively. The mean half-life ranged from 16.6 ± 3.80 hours to 17.5 ± 3.83 hours. The geometric mean ratios of dose-normalized C_{max}, $AUC_{0\text{-}t}$, and $AUC_{0\text{-}\infty;}$ between the 1 and 2 mg, 1 and 4 mg, and 2 and 4 mg doses were all dose proportional, except for the C_{max} between 1 and 2 mg (geometric mean ratio, 1.26; 90% CI=1.17–1.35). Treatment-emergent AEs were observed in 40 (77%) of the subjects. All were mild (99%) or moderate (1%) in intensity and generally resolved without treatment. No discontinuations due to AEs were observed. The most common treatment-emergent AE was somnolence. All postdose mean vital signs and ECG parameters remained within normal limits.
CONCLUSIONS: The pharmacokinetics of GXR tablets are generally linear over doses ranging from 1 mg to 4 mg. Overall, GXR was well tolerated, with no AE-related withdrawals or severe AEs.

237. Antibiotic level monitoring: are centrally drawn levels accurate? *Gretchen L. Brummel, Pharm.D.*, Kevin M. Mulieri, Pharm.D., Patricia A. Light, R.N., M.S., CPN, Neal J. Thomas, M.D., MSc, Missy McClure, R.N., W. Stuart Warren, M.D., Gavin R. Graff, M.D.; Penn State Milton S. Hershey Medical Center, Hershey, PA.

PURPOSE: Serum concentration monitoring is routinely performed with certain antibiotics to optimize therapeutic response and decrease adverse effect potential. However, controversy exists as to whether levels should be drawn peripherally or if they can be obtained through a central venous line. Often, centrally obtained levels are taken from the same line through which the dose has been administered. An inaccurate value has the potential to result in subtherapeutic levels which has been demonstrated to induce bacterial resistance and cause treatment failures. In addition, there is potential for drug toxicity if a level is falsely low. Our objective was to determine whether antibiotic levels obtained from a single lumen central line correlate with those drawn through a peripheral blood draw.
METHODS: Pediatric patients receiving intravenous antibiotics (vancomycin or tobramycin) were enrolled if they had a single lumen central catheter. Peripheral and central antibiotic levels were taken simultaneously. The central line draw was completed adhering to the institution's central venous catheter blood withdrawal protocol. A paired t-test was used to compare the central and peripheral levels.
RESULTS: Twenty-five pairs of levels were available for analysis. The mean differences in tobramycin peaks (n=10) and troughs (n=8) were 2.4 µg/mL ± 2.7 and 0.15 µg/mL ± 0.17, respectively. The mean differences in vancomycin peaks (n=2) and troughs (n=5) were 32.7 µg/mL ± 43.9 and 1.88 µg/mL ± 1.13, respectively. The difference was statistically significant (p<0.05) for tobramycin levels and vancomycin troughs.
CONCLUSIONS: Centrally obtained antibiotic levels drawn from the same line through which they were infused resulted in statistically significantly different values than peripheral levels for vancomycin troughs, tobramycin peaks and tobramycin troughs. The clinical significance is yet to be determined. To optimize therapeutic response and decrease potential adverse effects, we recommend that antibiotic levels be obtained from a peripheral blood draw.

238E. Abuse liability of intravenous lisdexamfetamine dimesylate (LDX; NRP104). *Michael Arora, Pharm.D.*[1], Donald Jasinski, M.D.[2], Suma Krishnan, M.S.[3]; (1)Shire Development Inc, Wayne, PA; (2)Johns Hopkins Bayview Medical Center, Baltimore, MD; (3)New River Pharmaceuticals, Blacksburg, VA.

Presented at the College on Problems of Drug Dependence, Scottsdale, AZ, June 17-22, 2006.

239E. Evaluation of preservative-free, highly purified hyaluronidase ovine (Vitrase®), 200 USP units/mL, as an adjuvant to increase the absorption and dispersion of other injected drugs prior to ocular surgery. Eric D. Donnenfeld, M.D.[1], Edward J. Holland, M.D.[2], John D. Hunkeler, M.D.[3], David E. Silverstone, M.D.[4], Rachel M. Sacks, B.S.[5], *James A. Gow, M.D.*[5], Lisa R. Grillone, Ph.D.[5]; (1)Ophthalmic Consultants of Long Island, Rockville Centre, NY; (2)Cincinnati Eye Institute, Cincinnati, OH; (3)Hunkeler Eye Institute, Kansas City, MO; (4)Yale School of Medicine, New Haven, CT; (5)ISTA Pharmaceuticals, Inc., Irvine, CA.

Presented at the 19th Annual Meeting of the Ophthalmic Anesthesia Society, Chicago, IL, September 23-25, 2005.

240E. Modified diet in renal disease versus Cockroft-Gault equation use in assessment of antibiotic pharmacokinetics. *Ealaf Shemmeri, Pharm.D.*[1], Thomas C. Dowling, Pharm.D., Ph.D.[2], Sharon Wilson, Pharm.D., BCPS[1]; (1)University of Maryland Medical Center, Baltimore, MD; (2)University of Maryland, Baltimore, MD.

Presented at the Eastern States Residency Conference, Baltimore, MD, May 13-16, 2006.

241. A population model of naltrexone using MC-PEM. *Olanrewaju O. Okusanya, Pharm.D.*, Ahmed Amer, M.D., M.S., Elizabeth Shang, Ph.D, Robin DiFrancesco, M.T., M.B.A., Alan Forrest, Pharm.D, Edward Bednarczyk, Pharm.D; University at Buffalo, Buffalo, NY.

PURPOSE: Naltrexone is an opioid receptor antagonist used primarily in the management of opioid addiction and alcoholism. In spite of widespread use, the pharmacokinetics of naltrexone haven't been extensively studied. We have developed a population model to describe the pharmacokinetics of naltrexone and its metabolite, 6-β-naltrexol.
METHODS: Fifteen healthy subjects were randomized to a single 12.5, 25, or 50 mg dose of oral naltrexone. Serial blood samples were obtained at 20, 40, and 60 minutes, and 1.5, 2, 3, 4, 6, 8, 12, 24, 72, and 96 hours following dosing. Samples were analyzed, for naltrexone and its metabolite, with a LLQ of 10 ng/mL and 1 ng/mL respectively with CV% < 9.3. The data were fit to a compartmental model using a Monte-Carlo parametric expectation maximization method implemented in S-ADAPT 1.52; with all volumes and clearances, for the parent, conditioned on bioavailability (BA) and, for the metabolite, also on the fraction of BA parent which is transformed into the metabolite. The data were weighted by the inverse of the estimated measurement error variance; model discrimination was by evaluating the difference in objective function (-2LL) assuming a χ^2 distribution.
RESULTS: The data were fit to a 2-compartment model for both the parent and metabolite, with a fraction of the dose absorbed as metabolite, due to a high first pass effect. Mean estimates for the parameters are shown below:

	CL/F (CV), L/hr	Vc/F (CV), L	Vp/F (CV), L	CLd/F (CV), L/hr
Naltrexone	762 (0.40)	193 (0.99)	7810 (0.53)	1830 (0.58)
6-β-Naltrexol	80.3 (0.30)	171 (0.49)	468 (0.57)	90.5 (0.80)

The goodness of fit was excellent with an overall r^2 of 0.97 and 0.89 for the parent and metabolite respectively.
CONCLUSIONS: Naltrexone PK can be well described using a 2-cmpt model for the parent and metabolite, which will be useful in modeling its pharmacodynamic effects.

242. The pharmacokinetics of pantoprazole delayed-release granules administered by three different methods in healthy subjects. *Brinda K. Tammara, Ph.D*, Kathy Weisel, M.S., Arie Katz, M.D., Xu Meng, Ph.D.; Wyeth Research, Collegeville, PA.

PURPOSE: A new oral delayed-release granule formulation of pantoprazole was developed as an alternative for adult subjects who cannot swallow tablets. The primary objective of this study was to determine the bioequivalence of this new formulation administered by 3 different methods in healthy subjects.
METHODS: This was a randomized, open-label, 3-period, crossover, in-patient study in 25 healthy adult subjects aged 18–50 years. Each subject received a single 40 mg dose of pantoprazole after at least a 10-hour fast for each of the following administration methods separated by a washout period: 1) granules sprinkled over applesauce; 2) granules mixed with apple juice; 3) granules mixed with apple juice and administered through a nasogastric (NG) tube. Blood samples were collected up to 24 hours post dose and analyzed for pantoprazole levels by a validated LC/MS/MS method. Standard safety evaluations were performed. The PK parameters were estimated using non-compartmental methods. The 90% confidence limits for the test-to-reference geometric mean ratio were calculated for C_{max} and AUC.
RESULTS: The mean C_{max}, AUC_T,and AUC values were similar for the 3 dosing methods. For C_{max}, AUC_T, and AUC, the 90% CIs for the ratio of the geometric means were within the bioequivalent limits of 80%–125%. Four subjects reported adverse events while on treatment including: headache, diarrhea, bronchitis, increased cough, epistaxis, and local reaction to the NG tube. There were no deaths, serious adverse events, or discontinuations.
CONCLUSIONS: Pantoprazole granules administered with apple juice orally or through an NG tube, or with applesauce are bioequivalent. Pantoprazole granules were safe and well tolerated when administered by the above methods.

243. Monte Carlo analysis (MCA) using multicenter databases: is it useful in individual hospitals? *Roger L. White, Pharm.D.*, Samantha Griner, Governors School Scholar; Medical University of South Carolina, Charleston, SC.

PURPOSE: MCA is used to assess pharmacodynamic profiles in patient populations and is often performed with multicenter MICs. Because MICs vary among hospitals, multicenter MCA may not be useful in individual hospitals.
METHODS: Levofloxacin (L), and gatifloxacin (G) MICs (Etest) were determined for 2267 blood and sputum *S. pneumoniae* from 56 U.S. hospitals. Published PK parameters and a CrCl distribution from a tertiary care hospital were used to simulate unbound AUCs for: L750 mg (L750), L500 mg (L500), and G400 mg (dosed per product label). MCA (10,000 simulations) for each regimen was performed using the combined MICs (ALL) and MICs from each hospital (n=56). Target attainment (TA) at AUC/MIC≥ 30 and ≥ 60 were assessed. Chi square ($p<0.05$) was used to assess %TA differences between each hospital and ALL.
RESULTS: ALL MIC_{50}, MIC_{90}, and range were: 0.75, 1.0, 0.023–32 mg/L for L; 0.19, 0.25, 0.016–32 mg/L for G. Susceptibility (%) was 98.7 for L; 99.4 for G.

Parameter	L750	L500	G
%TA at AUC/MIC ≥ 30/≥ 60 (ALL)	99/87	95/56	99/99
%TA range among hospitals (AUC/MIC ≥ 30)	95–100	84–100	97–100
%TA range among hospitals (AUC/MIC ≥ 60)	56–100	10–96	94–100
% of hospitals with TA (AUC/MIC ≥ 30) ≥ 90%	100	86	100
% of hospitals with TA (AUC/MIC ≥ 60) ≥ 90%	59	11	100

Differences in TA between hospitals and ALL occurred in > 80% of the hospitals. Differences in TA between L750 and L500 at AUC/MIC ≥ 30 and ≥ 60 was 0–13 and 4–54%, respectively. Differences in TA between L750 and G at AUC/MIC ≥ 30 and ≥ 60 was 0–4 and 0-44%, respectively.
CONCLUSIONS: TA varied widely among hospitals. These findings suggest that a hospital may select a different drug or perhaps even a different dose when hospital-specific, rather than combined, MCA is used; thus, MCA should be based on hospital-specific data.

244E. Bioavailability of extended-release tramadol compared with immediate-release tramadol. *Okponanabofa Eradiri, Ph.D.*[1], Suryanarayana Sista, Ph.D.[1], John C-K Lai, M.Sc[1], Alexander Danyluk, Pharm.D.[2], Vincent V. Brett, M.S., R.Ph.[2]; (1)Biovail Technologies, Ltd., Chantilly, VA; (2)Ortho-McNeil Janssen Scientific Affairs, LLC, Raritan, NJ.

Presented at the 35th Annual Meeting of the American College of Clinical Pharmacology, Cambridge, MA, September 17-19, 2006.

245. Pharmacokinetics of alvimopan and its amide hydrolysis metabolite: effect of perioperative antibiotic use in patients undergoing laparotomy. *Joseph Foss, M.D.*[1], Virginia Schmith, Ph.D.[2], John G. Fort, M.D.[3], Wei Du, Ph.D.[3], Lee Techner, D.P.M.[3]; (1)The Cleveland Clinic, Cleveland, OH; (2)GlaxoSmithKline, Philadelphia, PA; (3)Adolor Corporation, Exton, PA.
PURPOSE: To characterize the pharmacokinetics of alvimopan and its primary amide hydrolysis metabolite in patients undergoing laparotomy in a phase III postoperative ileus trial. The effect of perioperative antibiotic treatment on metabolite production was also explored.

METHODS: Alvimopan (6 mg or 12 mg) or placebo was administered ≥ 2 hours preoperatively and twice-daily postoperatively until hospital discharge (HD) (≤ 7 postoperative days [PODs]). Blood was collected 2 hours after study drug administration (POD 0) and on the day of HD (n=242/615) or on the day of HD (n=212/615) for pharmacokinetic analysis. The effect of antibiotic use on efficacy was examined in this trial and 2 additional phase III trials. Gastrointestinal (GI) recovery data were calculated using Cox proportional hazard models; P values were calculated using the Wald Chi-square test.

RESULTS: Mean alvimopan plasma concentrations were higher on POD 0 (alvimopan 6 mg, 4.12 ± 4.35 ng/mL; alvimopan 12 mg, 6.26 ± 11.03 ng/mL) than at HD (alvimopan 6mg, 1.20 ± 1.79 ng/mL; alvimopan 12 mg, 2.53 ± 8.03 ng/mL). The amide hydrolysis metabolite was not detectable in plasma, in general, until 6–8 hours after alvimopan dosing, and mean levels were lower at POD 0 (alvimopan 6 mg, 0.13 ± 0.10 ng/mL; alvimopan 12 mg, 0.13 ± 0.17 ng/mL) than at HD (alvimopan 6 mg, 0.91 ± 10.50 ng/mL; alvimopan 12 mg, 1.49 ± 25.10 ng/mL). At HD, the amide hydrolysis metabolite was detectable in only half the patients. The amide hydrolysis metabolite was detected in almost no patients (3/39) who received oral bowel-preparation antibiotics, half (23/47) who received broad-spectrum intravenous antibiotics, and most (27/33) who received intravenous non-GI–targeted antibiotics. Alvimopan significantly accelerated GI recovery (Hazard ratios=1.3–1.5; p<0.001) in patients who received GI-targeted antibiotics despite low/absent metabolite levels.
CONCLUSIONS: Patients who received GI-flora–targeted oral or intravenous antibiotics were likely to have low or absent metabolite levels, supporting the hypothesis that gut flora contribute to metabolite production. The alvimopan amide hydrolysis metabolite is not required for efficacy.

246E. Pharmacokinetic modeling for dose conversion of immediate-release to extended-release tramadol. *Bindu P. Murthy, Pharm.D.*[1], Alexander Danyluk, Pharm.D.[2], Donna Skee, B.S.[1], Gary Vorsanger, Ph.D., M.D.[3], Vincent Brett, M.S., R.Ph.[2], Bruce Moskovitz, M.D.[3]; (1)Johnson & Johnson, PRD, Raritan, NJ; (2)Ortho-McNeil Janssen Scientific Affairs, LLC, Raritan, NJ; (3)PriCara, Raritan, NJ.

Presented at the 17th Annual Clinical Meeting of the American Academy of Pain Management, Orlando, FL, September 7-10, 2006.

247E. Tolerability of switching from an oral dopamine agonist to transdermal rotigotine in Parkinson's disease. Paul Nausieda, MD[1], James M. Patton, M.D.[2], *Katherine L. Widnell, M.D., Ph.D.*[1], Steven Neilson, M.S.[3], Babak Boroojerdi, Ph.D.[4]; (1)Aurora Sinai Medical Center, Milwaukee, WI; (2)Asheville Neurology Specialists, P.A., Asheville, NC; (3)Schwarz Biosciences, Inc, Research Triangle Park, NC; (4)Schwarz Pharma AG, Monheim, Germany.

Presented at the 16th Annual Meeting of the European Neurological Society, Lausanne, Switzerland, May 29, 2006.

248. Pharmacokinetics of terbinafine 1% emulsion gel in healthy volunteers and in patients with tinea cruris/corporis. Jannick Denouel[1], Pascale Burtin, M.D.[2], *Bhakti Kshatriya, Pharm.D.*[3], Andrew Snoddy, Ph.D.[3]; (1)Novartis Pharma SAS, Paris, France; (2)Novartis Pharma AG, Paris, France; (3)Novartis Consumer Health Inc, Parsippany, NJ.

PURPOSE: Two studies were conducted to examine the pharmacokinetics of terbinafine after application of the 1% emulsion gel in healthy volunteers and in patients with tinea cruris/corporis.
METHODS: Two open-label, multiple-dose studies were conducted. In study 1, terbinafine gel was applied once daily for 7 days in 12 healthy volunteers. Study medication was applied onto 20% of each subject's total body surface area (BSA). Study 2 examined 12 patients with tinea cruris/corporis. Study medication was applied once daily for 7 days onto the diseased areas of skin as well as a 2.5 cm-wide margin of healthy skin. T_{max}, C_{max}, $AUC_{(0\text{-}24h)}$ were calculated on day 7 in both studies. Adverse event data were collected for all patients. Terbinafine concentrations were measured using HPLC. Descriptive statistics were generated for the outcome measures, and PK parameters were determined by standard non-compartmental methods.
RESULTS: Pharmacokinetic variables are reported below for study 1 (6 men, 6 women, age 19–42 years) and study 2 (6 men, 6 women, age 19–64 years). The mean amount of terbinafine applied in study 1 was 67.5 mg/day (± 5.5 mg/day) and ranged from 20.4 mg/day to 92.1 mg/day in study 2.

	Mean	SD	Range
Study 1			
t_{max} (h)	7.33	3.45	4.0–14.0
C_{max} (ng/ml)	3.82	2.05	1.97–9.72
$AUC_{0\text{-}24h}$ (h.ng/ml)	62.55	46.54	13.45–190.28
Study 2			
t_{max} (h)	7.83	7.11	0–24.0
C_{max} (ng/ml)	2.48	1.85	0–6.8
$AUC_{0\text{-}24h}$ (h.ng/ml)	40.54	36.30	0–133.6

One adverse event was reported in each study (headache, tooth pain). Investigators considered both unlikely related to study medication.
CONCLUSIONS: Systemic exposure of terbinafine was low with once daily application of 1% emulsion gel, and was similar in healthy subjects and in patients with tinea cruris/corporis.

249. Skin pharmacokinetics of terbinafine in healthy subjects following once-daily application of 1% emulsion gel or 1% cream for 1, 5 or 7 days. Jeffrey Cramer, Ph.D.[1], *Bhakti Kshatriya, Pharm.D.*[2], Andrew Snoddy, Ph.D.[2]; (1)Novartis Pharmaceuticals Corp, Florham Park, NJ; (2)Novartis Consumer Health Inc, Parsippany, NJ.

PURPOSE: To compare skin pharmacokinetics of terbinafine following once-daily applications of gel or cream for 1, 5 or 7 consecutive days.
Methods: In this prospective, randomized, open, parallel-group study, 36 adults (3 males, 3 females/regimen) applied gel or cream to the back once daily for 1, 5, or 7 days. Skin biopsies were taken before treatment on day 1 (1-day regimen), days 1 and 5 (5-day regimen) or days 1, 3, 5, and 7 (7-day regimen). Biopsies were also taken 4, 8, 12, and 24 hours and 2, 3, 4, and 7 days following the last application.
RESULTS: AUC values in the total stratum corneum were significantly greater for gel *vs* cream after 1 and 5 days, while mean C_{max} values were significantly higher for gel after 5 days. The t_{fi} with gel was significantly longer than with cream after 5 days. Both gel and cream were well tolerated.
CONCLUSIONS: Skin penetration was greater and occurred sooner during the treatment with terbinafine 1% gel than with 1% cream. This improved penetration may allow for 7-day once daily treatment with terbinafine 1% gel.

	Gel		
Mean ± SD	1 day	5 days	7 days
AUC_{0-t} (ng•hr/cm²)	8295 ± 956[a,b,c]	10,287 ± 551[d,e]	12,650 ± 626
C_{max} (ng/cm²)	683.7 ± 54.1[g,b]	891.2 ± 93.5[c,h]	908.8 ± 91.0[g]
t_{fi} (hrs)	n/a	36.7 ± 5.5[d]	47.2 ± 3.0[i]

Table continued

	Cream		
Mean ± SD	1 day	5 days	7 days
AUC_{0-t} (ng•hr/cm²)	7271 ± 951[c,f]	8480 ± 268[e]	11,754 ± 256
C_{max} (ng/cm²)	717.7 ± 76.1[c]	746.0 ± 54.1[e]	944.0 ± 105.9[e]
t_{fi} (hrs)	n/a	21.3 ± 1.5	44.1 ± 3.4[i]

[a]*P*=0.008 *vs* cream; [b]*P*=0.001 *vs* 1 and 5 days; [c]*P*<0.001 1 day *vs* 7 days; [d]*P*<0.001 *vs* cream; [e]*P*<0.001 5 days *vs* 7 days; [f]*P*=0.002 1 day *vs* 5 days; [g]*P*<0.001 *vs* 1 day; [h]*P*=0.004 *vs* cream; [i]*P*<0.001 *vs* 5 days

250. Evaluating the effects of St. John's wort (hypericum perforatum) on pharmacokinetic, pharmacodynamic and physiologic characteristics of third-generation oral contraceptive agents in young women. *Priscilla How, Pharm.D.*[1], Lingtak-Neander Chan, Pharm.D.[2], Jennifer Hardman, Pharm.D.[1], Allison Cowett, M.D.[1], Mark Vajaranant, M.D.[1], Lee Shulman, M.D.[1], Alan Lau, Pharm.D.[1]; (1)University of Illinois at Chicago, Chicago, IL; (2)University of Washington, Seattle, WA.

PURPOSE: The interaction between St. John's Wort (SJW) and less prescribed, older generation oral contraceptives (OC) has been reported. Additionally, SJW showed conflicting effects on OC disposition. The effect of SJW on more potent and widely prescribed third-generation OC is unknown. This study was conducted to assess the impact of SJW on pharmacokinetic (PK), pharmacodynamic (PD), and physiologic effects of the estrogen and progestin components of a third-generation OC.
METHODS: A monophasic OC containing ethinyl estradiol (EE) and norgestimate (NGM) was administered to 14 healthy women in this prospective, single-blind study for 2 months, followed by 2 months with placebo, then 2 months with SJW. Serial blood draws and endovaginal ultrasound were performed at the end of the placebo and SJW phases. Liquid-chromatography mass spectrometry (LCMS) was used to determine the plasma concentrations of EE and NGM. All results were compared using the paired Student's *t*-test.
RESULTS:

Parameters	Placebo	SJW
$AUC_{0\text{-}24}$ of EE (ng·h/L)[#]	2303 ± 1138	2186 ± 1204
$T_{1/2}$ of EE (h)[#]	24.15 ± 4.96	23.73 ± 6.08
Cmax of EE (ng/L)[#]	272 ± 200	266 ± 121
Tmax of EE – median (h)	1.25	1.25
FSH (MIU/ml)^	1.9 (0.6–3.4)	2.1 (0.6–5.8)
LH (MIU/ml)^	1.8 (0.1–7.1)	2.1 (0.1–5.5)
Factor II activity (% normal)^	126 (108–181)	123 (108–139)
Factor VII activity (% normal)^	150 (101–208)	132 (73–181)
Ovarian follicle size (mm)^	6.4 (4.1–33.4)	5.7 (3.6–45.9)

[#]Mean ± standard deviation
^Median (range)

SJW did not significantly affect the PK, PD and physiologic effects of EE and NGM (data not shown but will be presented) [p>0.05].
CONCLUSIONS: SJW does not appear to have significant effects on the PK, PD and physiologic effects of third-generation OCs. The clinical significance of drug interaction between SJW and OC is doubtful.

Psychiatry

251. Pharmacokinetic evaluation of SPD465, a novel long-acting mixed amphetamine salts extended-release formulation. *Sharon H. Youcha, M.D.*[1], Michael Pennick, B.Sc., (Hons)[2], Colleen S. Anderson, M.Ed., B.A.[1], James C. Ermer, M.S.[1]; (1)Shire Development, Inc., Wayne, PA; (2)Shire Development, Inc., United Kingdom.

PURPOSE: SPD465 (Shire Development, Inc.) is a long-acting mixed amphetamine salts extended-release product in clinical development to provide full-day symptom control (up to 16 hours) for the treatment of adults with attention-deficit/hyperactivity disorder (ADHD). This study evaluated the bioavailability of SPD465 compared with Adderall XR supplemented with mixed amphetamine salts (MAS) immediate-release (IR) in healthy subjects.
METHODS: This was a phase I, open-label, single-dose, 2-period, crossover study in 20 healthy adult volunteers, designed to evaluate the bioavailability of SPD465 over the course of a full day. Comparisons were made between SPD465 37.5 mg (Treatment A) and Adderall XR 25 mg augmented with 12.5 mg MAS IR dosed 8 hours later (Treatment B). Plasma samples were assayed for *d*- and *l*-amphetamine concentrations using a validated LC/MS/MS method. The pharmacokinetic parameters maximum plasma concentration (C_{max}) and area under the plasma concentration-time curve from time 0 to infinity ($AUC_{0\text{-}inf}$) were evaluated by standard bioequivalence (BE) tests. Vital signs, electrocardiograms (ECG), Lab, and Adverse Event (AE) data were also collected.
RESULTS: Exposure of both *d*-amphetamine and *l*-amphetamine was equivalent based on standard BE tests for C_{max} (least square mean ratio-Treatment A/B) of *d*-amphetamine and *l*-amphetamine (101.0 and 90.9, respectively) and for $AUC_{0\text{-}inf}$ (104.4 and 95.3, respectively). The 90% confidence intervals of all test-to-reference ratios were within the range of 80%–125%. There were no clinically significant differences between the study formulations on laboratory evaluations or number of AEs. One subject experienced an ECG abnormality leading to early study termination. All AEs were mild.
CONCLUSIONS: The results of this study indicate that the exposure observed with SPD465 37.5 mg was bioequivalent, according to current standards, to that of Adderall XR 25 mg supplemented by 12.5 mg of MAS IR administered 8 hours later. SPD465 was generally well tolerated.
Supported by Shire Development, Inc.

252. The effect of food on the pharmacokinetic profile of SPD465, a novel long-acting mixed amphetamine salts extended-release formulation. *James C. Ermer, M.S.*[1], Michael Pennick, B.Sc., (Hons)[2], Colleen S. Anderson, M.Ed., B.A.[1], Sharon H. Youcha, M.D.[1]; (1)Shire Development, Inc., Wayne, PA; (2)Shire Development, Inc., United Kingdom.

PURPOSE: To evaluate the bioavailability under fasted and fed conditions of SPD465 (Shire Development, Inc.), a novel, long-acting mixed amphetamine salts extended-release formulation in clinical development for full day symptom control (up to 16 hours) for the treatment of adult attention-deficit/hyperactivity disorder (ADHD).
METHODS: In this Phase I, open-label, single-dose, 3-period, crossover study, healthy adult subjects (N=16) received a single 50-mg dose of SPD465 under fasted conditions (following a 10-hour fast-Treatment A), fed conditions (following a standard high-fat meal-Treatment B), and sprinkled on applesauce under fasted conditions (following a 10-hour fast-Treatment C). Plasma samples were obtained over a 60-hour period and were assayed for *d*- and *l*-amphetamine using a validated LC/MS/MS method. The maximum plasma concentration (C_{max}) and area under the plasma concentration-time curve from time 0 to infinity ($AUC_{0\text{-}inf}$) were evaluated by standard bioequivalence tests. Vital signs, electrocardiograms (ECG), Lab, and Adverse Event (AE) data were also collected.
RESULTS: The mean C_{max} and AUC data in each of the 3 treatment conditions demonstrates equivalent exposure for both *d*- and *l*-amphetamine. The mean *d*-amphetamine C_{max} and $AUC_{0\text{-}inf}$ were 72.3, 60.0 and 67.3 ng/mL and 1590, 1434 and 1498 ng-h/mL for Treatments A, B and C respectively. The mean *l*-amphetamine C_{max} and $AUC_{0\text{-}inf}$ were 21.1, 17.6 and 20.0 ng/mL and 545, 482, and 511 ng-h/mL for Treatments A, B and C respectively. The 90% confidence intervals of all ratios were within the range of 80%–125%. No clinically significant differences on laboratory evaluations, ECG results, or number of AEs were observed. Most AEs were mild.
CONCLUSIONS: The results of this study indicate that SPD465 exposure is not affected by food and was generally well tolerated. SPD465 can be taken without regard to meals or sprinkled over applesauce, providing increased flexibility in dosing.
Supported by Shire Development, Inc.

253E. Recurrence prevention in patients with recurrent unipolar major depression: a placebo-controlled trial of venlafaxine XR. Martin Keller, M.D.[1], *Bing Yan, M.D.*[2], David Dunner, M.D.[3], James Ferguson, M.D.[4], Edward Friedman, M.D.[5], Alan Gelenberg, M.D.[6], Robert Hirschfeld, M.D.[7], James Kocsis, M.D.[8], Susan Kornstein, M.D.[9], Charles Nemeroff, M.D., Ph.D.[10], Philip T. Ninan, M.D.[2], Anthony Rothschild, M.D.[11], Alan Schatzberg, M.D.[12], Richard Shelton, M.D.[13], Michael E. Thase, M.D.[5], Madhukar H. Trivedi, M.D.[14], John Zajecka, M.D.[15], Saeed Ahmed, M.D.[2], Jeff Musgnung, M.T.[2], Ron Pedersen, M.S.[2]; (1)Brown University, Providence, RI; (2)Wyeth Pharmaceuticals, Collegeville, PA; (3)University of Washington, Seattle, WA; (4)Radiant Research, Salt Lake City, UT; (5)University of Pittsburgh Medical Center, Pittsburgh, PA; (6)Univeristy of Arizona, Tucson, AZ; (7)University of Texas Medical Branch, Galveston, TX; (8)Weill Cornell Medical College, New York, NY; (9)Virginia Commonwealth University, Richmond, VA; (10)Emory University School of Medicine, Atlanta, GA; (11)University of Massachusetts Medical School, Worcester, MA; (12)Stanford University School of Medicine, Stanford, CA; (13)Vanderbilt University, Nashville, TN; (14)University of Texas Southwestern Medical School, Dallas, TX; (15)Rush University Medical Center, Chicago, IL.

Presented at the Annual Meeting of the College of Psychiatric and Neurologic Pharmacists, Baltimore, MD, April 23-26, 2006.

254E. Recurrence prevention during 2 years of maintenance treatment with venlafaxine XR in patients with recurrent unipolar major depression. Martin Keller, M.D.[1], *Bing Yan, M.D.*[2], David Dunner, M.D.[3], James Ferguson, M.D.[4], Edward Friedman, M.D.[5], Alan Gelenberg, M.D.[6], Robert Hirschfeld, M.D.[7], James Kocsis, M.D.[8], Susan Kornstein, M.D.[9], Charles Nemeroff, M.D., Ph.D.[10], Philip T. Ninan, M.D.[2], Anthony Rothschild, M.D.[11], Alan Schatzberg, M.D.[12], Richard Shelton, M.D.[13], Michael E. Thase, M.D.[5], Madhukar H. Trivedi, M.D.[14], John Zajecka, M.D.[15], Saeed Ahmed, M.D.[2], Jeff Musgnung, M.T.[2], Ron Pedersen, M.S.[2]; (1)Brown University, Providence, RI; (2)Wyeth Pharmaceuticals, Collegeville, PA; (3)University of Washington, Seattle, WA; (4)Radiant Research, Salt Lake City, UT; (5)University of Pittsburgh Medical Center, Pittsburgh, PA; (6)Univeristy of Arizona, Tucson, AZ; (7)University of Texas Medical Branch, Galveston, TX; (8)Weill Cornell Medical College, New York, NY; (9)Virginia Commonwealth University, Richmond, VA; (10)Emory University School of Medicine, Atlanta, GA; (11)University of Massachusetts Medical School, Worcester, MA; (12)Stanford University School of Medicine, Stanford, CA; (13)Vanderbilt University, Nashville, TN; (14)University of Texas Southwestern Medical School, Dallas, TX; (15)Rush University Medical Center, Chicago, IL.

Presented at the Annual Meeting of the American Psychiatric Association, Toronto, ON, Canada, May 20-25, 2006.

255E. Efficacy and safety of lisdexamfetamine dimesylate (LDX) in children aged 6–12 years with attention-deficit/hyperactivity disorder. *Michael Arora, Pharm.D.*[1], Joseph Biederman, M.D.[2], Suma Krishnan, M.S.[3], Robert L. Findling, M.D.[4]; (1)Shire Development Inc, Wayne, PA; (2)Clinical and Research Program in Pediatric Psychopharmacology, Massachusetts General Hospital, Harvard Medical School, Boston, MA; (3)New River Pharmaceuticals, Blacksburg, VA; (4)Department of Psychiatry, University Hospitals of Cleveland, Case Western Reserve University, Cleveland, OH.

Presented at the Annual Meeting of the American Psychiatric Association, Toronto, ON, Canada, May 20–25, 2006.

256. Pharmacotherapy use in mental health disorders in Lebanon. Elie G. Karam, M.D.[1], *Soumana A. Nasser, Pharm.D.*[2], Zeina N. Mneimneh, M.P.H.[1], Hani Dimassi, Ph.D.[3], Maya M. Helbaoui, Pharm.D.[2], John A. Fayyad, M.D.[1], Aimee N. Karam, Ph.D.[1]; (1)Institute for Development, Research, and Applied Care (I.D.R.A.C.), Balamand University Medical School, Beirut, Lebanon; (2)School of Pharmacy, Lebanese American University, Beirut, Lebanon; (3)American University of Beirut, Beirut, Lebanon.

PURPOSE: To assess the rate and type of pharmacotherapy use for mental health disorders in Lebanon as part of the L.E.B.A.N.O.N-WMH (Lebanese Evaluation of the Burden of Ailments and Needs Of the Nation - World Mental Health) study.
METHODS: This study is part of the WHO/WMH survey initiative conducted by IDRAC, between September 2002 and September 2003. Face-to-face interviews using the CIDI, version 3.0 were carried out on a national sample of 2856 Lebanese adults (age ≥ 18 years). Pharmacotherapy data is available on sub-sample of 1031 adults.
RESULTS: There were 94 respondents (5.1% ± 0.913(se)) receiving psychiatric drugs during the past 12 months: 25 respondents (1.1% ± 0.269%) were receiving antidepressants; 9 respondents (0.4% ± 0.123%) were on tricyclic antidepressants (TCAs), and 19 respondents (0.8% ± 0.240%) were on serotonin-selective-reuptake-inhibitors (SSRIs). There were 77 respondents (4.0% ± 0.740%) receiving anxiolytics, out of which 74 respondents (3.8% ± 0.716%) were on benzodiazepines. Five respondents (0.3% ± 0.095%) were using anti-psychotic agents. Among those who consulted either a health-care provider (n=55) or a non-health-care provider

(n=11) in the past 12 months, there were 40 respondents (61.54%) on any type of psychiatric drug; 19 (29.23%) were on antidepressants out of which 16 (24.62%) were on SSRIs, and 30 respondents (46.15%) on anxiolytics out of which 29 (44.62%) were on benzodiazepines.
CONCLUSIONS: Benzodiazepines and the SSRIs were the most commonly used agents, and the majority of respondents who are consulting a professional take medication. This study highlights the need toward improving the management of mental health disorders and implementing treatment policy in this field in Lebanon.

257. Zolpidem extended-release 12.5-mg, evaluated for 6 months in adult patients with primary insomnia, displays efficacy in multiple patient-reported sleep measurements. Milton Erman, M.D.[1], Andrew Krystal, M.D.[2], *Gary Zammit, Ph.D.*[3], Christina Soubrane, M.D.[4], Thomas Roth, Ph.D.[5]; (1)Pacific Sleep Medicine Services, San Diego, CA; (2)Duke University Hospital, Trent Drive, Durham, NC; (3)Clinilabs, Inc., New York, NY; (4)Sanofi-aventis Clinical Development, Chilly-Mazarin, France; (5)Henry Ford Hospital Sleep Disorders Center, Detroit, MI.

PURPOSE: To investigate the long-term efficacy and safety of zolpidem extended-release (Zolpidem CR) in the treatment of insomnia (sleep onset and maintenance difficulties) and impact on next-day functioning.
METHODS: Multicenter, double-blind, placebo-controlled study of zolpidem CR 12.5-mg, taken "as needed" 3–7 nights/week for 24 weeks, in adults with chronic primary insomnia (age 18–64 years, N=1025 randomized). Efficacy was measured every 4th week by Patient Global Impression (PGI) and Clinical Global Impression (CGI) scales, and by daily morning questionnaires assessing sleep parameters, next-day concentration, and morning sleepiness.
RESULTS: 1018 patients treated (395 male (38.8%), median age 47.0). Randomized patients: 436/674 (64.7%) zolpidem CR and 184/351 (52.4%) placebo patients completed the 6-month treatment period. PGI scores were superior for zolpidem CR versus placebo (P<.0001, all time points); a greater percentage of patients reported a treatment benefit to sleep with zolpidem CR compared with placebo at all time points (at week 24: 92.3% vs 59.7%). CGI scores were significantly improved with zolpidem CR versus placebo (p<0.0001, all time points). Baseline-adjusted analysis of daily questionnaires data demonstrated that zolpidem CR 12.5-mg treatment significantly improved sleep versus placebo (p<0.002) throughout the study (Months 1–6: sleep onset latency, wake time after sleep onset, total sleep time, and quality of sleep; Months 2–6; number of awakenings). No evidence of tolerance based on stable zolpidem tablet intake (mean treatment days per month across months: range 18.9–20.1). Baseline-adjusted analysis of next-day functioning demonstrated that zolpidem CR significantly improved the ability to concentrate (p<0.0014, each month), and significantly decreased ratings of morning sleepiness (p<0.0001, each month). Zolpidem CR was well tolerated. Most frequent AEs: zolpidem CR/placebo: headache (10.5%/9.5%), anxiety (6.3%/2.6%), somnolence (5.7%/2.0%).
CONCLUSIONS: Zolpidem extended-release 12.5-mg, taken up to 7 nights/week for 6 months, demonstrated sustained improvements in sleep onset, sleep maintenance, and next-day functioning, with no evidence of tolerance.

258. 6-Month evaluation of zolpidem extended-release 12.5 mg in adult patients with primary insomnia: improvements in next-day functioning with no observed tolerance and no rebound insomnia. *Gary Zammit, Ph.D.*[1], Milton Erman, M.D.[2], Andrew Krystal, M.D.[3], Christina Soubrane, M.D.[4], Thomas Roth, Ph.D.[5]; (1)Clinilabs, Inc., New York, NY; (2)Pacific Sleep Medicine Services, San Diego, CA; (3)Duke University Hospital, Trent Drive, Durham, NC; (4)Sanofi-aventis Clinical Development, Chilly-Mazarin, France; (5)Henry Ford Hospital Sleep Disorders Center, Detroit, MI.

PURPOSE: To evaluate the impact on next-day functioning of long-term zolpidem extended-release (Zolpidem CR) use in adult patients with primary insomnia.
METHODS: Multicenter, double-blind, placebo-controlled study in adult patients with chronic primary insomnia (age 18–64 years, n=1025 randomized). Zolpidem CR 12.5 mg or placebo taken "as needed" 3–7 nights/week for 24 weeks followed by a 1-week discontinuation period. Safety was evaluated by daily morning questionnaires examining drug-taking behavior, ability to concentrate, and sleepiness in the morning. Rebound insomnia was measured over the first 3 nights of the discontinuation period.
RESULTS: 1018 patients were treated (395 [38.8%] male, median age 47.0), with 436/674 of randomized zolpidem CR and 184/351 placebo patients completing 6-months of treatment. Most common reasons for study discontinuation for zolpidem CR and placebo groups were lack of efficacy/disease progression (4.7% and 23.4%), subject's request (9.5% and 6.0%), and lost to follow-up (7.4% and 7.7%). Tablet intake by patients in the zolpidem CR 12.5-mg group remained stable, indicating a lack of tolerance. Mean treatment days/month ranged from 18.9 to 20.1 during the 6-month treatment period (placebo range: 16.5–17.9). Baseline-adjusted analysis of daytime functioning demonstrated that zolpidem CR 12.5 mg significantly improved patient-reported ability to concentrate, compared with placebo (p<0.0014, for each month). Zolpidem CR 12.5 mg also significantly decreased patient-reported sleepiness in the morning, compared with placebo (p<0.0001, for each month). Following treatment discontinuation at study end, no rebound insomnia occurred based upon analysis of total sleep time and wake time after sleep onset (sleep onset latency not measured). The most frequently occurring AEs in the zolpidem CR 12.5 mg and placebo groups were headache (10.5% and 9.5%), anxiety (6.3% and 2.6%), and somnolence (5.7% and 2.0%).
CONCLUSIONS: 6 months of treatment with zolpidem extended-release 12.5 mg demonstrated sustained improvements in patient-reported next-day functioning without evidence of tolerance during treatment or rebound insomnia following discontinuation.

259. Aripiprazole prescribing patterns and side effects in elderly psychiatric inpatients. *Tina M. Scipio, Pharm.D.*[1], Kim Coley, Pharm.D.[1], Tanya J. Fabian, Pharm.D., Ph.D.[2], Eric J. Lenze, M.D.[3]; (1)University of Pittsburgh School of Pharmacy, Pittsburgh, PA; (2)Western Psychiatric Institute and Clinic, Pittsburgh, PA; (3)University of Pittsburgh School of Medicine, Pittsburgh, PA.

PURPOSE: Aripiprazole use in elderly persons is increasing, yet there are new concerns about atypical antipsychotics in this age group. Because no data are available on aripiprazole in the inpatient setting, we set out to describe its use and adverse effects in elderly psychiatric inpatients.
METHODS: All elderly inpatients prescribed aripiprazole between 1/1/2003 and 12/31/2005 at a psychiatric hospital were identified from an electronic medical records data repository. Patient records were reviewed retrospec-tively for diagnoses, dosing, side effects, and reason for drug discontinuation.
RESULTS: There were 55 elderly inpatients who were treated with aripiprazole: the mean age was 73 years, 75% were female, and 95% were Caucasian. Eighteen patients (33%) were receiving aripiprazole on admission and 67% received treatment with other atypical antipsychotics prior to aripiprazole. The average maximum dose of aripiprazole prescribed was 13.4 ± 7.0 mg (range 2.5–30 mg). Twenty-four (44%) of the patients had dementia, usually due to Alzheimer's Disease and the mean dose in these patients was 12.5 mg. Those with schizophrenia or schizoaffective disorder (18/55, 33%) received a mean dose of 16.1mg. Treatment with aripiprazole was continued at discharge in 53% of the patients. Of the 26 patients where aripiprazole was discontinued, adverse effects were the most common (23%) reason. Overall, adverse effects were reported in 11 (20%) patients, with increased activation/agitation recorded most often (4 of 55, 7%). Most adverse effects occurred at doses between 10 mg and 15 mg, and no adverse effects were reported with doses over 25 mg. Logistic regression demonstrated that males (OR=9.5) and patients with schizophrenia (OR=10.7) were more likely to experience side effects.
CONCLUSIONS: In this evaluation of aripiprazole in elderly psychiatric inpatients, the treatment continuation rate was 53%. Adverse effects were the most common reason for drug discontinuation, and were more common in male patients and those with schizophrenia. Increased activation/agitation was reported most frequently.

260. An open-label assessment of aripiprazole in the treatment of PTSD. *Sophie Robert, Pharm.D.*[1], Mark B. Hamner, M.D.[1], Valerie L. Durkalski, Ph.D., M.P.H.[2], Helen Ulmer, R.N.[1], Jeffrey P. Lorberbaum, M.D.[1], Mary W. Brown, R.N.[1]; (1)Ralph H. Johnson VAMC/Medical University of South Carolina, Charleston, SC; (2)Medical University of South Carolina, Charleston, SC.

PURPOSE: Antidepressants are considered first-line medication treatment for posttraumatic stress disorder (PTSD), yet they provide minimal or partial benefits to many patients. Recent studies suggest that atypical antipsychotics are effective augmentation strategies. Limited data were available on the newest agent, aripiprazole, so we aimed to evaluate its efficacy and tolerability in the treatment of PTSD.
METHODS: A 12-week, prospective, open-label, flexible-dose, adjunctive trial of aripiprazole was conducted in combat veterans meeting DSM-IV criteria for PTSD. Concomitant psychiatric medications continued unchanged, except for other neuroleptics, which were not allowed. The primary outcome variable was the Clinician Administered PTSD scale (CAPS). Secondary efficacy measures included several other rating scales as well as a battery of attention and memory tests.
RESULTS: Seventeen of 20 patients had at least one post-baseline efficacy evaluation and thus were included in the efficacy analysis. All subjects were male, with an average age of 57 years. Total CAPS scores decreased from 78.2 (SD=17.8) at baseline to 60.0 (23.5) at study end (p=0.002). Reexperiencing (CAPS-B) and avoidance/numbing symptoms (CAPS-C) were significantly improved, and trend level reductions were observed in hyperarousal symptoms (CAPS-D). Fifty-three percent (9/17) were considered responders, as defined by a decrease in total CAPS scores of at least 20%. Reductions in total score and subscale scores on the Positive and Negative Symptom Scale (PANSS) were all statistically significant. Other secondary measures showed

non-significant or trend level improvement. The final average dose of aripiprazole was 13.06 (SD=6.45) mg daily. Seven patients discontinued because of adverse effects. The most common adverse events consisted of gastro-intestinal disturbances, restlessness, and sedation. Tolerability was improved with lower starting doses (e.g., 5 mg daily) and slow titration.
CONCLUSIONS: Addition of aripiprazole to ongoing treatment further reduced PTSD symptoms in combat veterans with chronic, severe PTSD. These preliminary findings await confirmation in randomized, controlled trials.

261E. Self-reported efficacy of 8 mg ramelteon in elderly chronic insomnia patients with severe sleep-initiation difficulty. *Louis Mini, M.D.*[1], Sherry Wang-Weigand, M.D., Ph.D.[2], Jeffrey Zhang, M.S.[2], Kathy Kasten, M.S.[2]; (1)Takeda Pharmaceuticals North America, Inc., Lincolnshire, IL; (2)Takeda Global Research & Development Center, Lincolnshire, IL.

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262. Antipsychotic use in a pediatric inpatient population. *Jessica L. Gören, Pharm.D.*; University of RI, Cambridge Health Alliance, Harvard University, Somerville, MA.

PURPOSE: Use of antipsychotic medications in pediatric populations is increasing despite limited evidence demonstrating their safety or efficacy in this population. Although use of antipsychotic polypharmacy is increasing in adults, it is unknown how common this practice is in the pediatric inpatient psychiatric population. The aim of this study was to evaluate current antipsychotic prescribing patterns on a pediatric inpatient psychiatric unit.
METHODS: Data were drawn for all patients prescribed an antipsychotic medication and admitted to the child psychiatric unit between August 2005 and October 2005. Age, gender, diagnoses, length of stay, current antipsychotic medications and doses, and concomitant medications were recorded. Data were tabulated and analyzed to describe antipsychotic prescribing patterns.
RESULTS: From August 2005 until October 2005, 35 pediatric patients were admitted to the inpatient psychiatric unit. Twenty-four (68%) were prescribed antipsychotic medications. In patients prescribed antipsychotic medications the mean age was 9.8 years (range 7–13). The most frequent psychiatric diagnoses were bipolar disorders and attention-deficit/hyperactivity disorder. Boys were more likely to receive antipsychotic medication than girls (18 boys vs. 6 girls). The average length of stay was 19.8 days (range 1–63 days). Patients received an average of 4 medications. No patient received only one medication. 37.5% (9/24) of patients received two or more concomitant antipsychotic medications (PRN and scheduled), and 30% (7/24) received two concomitantly scheduled antipsychotic medications. The most commonly prescribed antipsychotic medications were risperidone and quetiapine. Antidepressants and α_2-agonists were the most commonly co-prescribed medication classes. Six patients were prescribed medications for the treatment of adverse effects commonly observed with antipsychotic medications. Two patients were treated for diabetes.
CONCLUSIONS: Antipsychotics are frequently prescribed for nonpsychotic conditions in the pediatric inpatient population despite limited evidence to support the safety or efficacy of this practice. Co-prescribing represents a substantial proportion of prescribing practice.

Pulmonary

263. Improvement in lung function in patients with moderate-severe persistent allergic asthma treated with omalizumab. *Marc Massanari, M.D.*; Novartis Pharmaceuticals Corporation, East Hanover, NJ.

PURPOSE: A significant percentage of patients with moderate-severe persistent asthma do not achieve guideline defined asthma control despite treatment with combination therapy with inhaled corticosteroids (ICS) and long-acting beta-agonists (LABAs). (Bateman, 2004). Omalizumab (OMA) binds serum IgE and reduces asthma exacerbations when added to ICS and ICS/LABAs. We examined the effect of adding OMA on lung function in patients with moderate-severe persistent allergic asthma inadequately controlled with ICS/LABAs.
METHODS: INNOVATE was a 28-week double-blind, randomized, placebo (PBO)-controlled trial that evaluated OMA in pts taking high-dose ICS (> 1000 µg beclomethasone equivalent) and LABAs. The efficacy assessments included change from baseline in FEV_1 and characterization according to investigator global evaluations of treatment effectiveness (IGETE), a 5-point scale with 1 denoting complete asthma control and 5 denoting worsening. Change in FEV_1 was analyzed using analysis of covariance. IGETE were analyzed using the Cochran-Mantel-Haenszel test, for the distribution of responses categorized as excellent/good, moderate and poor/worse.
RESULTS: A total of 419 pts were randomized, 209 to OMA and 210 to PBO. Mean duration of allergic asthma was 23 years. Baseline FEV_1 was 60%–80% of predicted in 49% and <60% of predicted in 44% of pts. Overall, mean FEV_1 improved by 196 mLs vs. 89 mls compared with baseline, OMA vs PBO respectively, p=0.012. Improvements in IGETE were observed in OMA vs. PBO (p=0.001). In OMA pts for whom IGETE was rated as excellent-good, mean FEV_1 increased 256 mLs compared with 90 mLs in pts with IGETE rated as no change or worse.
CONCLUSIONS: Addition of OMA significantly improved FEV_1 and was rated significantly more effective than placebo in moderate-severe persistent allergic asthmatics inadequately controlled with ICS/LABA combination therapy.

264. Addition of omalizumab improves lung function and treatment effectiveness in patients with moderate-severe persistent allergic asthma inadequately controlled with inhaled steroids and long-acting beta agonists. *Marc Massanari, Pharm.D.*, Robert J. Maykut, M.D., Robert K. Zeldin, M.D., Farid Kianifard, Ph.D., Gregory P. Geba, M.D.; Novartis Pharmaceuticals Corporation, East Hanover, NJ.

PURPOSE: A significant percentage of patients with moderate-severe persistent asthma do not achieve guideline-defined asthma control despite treatment with inhaled corticosteroids (ICS) and long-acting beta-agonists (LABAs) (Bateman, 2004). Omalizumab (OMA) binds serum IgE and reduces asthma exacerbations when added to ICS and ICS/LABAs. We examined the effect of adding OMA on lung function in patients with moderate-severe persistent allergic asthma inadequately controlled with ICS/LABAs.
METHODS: INNOVATE was a 28-week, double-blind, randomized, placebo (PBO)-controlled trial that evaluated OMA in patients taking high-dose ICS (> 1000 µg beclomethasone equivalent) and LABAs. The efficacy assessments included change from baseline in FEV_1 and investigator global evaluations of treatment effectiveness (IGETE), a 5-point scale ranging from excellent (complete control) to worse (worsening in control). Change in FEV_1 was analyzed using analysis of covariance. Responder (IGETE rated excellent/good) vs. non-responder (IGETE rated moderate/poor/worse) rate was analyzed using the Chi-squared test. The Spearman correlation coefficient was computed to examine the association between change from baseline in FEV_1 and IGETE.
RESULTS: A total of 419 patients were randomized; 209 to OMA and 210 to PBO. Mean duration of allergic asthma was 23 years. Baseline FEV_1 was 60%–80% predicted in 49% and < 60% predicted in 44% of patients. Overall, mean FEV_1 improved 134 mL vs. 17 mL compared with baseline (least squares means), OMA vs. PBO respectively, p=0.012. Sixty-one percent (61%) of OMA patients compared with 43% of PBO patients (p<0.001) were responders. In OMA responders, mean FEV_1 increased 256 mL compared with 90 mL in OMA non-responders. Improvement in FEV_1 was associated with better IGETE (Spearman correlation coefficient = -0.21, p<0.001).
CONCLUSIONS: Addition of OMA significantly improved FEV_1 and was rated significantly more effective than placebo in moderate-severe persistent allergic asthmatics inadequately controlled with ICS/LABA combination therapy.

265E. Efficacy of tiotropium inhalation powder in COPD patients of African descent. *Julie Kenkel, Pharm.D.*[1], Gerard J. Criner, M.D.[2], Cara Cassino, M.D.[1], Philip A. Johnson, M.S.[1], Craig S. Conoscenti, M.D.[1]; (1)Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT; (2)Temple University Hospital, Philadelphia, PA.

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266. Hospitalization and emergency room visit rates in asthma and chronic obstructive pulmonary disease patients taking beta-blockers. *Tyson WA Brooks, Pharm.D.*[1], Freddy M. Creekmore, Pharm.D.[2], David C. Young, Pharm.D.[2], Carl V. Asche, Ph.D.[3], Brian Oberg, M.B.A.[3], Wayne M. Samuelson, M.D.[1]; (1)University of Utah Hospitals & Clinics, Salt Lake City, UT; (2)University of Utah College of Pharmacy, Salt Lake City, UT; (3)University of Utah Pharmaceutical Outcomes Research Center, Salt Lake City, UT.

PURPOSE: To determine the incidence of hospitalizations and emergency room (ER) visits during cardioselective and nonselective beta blocker (BB) use in patients with asthma or chronic obstructive pulmonary disease.
METHODS: Design is an observational cohort design. Data Source is General Electric Logician's Electronic Medical Records Database. A total of 11,592 adult patients with asthma and/or COPD identified between August 1, 1997, and December 31, 2005, were included. 3062 were taking a cardioselective BB, 690 were taking a nonselective BB, and 7840 control patients were not taking a BB.
RESULTS: The primary end point for each BB group was the incidence rate of hospitalizations and ER visits per patient year of beta blocker use relative to the control group. In asthma patients, cardioselective BB use was associated with RR=1.40 (p<0.001) and RR=1.34 (p<0.001) for ER visits and total visits respectively. Nonselective BB use was associated with a RR=2.47 (p=0.009)

and RR=1.34 (p=0.032) for hospitalizations and total visits compared with controls. In COPD patients, cardioselective BB use was associated with a RR=0.64 (p=0.026) and RR=1.19 (p=0.033) for hospitalizations and ER visits respectively. Nonselective BB use was associated with a RR=0.51 (p=0.002) and RR=0.61 (p=0.006) for ER visits and total visits.
CONCLUSIONS: Until further long-term data are published regarding BB use specifically in patients with asthma, both cardioselective and nonselective BB should be avoided as both classes increase healthcare visits compared with controls. For patients with COPD, a cardioselective BB may be considered after weighing the risk of pulmonary exacerbation versus cardiovascular benefit on an individual basis. No strong conclusions can be made about nonselective BB use for COPD patients because of significant differences in baseline demographics between the nonselective BB and control groups.

Rheumatology

267E. Febuxostat vs. allopurinol and placebo in subjects with hyperuricemia and gout: the 28-Week APEX Study. *Patricia A. MacDonald, N.P.*[1], H. Ralph Schumacher Jr., M.D.[2], Michael A. Becker, M.D.[3], Robert L. Wortmann, M.D.[4], Barbara J Hunt, M.S.[1], Janet K Streit, M.S.[1], Christopher Lademacher, M.D.[1], Nancy Joseph-Ridge, M.D.[1]; (1)TAP Pharmaceutical Products Inc., Lake Forest, IL; (2)University of Pennsylvania School of Medicine, Veterans Affairs Medical Center, Philadelphia, PA; (3)University of Chicago, Pritzker School of Medicine, Chicago, IL; (4)University of Oklahoma, Dept of Internal Medicine, Tulsa, OK.

Presented at the Annual Scientific Meeting of the American College of Rheumatology, San Diego, CA, November 12-16, 2006.

Substance Abuse/Toxicology

268. Medication errors in children reported to a regional poison control center. Sasko D. Stojanovski, Pharm.D.[1], S. David Baker, Pharm.D.[2], Renee F. Robinson, Pharm.D.[3], Marcel J. Casavant, M.D.[4], John R. Hayes, Ph.D.[5], *Milap C. Nahata, Pharm.D., FCCP*[6]; (1)The Ohio State University College of Pharmacy, Children's Research Institute, Columbus, OH; (2)Central Ohio Poison Center, Columbus, OH; (3)The Ohio State University College of Medicine, Children's Hospital, Department of Pediatrics, Children's Research Institute, Columbus, OH; (4)The Ohio State University College of Medicine, Children's Hospital, Department of Pediatrics, Central Ohio Posion Center, Columbus, OH; (5)Children's Research Institute, Columbus, OH; (6)The Ohio State University Colleges of Pharmacy and Medicine, Children's Research Institute, Columbus, OH.

PURPOSE: Medication errors (MEs) in the pediatric population remain a significant problem. Calculation and measurement of doses, improper drug administration, and lack of understanding by caregiver may result in fatal errors.
METHODS: A retrospective study was conducted on all unintentional MEs in children ≤ 12 years of age referred to a regional poison control center from January 2000 to December 2005. The data, including demographics, drugs, symptoms, time of call, and reported outcomes, were obtained. A relationship between age and drug ingested, and age versus category of ME, was assessed. Data were analyzed using Chi-square test. A $p<0.05$ indicated statistical significance.
RESULTS: A total of 10,704 patient referrals were reviewed. The leading drug categories for MEs were cough and cold products (CCP) (29%), analgesic (18%), and antihistamines (12%). The relationship between age and drug ingestion was significant ($p<0.0001$). Children ≤ 23 months of age had greater amount of MEs with analgesics, gastrointestinal, and antimicrobial agents compared with other age groups. MEs with CCP and vitamins occurred more often in children ages 2–5 years. MEs with stimulants, cardiovascular, antipsychotic and antidepressant agents occurred more often in children 6–12 years. The relationship between age and category of ME was significant for all age groups ($p<0.0001$). Different types of MEs were identified for various age groups: 10-fold dosing errors and incorrectly measured dose was noted in ≤ 23 months of age; inadvertently administered, repeated dosing by different caregivers, and wrong medication given occurred more frequently among 6–12 years. As a result, 41% of children were symptomatic and two deaths occurred.
CONCLUSIONS: A relationship was identified between age and drug category, and age and category of ME. Dose calculation errors and overdosing of medications were identified frequently. Proper usage of medications among children needs to be emphasized to prevent potential harm.

Transplant/Immunology

269. Testing limited sampling strategies developed in lung transplant recipients for mycophenolic acid area under the curve in heart transplant recipients. *Lillian S. L. Ting, B.Sc., M.Sc.(Pharm), Ph.D.., student*[1], Nilufar Partovi, B.Sc.(Pharm), Pharm.D.[2], Robert D. Levy, M.D., FRCPC[3], K. Wayne Riggs, B.Sc.(Pharm), Ph.D.[4], Mary H. H. Ensom, B.S.(Pharm), Pharm.D., FCCP[5]; (1)University of British Columbia, Vancouver, BC; (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, Vancouver, BC, Canada; (5)University of British Columbia and Children's & Women's Health Centre of British Columbia, Vancouver, BC, Canada.

PURPOSE: To test the predictive performance of mycophenolic acid (MPA) optimal limited sampling strategies (LSSs) previously developed in lung transplant recipients when applied to heart transplant recipients.
METHODS: In our previous study involving lung transplant recipients, optimal MPA LSSs were developed via multiple regression analysis with forward stepwise elimination (Statistica® 5.1). The best LSSs were: Equation 1: LogAUC=0.241 LogC0+0.406 LogC2+1.140. Equation 2: LogAUC=0.202 LogC0+0.411 LogC1.5+1.09. Equation 3: LogAUC=0.153 LogC0+0.327 LogC0.6+0.354 LogC2+1.000. Equation 4: LogAUC=0.131 LogC0+0.320 LogC0.6+0.333 LogC1.5+0.974. 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 heart 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). The heart transplant group data were used to test the predictive performance (bias and precision) of LSSs (equations 1–4) developed from the lung transplant group.
RESULTS: The predictive performance of LSS equations 1–4 when applied to heart transplant recipients were: Equation 1: bias= -7.44%; precision= 11.78%; 11/19 (58%) profiles within±15% bias and precision. Equation 2: bias= -9.28%; precision= 11.46%; 16/19 (84%) profiles within±15% bias and precision. Equation 3: bias= -7.78%; precision= 10.66%; 15/19 (79%) profiles within±15% bias and precision. Equation 4: bias= -9.35%; precision= 11.93%; 15/19 (58%) profiles within±15% bias and precision.
CONCLUSIONS: Although these LSSs are developed in lung transplant recipients, application to the heart transplant population for prediction of MPA AUC is feasible with satisfactory predictive performance. To our knowledge, currently there are no published validated LSSs for MPA specifically for heart transplant recipients. Our study template provides a guide for other centers to develop and test accurate and precise LSSs specific to their own patient population.

270. Pharmacokinetic predictors of adverse effects during mycophenolate mofetil therapy in thoracic transplant recipients. *Lillian S. L. Ting, B.Sc., M.Sc.(Pharm), Ph.D.-student*[1], Melissa Fritz, B.Sc.(MedChem), B.Sc.(Pharm)-student[1], Stephanie Tsang, B.Sc.(Pharm)[1], Sarah Pang, B.Sc..(Pharm)-student[1], Nilufar Partovi, B.Sc.(Pharm), Pharm.D.[2], Robert D. Levy, MD, FRCPC[3], Mary H. H. Ensom, B.S.(Pharm), Pharm.D., FCCP[4]; (1)University of British Columbia, Vancouver, BC; (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 adverse effects during mycophenolate mofetil (MMF) therapy in thoracic (heart or lung) transplant recipients.
METHODS: Following informed consent, pharmacokinetic parameters of mycophenolic acid (MPA) and its glucuronidated metabolites [MPAG (inactive) and AcMPAG (pro-inflammatory activity in vitro)] were determined via HPLC with UV detection from serial blood samples of 19 heart and 21 lung transplant recipients on steady-state MMF therapy. Pharmacokinetic parameters [MPA area-under-the-curve (AUC), MPA maximum concentration (Cmax), MPA minimal concentration (Cmin), MPAG AUC, AcMPAG AUC, MPAG/MPA AUC metabolic ratio, and AcMPAG/MPA metabolic ratio] were calculated using WinNonlin 4.1. Patients' medical charts were reviewed for occurrences of rejection and adverse effects. Events occurring between date of last immunosuppressant medication (MMF and cyclosporine, tacrolimus or sirolimus) change and pharmacokinetic sampling day were considered for statistical analyses (Chi-squared test).
RESULTS: Patients included: 27 males/13 females, mean (± SD) 4.7 ± 3.7 years post transplant, 53.9 ± 14.8 years old and 74.7 ± 16.0 kg bodyweight. Significant results ($p\leq0.05$): 1) AcMPAG AUC (> 50 vs. < 50 μg•h/mL) and infections (yes vs. no); 2) AcMPAG/MPA AUC ratio (> 4 vs. < 4) and gastrointestinal toxicities (yes vs. no). Trends ($p\leq0.2$): 1) MPA AUC (> 40 vs. < 40 μg•h/mL) and infections (yes vs. no); 2) AcMPAG AUC (> 50 vs. < 50 μg*h/mL) and gastrointestinal toxicities (yes vs. no); 3) AcMPAG AUC (> 27 vs. < 27 μg•h/mL) and anemia (yes vs. no); 4) AcMPAG/MPA AUC ratio (>0.8 vs. <0.8) and anemia (yes vs. no).
CONCLUSIONS: AcMPAG AUC and AcMPAG/MPA AUC ratio appear to be

the best predictors of clinical safety end points for thoracic transplant recipients on MMF therapy. This study is the first to demonstrate that AcMPAG's activity (observed only in vitro to date) may translate into important clinical events for thoracic transplant recipients. In the future, these AcMPAG pharmacokinetic parameters may be useful in individualizing MMF therapy.

271. Does avoiding steroids after renal transplantation improve cardiovascular risk profiles? *Karen L. Hardinger, Pharm.D.*[1], Terry Bloomer, RN[2], Liz Faldtz, R.N.[2], Jeffrey Reese, M.D.[2], Daniel Murillo, M.D.[2]; (1)UMKC School of Pharmacy, Kansas City, MO; (2)Transplant Institute at Research Medical Center, Kansas City, MO.

PURPOSE: Early corticosteroid withdrawal is becoming more commonplace in transplantation, with the minimization of cardiovascular side effects as the desired goal. The purpose of this study was to assess the cardiovascular risk profile of transplant recipients who received steroid withdrawal (at 5 days after transplant) versus chronic steroids.
METHODS: This single-center, observational trial monitored adult renal transplants between 1/04 and 12/05 who received thymoglobulin, mycophenolic acid, tacrolimus, and either withdrawal of (W, n=30) or chronic (C, n=67) steroids. Serum glucose, lipid profile, blood pressure (BP), medications, and weight were monitored for up to 12 months. Published guidelines recommend fasting glucose < 126 mg/dL, LDL < 100 mg/dL, and BP < 130/85.
RESULTS: The mean age (51 ± 12), cause of renal disease (DM= 40%), gender, DR match, donor age, delayed graft function (10%), acute rejection episodes (15%) and graft loss were similar. Three cases of PTDM occurred, but most (~2/3) met glucose goals. Cholesterol treatment was similar and most LDL targets were achieved (W 77% vs C 63%) at 2 months post-transplant. BPs were similar and there was a trend toward less post-transplant medication requirement in the W group (W 1.3 ± 1.0 vs C 1.7 ± 1.2 meds, p=0.08). Most patients did not meet BP goals at baseline (W 67% vs C 79%, p=NS), while both arms improved at 3 months (W 54% vs C 59% attained goals). The C group was heavier at pre-transplant (W 89 ± 20 vs C 83 ± 19 kg, p=0.06), while post-transplant weight gain (W 4 ± 11 vs C 7 ± 9 kg, p=NS) was similar.
CONCLUSIONS: When compared with patients on chronic steroids, a statistical improvement in cardiovascular profiles was not seen in steroid withdrawal patients although this was not at the expense of acute rejection or graft loss. Additional follow-up is needed to determine the long-term cardiovascular effects in patients with early steroid withdrawal.

272E. Abbreviated intravenous ganciclovir for cytomegalovirus prophylaxis in intermediate-risk liver transplant recipients. *Nancy E. Williams, Pharm.D.*[1], Derrick R VanBeuge, Pharm.D.[1], William L. Musick, Pharm.D.[1], Christine O'Mahony, M.D.[2], John Goss, M.D.[2]; (1)The Methodist Hospital, Houston, TX; (2)Baylor College of Medicine, Houston, TX.

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273. Biliary tract infections in liver transplant recipients. *Erin M. Megerle, Pharm.D.*, Shiv K. Seth, Ph.D, R.Ph.; The Ohio State University Medical Center, Columbus, OH.

PURPOSE: Determine the predominant organisms in bile fluid cultures of liver transplant recipients at The Ohio State University Medical Center and determine the use and effectiveness of antibiotics administered for treating biliary tract infections.
METHODS: Liver transplant recipients were reviewed retrospectively from January 2003 to January 2006. Inclusion criteria were positive bile fluid cultures and receipt of antibiotics during hospital admission. Exclusion criteria were pregnancy and age less than 18 or greater than 89 years. Data collected included demographics, bile fluid culture results, empiric and treatment antibiotic use, treatment duration, biliary infection etiology, and recurrence rate of infection. Recurrence rate is defined as repeat growth of the same organism(s) in bile fluid cultures after achieving no growth. The outcomes evaluated included predominant organisms in bile fluid cultures, empiric and treatment antibiotic utilization, and recurrence rate.
RESULTS: Sixty-six bile fluid culture results from 23 liver transplant recipients were evaluated. The mean age was 50.5 years. Biliary stricture was the etiology of infection in 52.2% of patients. Bile fluid cultures achieved no growth in 2 patients, neither of which had recurrence of infection. Thus, the recurrence rate was zero. Ninety-five percent of cultures were polymicrobial. Empiric therapy was tailored correctly in 68.2% of cases.

Predominant organisms present in bile culture (n=66)

Organism	Percentage
Enterococcus faecalis	53.0
Candida glabrata	33.3
Candida albicans	31.8
Vancomycin-resistant *E. faecium*	21.2
Pseudomonas aeruginosa	16.7
Klebsiella pneumonia	16.7
Escherichia coli	15.2

Antibiotic utilization (n=66)

Antibiotic spectrum	Empiric use (%)	Treatment use (%)
Gram-positive	33.3	40.9
Gram-negative	51.5	39.4
Broad spectrum	80.3	47.0
Antifungal	33.3	40.9
Anaerobic	6.1	1.5

CONCLUSIONS: Biliary infections in liver transplant patients are predominantly polymicrobial and virtually untreatable. Selecting appropriate antimicrobial therapy is important in preventing morbidity and mortality; however, further research is needed to identify effective drug therapy in treating biliary infections.

274. HMG-CoA reductase inhibitors in thoracic organ transplantation: a meta-analysis. *Rebecca Moon, Pharm.D.*[1], Paul E. Nolan, Pharm.D.[1], Marion K. Slack, Ph.D.[1], Kimberly L. Gandy, M.D.[2]; (1)University of Arizona College of Pharmacy, Department of Pharmacy Practice and Science, Tucson, AZ; (2)University of Arizona College of Medicine, Section of Cardiothoracic Surgery, Tucson, AZ.

PURPOSE: The purpose of this study was to use Meta-analysis to evaluate the efficacy of hydroxymethylglutaryl coenzyme A (HMG-CoA) reductase inhibitors (statins) in reducing all-cause mortality and death due to rejection when administered to thoracic organ transplant patients.
METHODS: Using the following Medical Subject Heading (MeSH) terms and text words: hydroxymethylglutaryl coenzyme A (HMG-CoA) reductase inhibitors, statins, heart transplantation, and lung transplantation, the following data bases were searched: Cochrane Central Register of Controlled Trials (First Quarter 2006), Cochrane Database of Systematic Reviews (First Quarter 2006), Database of Abstracts and Reviews of Effects (First Quarter 2006), ACP Journal Club (1991 to January/February 2006), International Pharmaceutical Abstracts (1970 to February 2006), and Medline (1966 to February 2006) for English language reports. Three prospective randomized controlled trials (RCTs) and 3 retrospective observational studies were identified as using statins to reduce mortality and death due to fatal rejection in thoracic organ transplant patients. Pooled odds ratios and 95% confidence intervals were calculated and forest plots constructed.
RESULTS: Using all 6 studies (n=1770 patients), statins significantly decreased mortality by 77% (OR=0.23; [95% confidence interval 0.16-0.34] Z-test, p<0.001). Sub-analysis using only RCT heart transplant data showed that statins significantly decreased mortality by 69% (OR=0.31; [95% confidence interval 0.09–1.07] Z-test, p<0.003). Sub-analysis using retrospective heart transplant data showed that statins significantly decreased mortality by 75% (OR=0.25; [95% confidence interval 0.16–0.39] Z-test, p<0.001). Retrospective lung transplant results (1 study) showed statins significantly decreased mortality by 90% (OR=0.10; [95% confidence interval 0.03-0.34] Z-test, p<0.001). In addition, when using all 6 studies, statins significantly decreased death due to rejection by 78% (OR=0.22; [95% confidence interval 0.13–0.37] Z-test, p<0.001).
CONCLUSIONS: In patients undergoing thoracic organ transplantation, statins significantly decrease all-cause mortality and death due to rejection. Therefore, statins should be routinely administered to these patients following transplant surgery.

275E. Highly variable mycophenolate mofetil bioavailabiltiy following nonmyeloablative hematopoietic cell transplantation (HCT). *Pamala A. Jacobson, Pharm.D*[1], Kathleen Green, Pharm.D.[1], John Rogosheske, Pharm.D.[2], Breta Ebeling, B.S. R.N.[1]; (1)Experimental and Clinical Pharmacology, College of Pharmacy, University of Minnesota, Minneapolis, MN; (2)University of Minnesota Fairview Hospital, Minneapolis, MN.

Presented at the Annual Meeting of the American Society of Hematology, Atlanta, GA, December 13, 2005.

276. Lung transplant patients' T-cell responses to influenza vaccine viruses between seasons. *Mary S. Hayney, Pharm.D.*, John Moran, BS, Nicholas A. Wiegert, B.S.; 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. Antibody responses to influenza vaccine viruses have been shown to be lower in lung transplant patients. In spite of this, we hypothesized that T-cell responses to influenza viruses by lung transplant and healthy individuals would be similar.
METHODS: Twelve lung transplant patients and 12 healthy individuals

received the 2004-05 and the 2005-06 influenza vaccines. Peripheral blood mononuclear cells (PBMC) were isolated for the trans-vivo 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 a 20 x 10-4 inches difference.
RESULTS: T-cell responses to all three influenza antigens from each season in a single injection were similar between the lung transplant and healthy groups (2004-05: 30.8+5.6 vs. 22.1+2.8x10-4inches; p=0.18; 2005-06: 32.5+3.7 vs. 28.3+7.1x10-4inches; p>0.6). The response in the 2004-05 season 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+3.5x10-4 inches; p<0.005; t test), but were similar in 2005-06. 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 six seasons, and the healthy group had all been immunized in both seasons eliminating this difference in the second season of the study.
CONCLUSIONS: The magnitude of influenza-specific T-cell responses by lung transplant patients is similar to those of healthy control individuals. These responses may be important in T-cell memory.

277. Treatment outcomes of pegylated interferon and ribavirin for the treatment of recurrent hepatitis C following liver transplantation. *Greg A. Smallwood, Pharm.D.*[1], Renee Devine, Pharm.D.[1], Rochelle Schmidt, Pharm.D.[2], Carlos Fasola, MD[1], Andrei C. Stieber, M.D.[1], Thomas Heffron, M.D.[1]; (1)Emory Healthcare, Atlanta, GA; (2)Emory University Hospital, Atlanta, GA.

PURPOSE: The number one reason for liver transplantation in the United States is currently complications of chronic hepatitis C viral (HCV) infection. Following liver transplantation, HCV recurs in 49.6% of patients within the first year and by year 4, all patients have recurrence. The aim of this study is to evaluate outcomes of a treatment protocol in a pharmacist-run HCV treatment clinic following liver transplantation.
METHODS: Patients with biopsy proven, recurrence of HCV following liver transplantation were directed to a pharmacist-run, protocol-driven, outpatient treatment clinic. Inclusion criteria for this IRB approved review included all patients that were treated for recurrence of HCV. Outcomes of peg. interferon/ribavirin treatment evaluation included biochemical, histological as well as virological responses to therapy. Other outcome measures evaluated included rejection, adverse effects, and patient/graph survival.
RESULTS: Of the 67 patients treated, 92.5% (62/67) were genotype I with 79.1% (53/67) having a biochemical response by month 3. At 3 months there was a decrease in ALT [123 (± 79) u/L vs. 69.3 (± 90) u/L; p=0.002], total bilirubin [1.7 (± 0.8) ng/dL vs. 1.1 (± 0.6) mg; p=0.05], viral load (2.2 X 106 vs. 0.7 X 106, p=0.02) and AST [156 (± 221) u/L vs 62 (± 78); p=0.002]. The normalization of transaminases was maintained through end of treatment. Viral clearance during treatment was 41.7% (28/67) at 3 months, end of treatment clearance was 51.7% (30/58) and sustained virological response was 34.8% (15/43). Only 16.4% (10/61) had to have dose interruption with 2 patients having rejection. Progression of biopsy results maintained Schuler score. Patient/graft 3 year survival was 75.9% ± 0.5.
CONCLUSIONS: Hepatitis C following liver transplantation can safely be treated under a protocol driven clinic to obtain similar viral clearance as is reported in the non-transplant population.

278E. Early sirolimus conversion is superior to late sirolimus conversion in reversing renal dysfunction in liver transplant recipients. *Christin Rogers, Pharm.D.*, Scott Johnson, M.D., Emily Snow, B.S., Douglas Hanto, M.D., Ph.D., Khalid Khwaja, M.D., Seth Karp, M.D., Ojo Egbuna, M.D., Didier Mandelbrot, M.D., Martha Pavlakis, M.D., Michael Curry, M.D.; Beth Israel Deaconess Medical Center, Boston, M.A.

Presented at the World Transplant Congress, Boston, MA, July 21-27, 2006.

279. The impact of broad-spectrum antifungal prophylaxis in lung transplant recipients. *William L. Musick, Pharm.D.*, Derrick R. Van Beuge, Pharm.D., Jennifer L. Christensen, Pharm.D.; The Methodist Hospital, Houston, TX.

PURPOSE: Despite advancements in antifungal therapies, invasive fungal infections in immunocompromised patients remain lethal. Although multiple antifungal prophylactic strategies exist, the ideal regimen remains to be elucidated. We report a single center's experience using voriconazole as prophylaxis following lung transplantation.
METHODS: We retrospectively evaluated the records of all lung transplant recipients from October 2002 through December 2004. During this period, the post-operative lung transplant protocol included voriconazole 200 mg every 12 hours, either intravenously or by mouth, starting at day zero and continuing for 6 weeks.
RESULTS: Thirty-three patients were evaluated. The median age at the time of transplantation was 53 years (range: 25–70 years). The most common indications for transplant were pulmonary fibrosis (33%), cystic fibrosis (18%), and chronic obstructive pulmonary disease (15%). Serial bronchoalveolar lavages (BALs) were conducted per protocol in all patients throughout the first year post-transplant. Eighty distinct fungal isolates were recovered from BALs in 28 of 33 patients (85%). Twenty-one Aspergillus isolates were recovered from 14 patients (38%). Nine of the 21 Aspergillus isolates were recovered during voriconazole therapy. *Aspergillus versicolor* was most commonly isolated. Of three patients having Aspergillus-positive BALs on day zero, only one did not have repeat positive cultures. Fifty-eight non-Aspergillus fungal isolates were recovered in BALs from 24 of 33 patients (73%). *Penicillium* spp. and *Candida* spp. were most commonly isolated. Of particular interest, Zygomycetes were isolated from BALs of three patients. Median time to positive BAL was 142 days post-transplant (range: 19–356). Overall mortality was 27% (9 of 33 patients).
CONCLUSIONS: Although the limitations of the current study preclude definitive answers regarding the effectiveness of this regimen, we call into question the efficacy of voriconazole as prophylaxis for invasive fungal infections following lung transplantation. Further investigation is needed to determine the ideal prophylactic strategy in this population.

280. Does rifampin use prior to liver transplantation affect post-transplant tacrolimus dosing? *Lisa M. McDevitt, Pharm.D., BCPS*, Hilina Aweke, Pharm.D., Gabriela Williams, Pharm.D.; Massachusetts College of Pharmacy and Health Sciences, Boston, MA.

PURPOSE: Rifampin is known to induce the cytochrome P450 3A (CYP3A) enzyme system and significantly decrease tacrolimus blood concentrations when taken concomitantly. CYP3A is predominantly found in the liver. The objective of this study was to analyze whether rifampin use prior to liver transplantation (and removal of the native liver) affects the ability to achieve target tacrolimus levels after transplant.
METHODS: We retrospectively evaluated 20 patients who received liver transplants between December 2004 and January 2006. The study arm included patients who were taking rifampin prior to transplant (n=5) and the control arm included those who were not on rifampin prior to their liver transplant (n=15). All patients initiated tacrolimus on the day of transplantation. Combined liver/kidney recipients, patients who started cyclosporine after transplant, and patients with SCr values > 2 mg/dL during the first week after transplant were excluded.
RESULTS: Patients receiving rifampin prior to liver transplantation achieved a target tacrolimus concentration of > 8 ng/mL a mean of 5.4 days and a median of 6 days postoperatively. Patients in the control group achieved target tacrolimus concentrations of > 8 ng/mL a mean of 3.6 days and a median of 3 days postoperatively. The average tacrolimus dose required to reach target trough concentrations was 0.13 mg/kg in the study group and 0.05 mg/kg in the control arm.
CONCLUSIONS: Rifampin is a potent inducer of CYP3A and has prolonged effects on tacrolimus metabolism despite discontinuation of rifampin at the time of transplant and removal of the native liver. This prolonged interaction may be attributable to rifampin's effect on CYP3A4 and p-glycoprotein present in the small bowel. Liver transplant recipients who use rifampin prior to liver transplantation require aggressive tacrolimus dosing to achieve target blood concentrations in a reasonable amount of time.

281E. Does interferon use prior to liver transplant influence hepatitis C outcomes following liver transplantation? *Greg A. Smallwood, Pharm.D.*, Renee Devine, Pharm.D., Carlos Fasola, M.D., Andrei C. Stieber, M.D., Thomas Heffron, MD; Emory Healthcare, Atlanta, GA.

Presented at Presented at the World Transplant Congress, Boston, Ma, July 22-26.

Urology

282. Transdermal oxybutynin and quality of life in patients with overactive bladder: results from the MATRIX trial. Vincent Lucente, M.D.[1], Roger Goldberg, M.D.[2], G. Willy Davila, M.D.[3], *Naomi V. Dahl, Pharm.D.*[4], MATRIX Investigators, -[4]; (1)Institute for Female Pelvic Medicine, Allentown, PA; (2)Evanston Continence Center, Northwestern University, Feinberg School of Medicine, Evanston, IL; (3)Department of Gynecology, Cleveland Clinic Florida, Weston, FL; (4)Watson Laboratories, Morristown, NJ.

PURPOSE: Quality of life (QOL) measurements are increasingly important in the evaluation of pharmacotherapy in patients with overactive bladder (OAB). Oral medications can improve QOL, but many patients discontinue therapy due to anticholinergic adverse effects, such as dry mouth. The Multicenter Assessment of Transdermal Therapy in Overactive Bladder with Oxybutynin (MATRIX) study assessed QOL and safety in a large, community-based

population of adults with OAB treated with transdermal oxybutynin (OXY-TDS).
METHODS: MATRIX, an open-label, multicenter, prospective trial, enrolled community-dwelling adults with OAB. OXY-TDS was administered at FDA-approved dose of 3.9 mg/d (2 patches per week) for up to 6 months. The King's Health Questionnaire® (KHQ), Work Productivity Questionnaire (WPQ), and Beck Depression Inventory®-II (BDI-II) were used to evaluate the impact of OAB on QOL. Patients self-rated OAB severity on a scale of 1 (no problems) to 6 (many severe problems). Clinic visits were conducted at 1, 3, and 6 months. Adverse events and concomitant medications were monitored throughout the study.
RESULTS: MATRIX enrolled 2878 patients; median age, 63 (range 18–100); 87.2% female. At baseline, 78.2% of patients rated OAB severity of 4 or greater, 46.4% had experienced OAB symptoms for at least 4 years, and 57.1% reported prior OAB treatment. At end of study, patients showed significant improvement in 9 of 10 domains of the KHQ ($p<0.0001$). Mean BDI-II summary score also improved (decreased) (baseline, 9.6; end of study, 7.4; $p<0.0001$). WPQ scores improved in all scales: physical ($p=0.002$), time, mental, and output scales (all $p<0.0001$), and overall index score ($p<0.0001$). Treatment was well tolerated, with a low incidence of anticholinergic side effects such as dry mouth (2.6%), constipation (1.5%), and dizziness (0.7%).
CONCLUSIONS: Quality of life impairment in OAB is common and encompasses physiologic, psychological, and social domains. Quality of life improves in OAB patients treated with OXY-TDS.

283. Does prior treatment for overactive bladder affect quality of life outcomes with transdermal oxybutynin? Results from the MATRIX study. Roger Goldberg, M.D.[1], *Naomi V. Dahl, Pharm.D.*[2], MATRIX Investigators[2]; (1)Evanston Continence Center, Northwestern University, Feinberg School of Medicine, Evanston, IL; (2)Watson Laboratories, Morristown, NJ.

PURPOSE: Treatment history may affect perceived effectiveness of antimuscarinic therapy for overactive bladder (OAB). This analysis of the Multicenter Assessment of Transdermal Therapy in Overactive Bladder with Oxybutynin (MATRIX) compares quality of life (QOL) in treatment-experienced vs -naive patients.
METHODS: MATRIX, an open-label, multicenter prospective trial, evaluated adults with OAB treated with transdermal oxybutynin 3.9 mg/day (Oxytrol®, Watson Pharma, Corona, CA) for ≤ 6 months. Study population included 3 predefined patient groups: treatment naive (n=973), recently discontinued (therapy stopped 0–29 days prior; n=785), lapsed (no therapy ≥ 30 days; n=566). King's Health Questionnaire® (KHQ) was used to evaluate QOL. P-values for within group changes from baseline were based on a 1-sample, 2-tailed t- test for significance of difference from zero, and those for between group differences were based on ANCOVA.
RESULTS: MATRIX enrolled 2878 patients (mean age 62.5 ± 14.8 years, range 18–100 year; 87% women, 84% white, 10% African American, 5% Hispanic). At baseline, 46% had OAB symptoms ≥ 4 years; 57% had prior oral OAB treatment (32% of whom with multiple drugs), predominantly extended release versions of tolterodine or oxybutynin. Baseline differences in impairment were seen between groups ($p<0.0001$) in 5 of 10 KHQ domains (trend for increasing severity: naive < recently discontinued < lapsed). At study end, statistically significant improvements were observed in all KHQ domains ($p<0.0001$), and were considered clinically meaningful in 9 of 10 domains. Magnitude of response was similar between groups in 6 domains, with greater improvement among lapsed and naive patients in 4 domains.
CONCLUSIONS: OAB patients benefit from transdermal oxybutynin, regardless of treatment history.

Women's Health

284. Use and knowledge of multivitamins containing folic acid among women of childbearing ages 18–45 years attending women, infant, children, and family planning clinics in Georgia. *Anthony G. Oladipo, Pharm.D., M.P.H*[1], Mary Beth Weber, M.P.H[2], Carol Hogue, Ph.D., M.P.H[2]; (1)Medimmune, Gaithersburg, MD; (2)Emory Univeristy, Atlanta, GA.

PURPOSE: To determine the proportion of women using multivitamins containing folic acid and the level of knowledge of folic acid among women of childbearing age.
METHODS: A cross-sectional survey was conducted among 2,353 women, aged 18–45 years, attending family planning clinics in Georgia between March 2003 and September 2004. We defined folic acid exposure as self-reported multivitamins or folic acid consumption within the last 2 days (MVFA users) and folic acid knowledge as awareness that 1) folic acid prevents birth defects, and 2) folic acid should be taken before pregnancy. We examined the associations between folic acid exposure and knowledge with selected variables using prevalence odds ratios (POR) and logistic regression analyses.
RESULTS: Overall, 38% of the respondents were MVFA users. MVFA use was associated with checking folic acid content on nutrition labels (POR 2.11; 95%CI: 1.59–2.81); pregnancy (POR 4.66 95%CI: 3.74–5.74); composite knowledge of folic acid (POR 1.33 95%CI: 1.04–1.72); doctor's or nurse's recommendation (POR 7.07; 95%; CI: 5.01–9.99); and multivitamins tablets as the most convenient source for daily folic acid (POR 2.31; 95%CI 1.91–2.98). Non-MVFA use was predominately because of lack of information 47%, and forgetfulness 27%. Overall 34% of the women had folic acid knowledge, which was associated with college/graduation (POR 1.12; 95%CI: 1.56–3.66); checking nutrition labels (POR 2.35; 95%CI: 1.87–2.96); white race (POR 1.12; 95% CI: 0.99–1.65); and learning about folic acid from a health care professional (POR 3.92; 95%CI: 2.51–4.42).
CONCLUSIONS: Sixty-two percent of women did not use MVFA, mainly due to forgetfulness and lack of knowledge on folic acid. Interventions to increase folic acid use should include targeted behavioral changes, aggressive public health and media campaigns involving active solicitation of health care professionals. Indirect folic acid delivery should include increased consumption of super-fortified cereals, and new formulations, such as oral contraceptives and folic acid combination tablets.

285. Relationship between hormonal contraceptive compliance and medical costs. *George J. Wan, Ph.D., M.P.H.*[1], Amy Grogg, Pharm.D.[2], Christopher E. Barnowski, M.D.[3], Lisa Berge, M.S.[3]; (1)Ortho Women's Health & Urology, Fort Washington, PA; (2)Applied Health Outcomes, Palm Harbor, FL; (3)Ortho Women's Health & Urology, Raritan, NJ.

PURPOSE: Analysis evaluated the relationship between compliance with different hormonal contraceptives and medical (inpatient, outpatient, emergency room, other/ancillary) costs incurred by health plans.
METHODS: Retrospective analysis was performed using the Pharmetrics medical and pharmacy claims database. Database yielded 38,495 women with administrative claims between 1/1/01 and 4/30/04 who had obtained a first time prescription for either norelgestromin/ethinyl estradiol (Ortho Evra®) or other commonly prescribed contraceptives: norgestimate/ethinyl estradiol (Ortho Tri-Cyclen Lo®); drosperinone/ethinyl estradiol (Yasmin®); or etonogestrel/ethinyl estradiol (NuvaRing®). Claims were reviewed for the period beginning 6 months prior to a patient's index claim and ending 12 months following the index claim. Women were excluded if they had a pregnancy diagnosis, cancer, liver disease, heart attack, stroke, or blood clots at any time during the study or were pregnant during the 6 months prior to the index claim. Compliance was measured using the medication possession ratio (MPR), which was calculated by dividing total number of days of medication supplied by total number of days (360). Pregnancy-related costs were excluded, because the focus was to examine the impact of compliance on medical costs other than pregnancy-related costs.
RESULTS: High compliance among all hormonal contraceptives examined was associated with costs-savings in medical costs compared with those that were less compliant ($829.19 cost-savings; $p<0.001$) (n=31,432). Among those not switching contraceptives, continuous users of Ortho Evra (n=4,117) had a greater likelihood of demonstrating high compliance (MPR of ≥ 0.80) with their medication compared with women on other medications (n=5,894) (OR=1.41; 95% CI=1.29–1.55; $p<0.0001$). Statistically significant cost-savings due to reductions in medical costs among highly vs. less than highly compliant patients were observed among Ortho Evra users ($923.91; $p<0.0001$) and not among users of other contraceptives.
CONCLUSIONS: Health plans with patients who are highly compliant to their hormonal contraceptive regimens see nonpregnancy-related cost-savings, regardless of the type of contraceptive prescribed.

286. Failure of primary care physicians to treat high risk osteoporosis patients. Carlos E. Ballestas, M.D.[1], *Eric J. MacLaughlin, Pharm.D.*[2], David S. Fike, Ph.D.[3], Dennis Zoller, M.D.[1]; (1)Texas Tech University Health Sciences Center School of Medicine, Amarillo, TX; (2)Texas Tech University Health Sciences Center School of Pharmacy, Amarillo, TX; (3)Amarillo College, Amarillo, TX.

PURPOSE: Despite wide availability of guidelines, screening and treatment of osteoporosis remains poor. However, data are lacking regarding the status in the outpatient family medicine environment. The purpose of this study was to determine whether patients with a diagnosis of osteoporosis or with a history of high risk fractures were receiving adequate care according to national treatment guidelines.
METHODS: Retrospective chart review of all patients ≥ 65 years from the Texas Tech Center for Community and Family Medicine with an ICD-9 code for hip, wrist, or pelvic facture and/or osteoporosis. Patient charts were reviewed and data collected regarding medical history, medication use, and osteoporosis diagnostic testing (i.e., dual x-ray absorptiometry [DXA] and standard radiography). Medications considered as treatments for osteoporosis included calcium/vitamin D, bisphosphonates, calcitonin, estrogen, raloxifene, and teriparatide.
RESULTS: One hundred seventeen patients (mean age 77.4 years) were identified and enrolled with 28 (24%) having had a high-risk fracture. For screening purposes, 73 (62.4%) of patients had received a DXA scan with 62

(53.0%) having documented osteoporosis at ≥ 1 site. In patients with a high risk of fracture or osteoporosis, only 62 (53.0%) had documented calcium use and 74 (63.2%) had any antiresorptive treatment. Of the 28 patients with a fracture, 1 (3.6%) was receiving treatment before the fracture and 16 (57.1%) received treatment after the fracture. There was an association between those that received a DXA scan and calcium use (r=0.577; p<0.001) any type of treatment (r=0.580; p<0.001).
CONCLUSIONS: Despite the presence of high risk factors for osteoporotic fractures, many patients are not being screened or treated by family physicians according to national guidelines. Future efforts must be made to improve care of patients at risk for debilitating fractures associated with osteoporosis.

287. What women want to know: an assessment of questions asked by women using an online ask-the-pharmacist service. Chad S. Jariangprasert, Pharm.D., *Shareen Y. El-Ibiary, Pharm.D., BCPS*, Candy Tsourounis, Pharm.D., Mitra Assemi, Pharm.D.; University of California, San Francisco, School of Pharmacy, San Francisco, CA.

PURPOSE: Ask-the-Pharmacist (ATP) services provide individualized clinical information to online consumers. The purpose of this study is to characterize the content of online drug information queries submitted by adult women to the ATP service for Blue Shield of California.
METHODS: This study is a retrospective review of online queries to the Blue Shield of California ATP service received in 2003–04. Clinical questions submitted by women ages 18 and older were evaluated.
RESULTS: A total of 1056 queries submitted by women were analyzed in this study. The mean age of female consumers was 44 (range 18–88). Thirty-three percent of all submissions inquired about drug adverse effects, of which 19% had reported experiencing acute adverse reactions. Drug efficacy or indications were the subject of 26% of submitted queries. The most common drug-related queries were antidepressants (8.6%) and contraceptives (8.2%), with a majority interested in the adverse effects of these drug classes. Herbal, nutritional, or vitamin supplements were the subject of 12% of queries. In terms of clinical topics, contraception and dermatology were most frequent for women ages 18–35, and osteoporosis and cardiovascular-related diseases for women over 55. Additional results to be presented.
CONCLUSIONS: The clinical questions posed by female consumers reflect the current trend of multiple treatment options. With many new medicines available for birth control and osteoporosis, women want to know the differences in drug efficacy and adverse effects. This information may help health plans, drug information centers, and pharmacies develop specific materials targeted toward these issues. In addition, healthcare providers need to be aware of these issues to better anticipate the healthcare needs of women.

288. Assessing knowledge and attitudes toward emergency contraception among Missouri pharmacists. *Alicia B. Forinash, Pharm.D., BCPS, CCD*, Evelyn Becker, Pharm.D., M.A.; St. Louis College of Pharmacy, St. Louis, MO.

PURPOSE: This study examined knowledge and attitudes about emergency contraception (EC) among licensed Missouri pharmacists.
METHODS: A survey was developed to assess knowledge and attitudes toward EC using responses to multiple choice and true/false questions. Participants were asked to provide information, including age, gender, marital status, years since graduation, and area of practice. This survey was mailed to 3000 pharmacists licensed and residing in Missouri using names and addresses provided by the Missouri Board of Pharmacy Web site. All names were computer randomized to generate the mailing list. The data were analyzed with SPSS.
RESULTS: The return rate for completed surveys was 16.5%. Responses to questions designed to assess knowledge base about EC varied in accuracy. More than half incorrectly identified RU- 486 as EC, and 45% thought that EC could induce an abortion of an already implanted embryo. However, the vast majority (91%) were aware of the time sensitive nature of EC, and 75% chose the correct response regarding redosing of EC in the event of nausea and vomiting. No significant correlations existed between demographic variables and knowledge base for most survey items. However, gender, practice setting, and years since graduation influenced knowledge about EC mechanism of action and efficacy. Although 64% supported the right of refusal, 58% believed that pharmacists are morally obligated to refer patients to another pharmacist if they refuse to fill EC.
CONCLUSIONS: Results of this survey may not be broadly applicable to all Missouri pharmacists because data were obtained from only about 10% of licensed pharmacists. Larger surveys will be needed to fully assess the need for educational programming. Since pharmacists' concerns about dispensing EC have been highlighted in public and professional media recently, further examination of pharmacists' attitudes toward EC is warranted.

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.

289. Acute renal failure in a comatose ICU patient on intraveous piperacillin-tazobactam, vancomycin, and levaquin therapy for the empiric treatment of hospital-acquired pneumonia. *Victoria L. Dillon-Bader, Pharm.D.*; Clinical Pharmacy Management, Inc., Mora, MN.

A 43-year-old admitted to the intensive care unit after a car accident developed a 102° Fever and was started on Zosyn, vancomycin, and Levaquin. On day 6, the patient experienced oliguric renal failure. The features supporting a piperacillin-tazobactam nephritis included the abrupt onset, 8-fold increase in eosinophils, elevated blood urea nitrogen (95), creatinine (8.84), edema of hand, negative cultures, unremarkable chest X-ray, normal WBC, and hypertension (210/120). The highest vancomycin trough was 16.2 ug/ml and levofloxacin was discontinued 2 days prior to the event. Within 24 hours of discontinuation of piperacillin-tazobactam the temperature and blood pressure normalized; however, the renal failure could not be reversed and the patient expired. Patients on triple antibiotic therapy should be closely monitored. This "evidence based" therapy encourages the use of either an intravenous beta-lactam cephalosporin or penicillin for the successful treatment of complicated pneumonia; however, the safety of piperacillin-tazobactam in combination with vancomycin and levofloxacin should be further investigated. In reviewing 10 years of drug safety data, there are more serious adverse events related to piperacillin-tazobactam than with cefepime or ceftazidime. The use of ceftazidime is discouraged, because of its ability to stimulate the production of beta-lactamase and its complicated dosing schedule. In view of this case, and the preliminary results of a retrospective follow up of 50 patients, the safest combination therapy for the empiric treatment of complicated pneumonia appears to be cefepime. References: FDA Medwatch; American Family Physicians, June 2003; American Thoracic Society, September, 2005; Clin Pharmacol Ther 1981;30(2)239-45; J Pharmacol 1997, Jan-Feb;17(1):166-9.

290. Evaluating the effectiveness of a pharmacist-managed pain consult service in postoperative knee replacement patients. Christine Yacoub, Pharm.D., Lisha Liang, Pharm.D., Julie Ryu, Pharm.D., Teresa Thongsinthusak, Pharm.D., *Mark Holtsman, Pharm.D.*; University of California, Davis Medical Center, Sacramento, CA.

PURPOSE: This study assessed the validity of a pharmacist-managed pain consult service in postoperative total knee replacement patients.
METHODS: A retrospective study that evaluates the effectiveness of a pharmacist-managed pain consult service in postoperative total knee replacement patients seen at UCDMC from June 1, 2004, to June 30, 2005. To assess the effectiveness of a pharmacist-managed pain consult service, pain relief was compared in patients who received a pain consult to those who did not receive a pain consult. Patients were analyzed for outcome measures such as length of stay, amount and duration of IV opioid use, adverse effects, and use of pain consult recommendations.
RESULTS: The patients were stratified into two distinct groups: patients without a pain consult (n=37) and patients given a pain consult (n=11). Average pain scores 12 hours post surgery for the group that received the pain consult were 6.6 compared with 5.5 for those without the consult (p<0.025). Of the patients evaluated by the pain pharmacist, the average pain score was 7.7 prior to the consult and 4.3 after the consult was implemented. Patients who received a pain consult had a statistically significant decrease in pain (p<0.005). Constipation, itching, and drowsiness were more prevalent in the group with a pain consult by 14.5%, 25%, and 14% although no difference in nausea and vomiting was seen between the two groups. Average daily morphine use was higher for patients who received a pain consult 105 ± 29.4 mg vs. (73.6 ± 35 mg) (p<0.005) for those without a consult.
CONCLUSIONS: This study demonstrates a pharmacist-managed pain consult service is effective at managing patients' pain. A majority of the pharmacist recommendations were followed by physicians. Patients who received a pain consult had more adverse effects than those who did not possibly as a result of their increased opioid use.

291. An evaluation of pharmacist-driven point-of-care lipid monitoring. *Kayce Clark, Pharm.D.*, Renee M. DeHart, Pharm.D.; Samford University McWhorter School of Pharmacy, Birmingham, AL.

PURPOSE: To evaluate the effectiveness of point-of-care (POC) cholesterol monitoring in a pharmacist-driven ambulatory clinic.
METHODS: A retrospective chart review at a Family Practice Residency clinic in Birmingham, Alabama. The study included patients that had two fasting POC lipid measurements drawn and analyzed by a pharmacist at least 3 months apart between October 2003 and December 2005. Primary end points measured were percent of patients at low-density lipoprotein cholesterol (LDL-C) goal, mean LDL-C, and the percent of patients that were on lipid-lowering therapy before and after POC monitoring.
RESULTS: Of the 98 patients meeting inclusion criteria, 62% reached their

National Cholesterol Education Panel (NCEP) Adult Treatment Program III (ATP III) LDL-C goal after POC monitoring compared with 43% before POC monitoring (p=0.001). The mean LDL-C of the total population was 123 mg/dL before POC monitoring and 109 mg/dL after POC monitoring (p=0.015). Additionally, 76% of patients were taking a lipid lowering agent after POC monitoring compared with 60% before POC monitoring (p=0.014).
CONCLUSIONS: Patients with dyslipidemia who participated in POC cholesterol monitoring offered by a pharmacist benefited from the service by having an increased likelihood of reaching their NCEP ATP III LDL-C goal. This is an important accomplishment in terms of patient care because it provides evidence that this type of POC clinic could be an asset to a patient's health care plan.

292. Pharmacist-driven cardiovascular risk-factor modification group clinic. Angelica Gomez, Pharm.D.[1], Kelly Parra, Pharm.D., BCPS[1], Nahla Lutfi, Pharm.D.[1], *David Parra, Pharm.D., BCPS*[1], Tamara Steiner, R.D.[2], Nick Beckey, Pharm.D., BCPS[1], Darin Rubin, D.O.[1], Israel Alvarez, M.D.[1]; (1)Veterans Affairs Medical Center, West Palm Beach, FL; (2)Veterans Affairs Medical Center, Tuscon, AZ.

PURPOSE: To pilot and evaluate a clinical pharmacy-driven group clinic targeting cardiovascular risk factors in a veteran population.
METHODS: Patients with coronary heart disease (or equivalents) and LDL-c levels > 100 mg/dL not receiving statin therapy were invited to participate. Patients with transaminase elevations > 1.5x ULN, a TSH > 10, or with clear documentation of provider's desire not to initiate statin therapy were excluded from enrollment. Patients received education by a pharmacist regarding disease state, signs/symptoms of coronary heart disease, dietary modifications (nutritionist or pharmacist), and the role of medications in reducing risk. Emphasis was placed on an interactive question-and-answer session as well an opportunity to share experiences among participants. Pharmacists prescribed lipid-lowering medications, antihypertensives, aspirin therapy, and nicotine replacement therapy as appropriate. Additional services offered included blood pressure monitors, weight reduction and smoking cessation classes, and individual dietitian appointments. Efficacy was measured via changes in lipid profiles, aspirin use, and blood pressures. Patient surveys were administered at follow-up to assess patient satisfaction.
RESULTS: Of the 61 initial participants, 85% of eligible participants agreed to statin therapy, resulting in a decrease in LDL-c from a baseline of 126 mg/dL to 93.6 mg/dL. Seventy-nine percent of participants had a diagnosis of hypertension with 38% requiring intervention to achieve blood pressure goal. All agreed to additional therapy resulting in a reduction in average blood pressure from 157/75 mm Hg to 147/76 mm Hg. In addition, 70% of the 33% of patients not on aspirin were successfully initiated on therapy. Results from the patient surveys reflected high levels of satisfaction demonstrating that the clinic not only effectively provided care, but was well received.
CONCLUSIONS: A pharmacist-driven cardiovascular risk-factor modification group clinic appears not only feasible, but also effective and well accepted by patients. Further studies are needed to assess clinical and economic outcomes.

293. Implementation of a thromboprophylaxis model in a community hospital setting: a multidisciplinary approach. *Stephen J. Ford, B.S., Pharm.D.*, Michael Cooney, M.D., Helen Parenti, R.N., M.S.N., Betsy DiSantis, R.N., B.S.N., Jane Miller, R.N., Elizabeth Felege, R.N., CCM, Pam Geopfarth, R.N., CCRN, RCIS; Saint Vincent Health Center, Erie, PA.

PURPOSE: Venous thromboembolism (VTE) remains the most common preventable cause of hospital-related mortality. To comply with national quality standards and ultimately improve patient care, our hospital recently established a "DVT Prevention Team." The purpose of this project was to adapt evidence-based guidelines to our hospital processes, leading to improved compliance with antithrombotic therapy for VTE prophylaxis.
METHODS: The DVT Prevention Team developed a strategy to accomplish this goal by focusing on two main quality outcome measures. The first focus measure was to improve the antithrombotic prophylaxis in hospitalized patients with two or more DVT risk factors. As a second focus measure, our team predicted that implementation of effective thromboprophylaxis would lead to a decrease in the actual DVT (e.g., nosocomial) occurrence rate. Using automated informational technology, patients with "DVT risk factors" were identified daily using a computer-generated worksheet. This worksheet was used to screen at-risk patients who had a history of DVT/PE or an admission to a critical care area on hospital day 1. All other patients with two or more risk factors on hospital day 2 were also screened. The chart was then reviewed daily (Monday through Friday) by an outcomes care manager or clinical pharmacist to determine eligibility for thromboprophylaxis. A "DVT Prevention" prompt is then placed under the Physician Progress Note section of the patient's chart with recommendations.
RESULTS: Our baseline thromboprophylaxis rate of 36% was consistent with the national average of 30%–40%. Subsequently, our hospital DVT program has been able to demonstrate a sustainable improvement with a current thromboprophylaxis rate of 47% overall and a cumulative average nosocomial DVT rate of 0.74%.
CONCLUSIONS: Implementation of a multidisciplinary DVT Prevention Team can improve the thromboprophylaxis rate in patients at risk for VTE and subsequently decrease the incidence of nosocomial DVTs.

294. Improving adherence to coronary heart disease secondary prevention medication guidelines at a community hospital. Thomas C. Bailey, M.D.[1], *Stuti Sinha, Pharm.D.*[2], Dennis A. Bouselli, Pharm.D.[3], Richard M. Reichley, R.Ph.[4], Laura A. Noirot, B.S.[4]; (1)BJC HealthCare and Washington University School of Medicine, St. Louis, MO; (2)Missouri Baptist Medical Center, St. Louis, MO; (3)Missouri Baptist Medical Center, St Louis, MO; (4)BJC HealthCare, St. Louis, MO.

PURPOSE: We previously reported that at an academic medical center, a technology assisted pharmacist intervention improved physician adherence to CHD secondary prevention guidelines for prescribing aspirin, beta-blockers, ACE-inhibitors and lipid lowering therapy. In this study, we tested whether the same approach is effective in a nonacademic, community hospital setting.
METHODS: Patients with elevated troponin-I levels were identified using a real-time clinical database, and a clinical pharmacist was notified via a secure Web site. In the observation phase, the study pharmacist confirmed the diagnosis of CHD and noted patient and medication level exclusions for secondary prevention, but did not intervene. Practices were then randomized to intervention or control groups. Patients in control practices continued to receive usual care, and data for exclusions continued to be collected, while the physicians in intervention practices received pharmacist-mediated recommendations regarding secondary prevention medications. Appropriate therapy was defined as a prescription at discharge for all four secondary prevention medication classes, or a valid exclusion for prescribing the medication.
RESULTS: The study was conducted between Nov. 7, 2004, and Jan. 20, 2006. The proportion of patients discharged on appropriate secondary prevention therapy increased from 69% to 73% in the control group and from 64% to 82% in the intervention group. The intervention had a statistically significant ($p<0.05$) impact on the composite end point of the proportion of patients discharged on appropriate secondary prevention medications.
CONCLUSIONS: Using an automated notification system to identify patients with CHD, and academic detailing of physicians by a clinical pharmacist, has a significant impact on the rate of adherence to CHD secondary prevention medication guidelines in a community hospital setting.

295. Intravascular ultrasound for the evaluation of novel cardiovascular therapies. Neil J. Weissman, M.D.[1], *Esteban Escolar, M.D.*[2]; (1)Cardiovascular Research Institute/Medstar Research Institute, Washington DC, WA; (2)Washington Hospital Center, Washington DC, WA.

PURPOSE: Cardiovascular therapies are traditionally evaluated in clinical end point trials. However, such trials must enroll large numbers of participants and have lengthy follow-up periods to have adequate statistical power to detect differences in clinical event rates between treatment arms. By contrast, surrogate markers (i.e., measures of a pathophysiological process that are characteristic of future clinical outcomes) allow trials that include smaller numbers of patients and are of shorter duration, which can expedite the introduction of novel therapies. While atherosclerotic progression is known to predict future cardiovascular events, and is therefore recognized as a surrogate marker for cardiovascular disease, the traditional method for measuring atherosclerotic progression, quantitative coronary angiography (QCA), has inherent limitations. This has driven the search for more accurate methods of evaluating atherosclerotic progression.
METHODS: Intravascular ultrasound (IVUS) is a catheter-based technique, which provides high-resolution, cross-sectional images of coronary arteries. During an IVUS procedure, the coronary artery is sub-selectively cannulated by a catheter incorporating a miniature transducer emitting high-frequency ultrasound. As the transducer is pulled back through the artery, ultrasonic reflections are electronically converted to cross-sectional images. Unlike QCA, which generates a 2-dimensional "silhouette" of the lumen, IVUS generates a 3-dimensional image of the arterial wall. This allows the detection of both early-stage atherosclerosis, where atherosclerotic plaque is developing in the arterial wall and luminal diameter is, as yet, unaffected, and end-stage atherosclerosis, where luminal diameter along an entire section of diseased artery is occluded to the same degree. IVUS is therefore considered to be more accurate for evaluating atherosclerotic burden than QCA.
RESULTS: There is growing evidence that atherosclerotic progression, as measured by IVUS, is highly predictive of cardiovascular outcomes.
CONCLUSIONS: Consequently, several ongoing trials, such as the ILLUSTRATE trial, are now using IVUS as a means of evaluating novel cardiovascular therapies.

296. Disease-specific health literacy and attitude toward treatment of hypertension. *Darcie L. Keller, Pharm.D., BCPS*[1], Julie Wright, Pharm.D.,

BCPS[2]; (1)University of Missouri-Kansas City/Truman Medical Center, Kansas City, MO; (2)University of Missouri at Kansas City/Truman Medical Center, Kansas City, MO.

PURPOSE: To evaluate subjects' disease-specific health literacy (DSHL) and attitudes toward treatment and to assess the correlation between these and self-reported adherence to antihypertensive therapy and blood pressure control.
METHODS: Forty-five subjects with a diagnosis of hypertension in an urban academic internal medicine clinic completed a survey designed to measure DSHL, attitudes toward treatment of hypertension, and self-reported adherence to antihypertensive therapy. Concurrent blood pressure (BP) and prescribed antihypertensive regimens were collected from the medical record.
RESULTS: The mean DSHL score was high (11.4/15); however, it was not associated with the subjects' BP control (p=0.163). Only 53% of subjects thought they would have hypertension for the rest of their life, and the majority of subjects thought they would have symptoms such as headache or dizziness when their BP was high, 76% and 73% respectively. Forty percent of the subjects did not have adequate knowledge of their antihypertensive regimen (drug or dosage). Although 97.8% of subjects thought it was very important (VI) or important (I) to control their BP and 100% thought it was VI or I to take their BP medicine everyday, 56% had uncontrolled BP and 42% reported that they had missed one or more doses in the last 7 days, including 44% of the patients with uncontrolled BP. In addition, 20% of subjects reported taking their BP medicines ≤ 6 days/week in a usual week. Level of education and DSHL score did not influence whether subjects missed doses.
CONCLUSIONS: Despite the relatively high DSHL score, the majority of subjects lacked insight into hypertension as a chronic asymptomatic disease and knowledge of their medication regimen. Although subjects reported a positive attitude toward the treatment of hypertension, adherence to antihypertensive medications and BP control are suboptimal, indicating a need for innovative interventions by pharmacists designed to improve adherence to antihypertensive therapy.

297. Presence of a pharmacy clinician in the intensive care unit 7 days a week decreases antibiotic utilization. *Lana Gerzenshtein, Pharm.D.*, Marc H. Scheetz, Pharm.D., Michael Postelnick, R.Ph., BCPS; Northwestern Memorial Hospital, Chicago, IL.

PURPOSE: Previous data has shown that a clinical pharmacist as an integral part of a critical care team in an Intensive Care Unit (ICU) improves patient care and decreases costs. We launched an ICU Pharmacist initiative providing a pharmacist on rounds 7 days per week in all our ICUs. One specific goal was to assess the difference in antibiotic use prior to and after the involvement of the ICU pharmacist.
METHODS: Daily pharmacist participation on rounds began in September 2005. Pharmacists suggested empiric antimicrobial therapy based on real-time antibiogram data and evidence based guidelines. Additionally, pharmacists streamlined antimicrobial coverage after report of culture and susceptibility data, optimized doses with regard to pharmacokinetics and pharmacodynamics, and advised on duration of therapy. To evaluate the impact of these interventions on antibiotic doses per patient day, two ICUs were evaluated between two time-periods, March and April of 2005 (pre-intervention) and March and April of 2006 (post-intervention).
RESULTS: Data reflect antibiotic use in the Medical Intensive Care Unit (MICU) and the Surgical Intensive Care Unit (SICU). There was a 23.7% decrease in antimicrobial doses/patient day in the MICU (3.97 in 2005, 3.03 in 2006). There was a 23.0% decrease in antimicrobial doses/patient day in the SICU (3.56 in 2005, 2.74 in 2006).
CONCLUSIONS: A critical care pharmacist as part of the ICU team 7 days per week was associated with decreased antibiotic doses per patient day. Future studies will need to quantify these benefits and assess the impact of these reductions on patient outcomes.

298. Impact of clinical pharmacy consult services on early goal-directed therapy for sepsis. *J. Audis Bethea, Pharm.D., BCPS*, Carol A. Morreale, Pharm.D., BCPS, Jeremy Fox, Pharm.D., BCPS, Christine Teague, Pharm.D., BCPS, M.P.H., Nicole Passerrello, Pharm.D., BCPS, David Rollins, Pharm.D., BCPS; Charleston Area Medical Center, Charleston, WV.

PURPOSE: To evaluate the impact of a clinical pharmacy consult service on the clinical management of sepsis.
METHODS: The complexity and significant mortality associated with sepsis has prompted the sepsis team at Charleston Area Medical Center (CAMC) to develop algorithms and order sets consistent with the recommendations of the Surviving Sepsis Campaign for early goal-directed therapy. Automatic consults to the clinical pharmacy on-call service are used to promote adherence to recommendations for early goal-directed therapy. This is achieved through direct interaction with nurses and physicians at the patient's bedside. Since the implementation of the order sets and algorithms, data has been retrospectively collected at 3-month intervals. Data will be analyzed to assess the impact of the clinical pharmacy on-call service in achieving therapeutic targets including, optimization of fluid resuscitation; selection of antibiotics; maintenance of tight glycemic control; and appropriate initiation of vasopressors, steroids, and drotrecogin alfa (Xigris®).
RESULTS: Twenty-six patients were seen by the pharmacy consult service in the initial 3-month period, February 2006 through April 2006. One hundred eighty-one clinical interventions were made addressing several areas of sepsis management including fluid resuscitation, vasopressors, antibiotics, steroids, and drotrecogin alfa (Xigris®) therapy.

	Clinical Interventions					
( ) = n	Resuscitation/ Vasopressors	Glycemic Control	Steroids	Anti-microbials	Xigris® Assessment	Other Interventions
February (4)	1	2	4	4	4	8
March (10)	11	7	3	16	10	31
April (12)	10	6	2	10	12	40
Total (26)	22	15	9	30	26	79

Analysis is ongoing; results will be added to the above data to include all sepsis consults from February to July of 2006. Additional pharmacoeconomic analyses are being conducted and will be included in the final analysis.
CONCLUSIONS: A clinical pharmacy consult service can make a significant impact in meeting the therapeutic targets associated with improved clinical outcomes in sepsis.

299. Antimicrobial administration times in a septic population: can implementation of a sepsis bundle shorten time to administration? *Jeff Biermann, Pharm.D.*[1], Tudy Hodgman, Pharm.D.[2], Aaron Joffe, D.O.[2]; (1)Midwesterrn University, Chicago College of Pharmacy, Downers Grove, IL; (2)Northwest Community Hospital/Midwestern University, Arlington Heights, IL.

PURPOSE: Severe sepsis has become an increasing problem as the population ages, more patients receive chemotherapy or antimetabolites and more invasive procedures are performed. The Surviving Sepsis Campaign advocates a "sepsis bundle" which includes "timely, effective, broad spectrum therapy." A recent study1 outlined delay in antimicrobial therapy to be the primary factor affecting increase in mortality. We undertook this study to examine the various processes in the continuum of ordering, pharmacy order entry and delivery, and nursing administration of antimicrobials to patients with severe sepsis.
METHODS: A retrospective chart review was performed on patients being followed by the Community Hospitals Against the Sepsis Epidemic group. Data collected include the time of sepsis diagnosis, time of first blood cultures, time antimicrobial orders written, time the order is entered into the pharmacy computer system, where the antimicrobial will be dispensed (PYXIS vs. pharmacy), location of first antimicrobial dose administered, antimicrobial ordered, culture results, time to appropriate empiric antimicrobial therapy and time to initiation of appropriate antimicorobial therapy based on culture results. Appropriate antmicrobial therapy is defined by the Infectious Disease Society of America empiric therapy guidelines.
RESULTS: This descriptive study was performed to evaluate potential issues in the processes by which patients receive antimicrobials. Analysis was performed on location of ordering, time of day, and day of week effects on the pharmacy turn-around time, time and day of week effect on nursing administration times. Pre to post bundle time to first antimicrobial administered decreased from 5.28 to 1.65 hours ($p<0.05$).
CONCLUSIONS: In this retrospective study, time to antimicrobial administration was significantly decreased by implementation of a protocol. Implementation of the surviving sepsis campaign requires a multidisciplinary approach. An assessment of all steps within a specific component of the bundle will allow process improvement and permit more effective implementation of the guidelines.

300. Treatment of patients with septic shock using sepsis bundles is cost-effective in a community-based non-teaching hospital. *Tudy M. Hodgman, Pharm.D.*, Aaron Joffe, D.O., Nathan M. Lidsky, M.D.; Northwest Community Hospital/Midwestern University Chicago College of Pharmacy, Arlington Heights, IL.

PURPOSE: Early goal-directed therapy (EGDT) decreases morbidity and mortality in severe sepsis and septic shock. Allocation of invasive monitoring and intensive care unit (ICU) resources in those with advanced age, severe comorbidities, and high risk of death is contentious. We aimed to study the effects of implementing a treatment bundle for septic shock—based on the recommendations of the Surviving Sepsis Campaign (SSC)—on direct patient cost using variable cost as its surrogate.
METHODS: Pre-printed order sets with clinical prompts were developed. "Emergent phase" orders emphasize early recognition, volume resuscitation, antibiotic administration, and intensivist notification. "Critical care" phase orders emphasized early goal-directed therapy (EGDT), adrenal testing, Xigris candidacy, and compliance with ARDSNet and must be evaluated and renewed every 12 hours for the first 48 hours. Presept catheters (Edwards

Lifescience, Irvine, Ca.) were placed in all patients by a 24/7 in-house intensivist who was also responsible for care of the patient in the ICU. Nursing and physician staff was educated regarding the initiative. Data for patients treated before (pre) and after (post) implementation were collected retrospectively using the hospital's cost accounting system and entered into a computerized database developed for the project.
RESULTS: 97 patients were included. Pre=46 and Post=51. Baseline age, APACHEII score, and number of acute organ dysfunctions in the first 24 hours were similar between groups. Overall mortality was 43%. Variable cost before implementation was $16,954 ± 18,854 and $13,100 ± 16,655 after (p=0.28). In the subgroup of patients under Medicare, the cost was $16,351 ± 14,834 before and $10,142 ± 6,568 after (p=0.03).
CONCLUSIONS: Implementation of the sepsis bundles decreased variable cost by approximately $3,800 per patient treated. Treatment of Medicare patients resulted in a statistically significant savings of more than $6,000 per patient. Treatment of patients with septic shock using treatment bundles is cost-effective in a community-based non-teaching hospital.

301. Cost justification of a critical care clinical pharmacist at a 254-bed community hospital. *Jennifer Priziola, Pharm.D.*, Molly Mullin, Pharm.D., Diana Steinl, Pharm.D., Craig Cooper, M.S., R.Ph., Keith Stevens, D.O.; William Beaumont Hospital, Troy, MI.

PURPOSE: The participation of clinical pharmacists in the ICU has been shown to decrease drug and ICU costs. A Critical Care Clinical Pharmacist joined the multidisciplinary Critical Care Team at William Beaumont Hospital-Troy, a 254-bed Community Hospital with 20 Critical Care beds, July 2004. The position is a full-time equivalent (FTE) funded by the Pharmacy Department and dedicated to optimizing medication management in the Critical Care Units. Internal cost justification of this new position was essential.
METHODS: A literature search was performed to define the cost savings and potential cost avoidance of the daily activities of the Critical Care Pharmacist. Using literature and internal data, the Pharmacy Department in collaboration with the Finance Department determined calculations for the cost savings and avoidance of daily interventions such as: discontinuation of therapeutic duplications or unnecessary medications, intravenous to oral conversion, dose adjustment, improved glycemic control, prevention of adverse drug events, addition of stress ulcer prophylaxis, addition of deep vein thrombosis prophylaxis, and overtime cost avoidance. Daily interventions were documented in an Excel® spreadsheet with defined cost savings and cost avoidance. Quarterly cost-containment summaries were submitted to the Finance Department and presented to the Board of Directors. The cost containment value did not include any cost savings or avoidance associated with administrative activities, development and implementation of protocols, clinical improvement projects, patient safety initiatives, formulary management, drug information, education, or any activity not associated with a direct cost savings or avoidance.
RESULTS: In 2005, the total cost savings and cost avoidance of the daily interventions performed by the Critical Care Pharmacist was $188,886. The documented cost containment was used to justify an additional pharmacist FTE when the Critical Care Units expanded by 13-beds.
CONCLUSIONS: The documented cost containment financially justifies the addition of a Clinical Pharmacist to the multidisciplinary Critical Care Team.

302E. Long-term safety of levalbuterol administered via metered dose inhaler in patients with asthma. *William K. McVicar, Ph.D.*[1], Anthony D. D'Urzo, M.D., M.S.C.[2], Michael G. Marcus, M.D.[3], Kenneth Tripp, M.S.[1], Merdad Parsey, M.D., Ph.D.[1], Rudolf A. Baumgartner, M.D.[1]; (1)Sepracor Inc, Marlborough, MA; (2)Primary Care Lung Clinic, Toronto, ON, Canada; (3)St Vincent Catholic Medical Centers, Staten Island, NY.

Presented at the Annual Meeting of the American College of Chest Physicians, Salt Lake City, UT, October 22, 2006.

303. Written versus oral recommendations made by pharmacy students during internal medicine rotations. *Melanie W. Pound, Pharm.D., BCPS*[1], Susan M. Miller, Pharm.D., BCPS[2]; (1)Campbell University School of Pharmacy and Cape Fear Valley Health System, Fayetteville, NC; (2)University of North Carolina at Chapel-Hill School of Pharmacy, Southern Regional AHEC and Cape Fear Valley Health System, Fayetteville, NC.

PURPOSE: Pharmacy students use a variety of methods to communicate with physicians during clinical rotations regarding pharmacotherapy concerns. Documented acceptance rates for oral or written interventions, when studied individually, range between 64% and 95%. No studies have directly compared the acceptance rates for medication-related interventions employing these two manners of communication. The purpose of this study was to compare the acceptance rates of written versus oral recommendations made by pharmacy students on internal medicine (IM) rotations.
METHODS: Fourth-year pharmacy students completing an IM rotation made oral or written recommendations to physicians at a large community-based medical center from November 2005 through April 2006 (excluding December). The types of recommendations and outcomes of the interventions were recorded using a data collection form. The primary end point was to determine differences in acceptance rates for written versus oral recommendations. Secondary end points included comparing the types of interventions and their corresponding acceptance rates. Additionally, the acceptance rate for evidence-based medicine (EBM) interventions was evaluated.
RESULTS: A total of 625 interventions were made by 10 pharmacy students during a 5-month period. Oral recommendations accounted for 47.5%. A total of 82.8% of oral recommendations were accepted compared with 54.2% of written recommendations ($p<0.0001$). More than 90% of the total interventions were drug-related. Overall, 68% of these drug-related recommendations were accepted. The major types of drug-related interventions were indication for use (42.7%), inappropriate dose (17.2%), inappropriate route (11.3%), inappropriate drug (8.5%), and duplicate therapy (6.5%). The remaining types of interventions were lab-related (6.4%) and requests for drug information (3.2%). The acceptance rate for EBM interventions was 36.3%.
CONCLUSIONS: Pharmacy student interventions are well received by physicians. Oral recommendations are accepted at a statistically significantly higher percentage compared with written recommendations. Higher acceptance rates for interventions may have the ability to positively affect patient care.

304. Development of a standardized training program for consultative clinical pharmacy services in a community hospital. *Laura H. Waite, Pharm.D.*, Tanya D. Gordon, Pharm.D.; Florida Hospital Orlando, Orlando, FL.

To promote the benefits of clinical pharmacy services and maintain physician support, pharmacy departments in community-based institutions must ensure consistent and reliable patient care via standardized, hospital-specific clinical training. At Florida Hospital Orlando, clinical pharmacy services are provided upon physician consultation only. Previously, the training program lacked formal selection criteria to define eligibility; ample documentation of performance, progress, initiative, or expansion of knowledge base; consistent standards for job performance; and adequate competency evaluation. To improve this process, we developed objective evaluation tools, competency assessments, an extensive training manual detailing pharmacy-specific procedures, and a training program syllabus outlining expectations and responsibilities of the clinical pharmacists. Each candidate must now undergo a formalized interview, including a presentation, to allow unbiased evaluation of the candidate's communication skills and clinical knowledge. Selection of candidates is based on predetermined eligibility criteria addressing clinical acumen and experience, staffing requirements, order entry proficiency, and communication skills. Upon entering the training program, the trainee must complete required reading assignments and baseline competency exams. He/she must document daily activities detailing the number of patients seen and what services were provided to ensure adequate experience with all services offered. The trainee receives a midpoint and final evaluation including written and verbal feedback of attitude and job performance based on prespecified criteria. At the culmination of the training program, the trainee must successfully complete case-based competency exams prior to providing clinical services independently. This program was implemented in spring 2006, and 3 clinical pharmacists have been successfully trained to date.

305. Pharmacist effect on glycemic control following institution of a post-prandial glucose correction scale. *Paul Juang, Pharm.D.*[1], John Khoury, Pharm.D.[2], Lawrence Prablek, M.D.[3]; (1)St. Louis College of Pharmacy, St. Louis, MO; (2)Missouri Baptist Medical Center, St. Louis, MO; (3)IPC The Hospitalist Company, St. Louis, MO.

PURPOSE: Studies have shown that strict glycemic control for hospitalized patients result in decreased morbidity and mortality. Recently the in-house insulin sliding scale was converted to a basal/bolus insulin model, with a post-prandial glucose correction scale. This study was conducted to evaluate the change in glycemic control and the effect of clinical pharmacist on the achievement of target glucose levels with the new model.
METHODS: A single-center, retrospective evaluation of patients admitted within an inpatient medicine service at a major metropolitan community hospital. Glucose readings were obtained for all patients admitted for 3 months prior to and after the institution of the new insulin scale, and were categorized to 5 groups: Blood glucose < 70, 70–79, 80–110, 111–150 and > 150 respectively. Statistical analysis was performed using the chi-square test.
RESULTS: A total of 4660 glucose readings were evaluated after the institution of the new insulin model as compared with 5116 glucose readings prior to institution. Following the institution of the new model, there was a significant greater number of readings > 150 (44.1% vs. 42.0%, P=0.039)

while fewer patients had readings of 70–79 (2.08% vs. 2.97%, P=0.0065) and 80–110 (18.3 vs. 19.6%, P=0.087). When a clinical pharmacist rounded on a daily basis, there were fewer glucose readings of < 70 (1.89% vs. 2.90%, P=0.0133), 70–79 (1.74% vs. 2.08%, P=0.36) and > 150 (41.9% vs. 44.1%, P=0.072) while more patients had glucose readings of 80–110 (20.6% vs. 18.3%, P=0.012) and 111–150 (33.8% vs. 32.7%, P=0.31).
CONCLUSIONS: The institution of the post-prandial glucose correction scale resulted in poor glycemic control throughout the entire institution. Extensive physician education of the new model has failed to improved institutional glycemic control. Poor glycemic control was observed within the inpatient medicine service; however, the presence of a clinical pharmacist was shown to improve overall glycemic control.

306E. Development of a model drug-usage utilization program at a community-based institution using enoxaparin as a template. *Jennifer Hunt, Pharm.D.*, Brian Buck, Pharm.D., Melissa C. Frank, Pharm.D.; Northeast Georgia Health System, Gainesville, GA.

Presented at the Southeastern States Regional Conference, Athens, GA, Aril 27-28, 2006.

307E. Implementing a tobacco cessation training program for healthcare professionals in a community hospital setting. *Timothy C. Chen, Pharm.D.*[1], Pamela Matten, R.N., O.C.N.[2], Dana Rutledge, R.N., Ph.D.[2], Ryan Quist, Ph.D.[1], Eunice P. Chung, Pharm.D.[1], Siu-Fun Wong, Pharm.D.[1]; (1)Western University of Health Sciences, College of Pharmacy, Pomona, CA; (2)St. Joseph Hospital of Orange, Orange, CA.

Presented at the 2nd Annual Conference of the Hematology/Oncology Pharmacy Association, Orlando, FL, June 15-18, 2006.

308. A pharmacist-managed continuous glucose monitoring program. *Jennifer D. Goldman-Levine, Pharm.D., CDE*; Massachusetts College of Pharmacy and Health Sciences, Tufts University Family Medicine Residency Program, Boston, MA.

This abstract will describe the rationale, development and implementation of a pharmacist-managed Continuous Glucose Monitoring Program. The poster will describe the CGMS, outline the process, and present actual patient examples. A pharmacist developed and manages diabetes services at the Tufts University Family Medicine Residency Program. For some patients, their in-office A1C determination does not correlate with their reported home glucose monitoring results. Continuous glucose monitoring can be used effectively in these patients. Physicians or the pharmacist refers for evaluation and placement of the device. The pharmacist evaluates the results and adjusts the medications as necessary. A CGMS records an average glucose value every 5 minutes for up to 72 hours for a total of 864 readings. Patients wear the cell phone-sized device for 3 days and continue with their usual daily activities. The user is expected to enter into the device at least 4 blood sugar readings, any insulin or oral medications taken, exercise engaged in, and when meals or snacks are consumed into the monitor by pushing a button to mark the times. In addition, the patient records these events on a paper diary, including specific details such as insulin doses, amount of exercise, and contents of food intake. The data are downloaded onto a computer for review of glucose levels in relation to the other data collected to make necessary adjustments in the patient's medication regimen. This extensive data can identify glucose level trends. Such trends may include previously unidentified dangerously low hypoglycemia that may go unnoticed, high postprandial readings and early morning blood sugar elevations. Other research has shown that CGMS leads to improved A1C values and fewer hypoglycemic episodes.

309. Clinical pharmacist-coordinated medication therapy management effect on diabetes clinical markers compared with standard care. *Patrick J. Kiel, Pharm.D.*[1], Ghada Ghannam, Ph.D.[2], Amie D. McCord, Pharm.D., BCPS, CDE[3]; (1)Rush University Medical Center, Chicago, IL; (2)Midwestern University, Downers Grove, IL; (3)St. Louis College of Pharmacy, St. Louis, MO.

PURPOSE: To evaluate and document clinical pharmacy medication management services on diabetes clinical markers over a 3-year period.
METHODS: Medical records of 321 patients were retrospectively reviewed to evaluate clinical markers such as A1C, lipid panel, adherence to preventive care, and medication profiles. Patients were stratified into 2 groups, an intervention group consisting of patients managed by clinical pharmacists (n=192) and a control group of patients receiving standard care (n=129).
RESULTS: Patients receiving medication management by a pharmacist had a mean A1C reduction of 1.89% within 6 months compared with a 0.58% reduction for those receiving standard care (p<0.001). Over 3 years, the mean A1C reduction was 2.01% and 1.02% for the intervention and control groups, respectively (p<0.001). Moreover, 28.6% of patients seen by a clinical pharmacist had an A1C goal of < 7% compared with 16.2% of patients receiving standard care over the course of 3 years (p=0.011). Clinical pharmacist-managed patients had a LDL reduction of 10.09 mg/dL over 3 years compared with 6.69 mg/dL for standard care (p=0.407). At 3 years, microalbuminaria screening adherence was recorded in 69.4% and 49% of patients within the pharmacist and standard care group, respectively (p<0.001). Additionally, 70.9% of the pharmacist managed group and 29.1% of the standard care group were negative for microalbuminaria (p=0.604).
CONCLUSIONS: Clinical pharmacist-coordinated medication therapy management was effective in improving diabetes associated clinical markers. Considerable improvement was observed in A1C and the frequency of preventative care. Improvements in these areas are known to reduce the risk of microvascular and macrovascular disease.

310E. Assessing classroom engagement utilizing student perceptions of faculty attributes and teaching techniques. *Michael J. Gonyeau, B.S., Pharm.D., BCPS*; Northeastern University, Boston, MA.

Presented at the Annual Meeting of the American Association of Colleges of Pharmacy, San Diego, CA, July 8-13, 2006.

311. Clinical pharmacy impact on aspirin prescribing for primary and secondary prevention of cardiovascular disease in diabetic patients. *Michael J. Gonyeau, B.S., Pharm.D., BCPS*; Northeastern University, Boston, MA.

PURPOSE: To evaluate the impact of pharmaceutical care on aspirin prescription for primary and secondary prevention of cardiovascular disease in diabetic patients in an urban, academic medical center.
METHODS: Data from a prospective 8-week intervention period were compared with baseline aspirin prescription rates from a 6-week observational chart review. Medical histories and medications of patients admitted to general medicine teams were reviewed and recommendations made per CHEST and ADA guidelines. The primary end point was discharge on aspirin or appropriate alternative. Secondary end points included influence of admitting diagnoses, acceptance of pharmacist recommendations and reasons for recommendation rejection.
RESULTS: 180 baseline and 255 intervention patients were assessed, resulting in 66 and 73 patients with diabetes respectively. The intervention group was 52% men, mean age 72, primary prevention (PP) candidates: 37%. For baseline patients, discharge aspirin (or appropriate alternative) use was 56% (PP) and 63% secondary prevention (SP). Intervention increased discharge prescription by 14% (PP) (p=0.389) and 11% (SP) (p=0.356) vs. baseline. Intervention significantly increased discharge prescription within the intervention group hospitalization (29% (PP) (p=0.027) and 20% (SP) (p=0.0038)). Aspirin was prescribed more often with cardiac admitting diagnoses (64% vs. 25% p=0.03). Recommendations were accepted in 82% of PP and 48% SP candidates. Common recommendation rejection reasons were assumed outpatient follow up (33%) and concomitant alternative therapy (18%).
CONCLUSIONS: Pharmaceutical care increases aspirin prescription for primary and secondary prevention of CAD in diabetic patients. Addressing the need for inpatient interventions on perceived outpatient issues may bridge the treatment gap.

312. Increase in *Clostridium difficile* rates after increased proton pump inhibitor prescribing. *John Belanger, Pharm.D., BCPS*, Patricia Triplett, M.D., Barney Hunter, Pharm.D., Lee Penry, M.I.E.; High Point Regional Hospital, High Point, NC.

PURPOSE: The objective of this study was to determine the impact of proton pump inhibitor (PPI) prescribing on the hospital *Clostridium difficile* rates.
METHODS: Medical records of all adult patients admitted to the hospital were retrospectively analyzed from October 1998 to present using Trendstar, the hospital's decision support system. Patients were identified by combining those with a primary or secondary diagnosis code for *Clostridium difficile* (008.45), and those who had used any PPI, any H-2 blocker, and any formulary antibiotic during their hospital stay.
RESULTS: Antibiotic use has increased from 18% of patients at the beginning of the study period to 35% currently. PPI use has increased from 13% to 37% over the same time period. When patients with *Clostridium difficile* were matched with all antibiotics on formulary, there were no discernable trends showing increased rates of infection. However, when patients were matched with PPI use, rates of *Clostridium difficile* infections were increased 4-fold over the study period. Rates of those with *Clostridium difficile* infections were not increased in those using H-2 blockers.
CONCLUSIONS: While hospital use of PPI's has grown rapidly since August 2002, the rate of *Clostridium difficile* infection related to that use has grown out of proportion. Our data seems to support that of recent publications highlighting the increased risk of *Clostridium difficile* infection in those using PPI's. Although there are many risk factors for *Clostridium difficile* infection that are well known, PPI's have become an emerging risk factor for

Clostridium difficile infection. PPI use will be heavily scrutinized to limit this potential threat to patient safety.

313E. An economic analysis comparing rifaximin and lactulose involving hospitalizations for the management of hepatic encephalopathy. Tiffany E. Kaiser, Pharm.D., N Kemmer, M.D., V Zacharias, M.S., PA-C, C Duncan, M.D., R McHenry, M.D., M Jonas, M.D., D Novick, M.D., C Willaimson, M.D., K Hess, M.S., ACNP, L Trumball, B.S., *G. Neff, M.D.*; University of Cincinnati, Cincinnati, OH.

Presented at the World Transplant Congress, Boston, MA, July 2006.

314. A bone-health screening, education, and referral project in northwest Iowa. *June F. Johnson, Pharm.D.*, Carrie Koenigsfeld, Pharm.D.; Drake University, Des Moines, IA.

PURPOSE: To enable community pharmacists to increase recognition and treatment of older women who may be at risk for osteopenia or osteoporosis.
METHODS: A collaboration between Drake University (DU) College of Pharmacy, Des Moines University (DMU) and its Geriatric Education Center (GEC), and community pharmacies was funded by the Community Pharmacy Foundation. Five pharmacies completed education on osteoporosis, received training on use of the Achilles InSight by GE Lunar, and served as sites for screening women > 60 years old for osteoporosis. A DU faculty and DMU graduate student coordinated pharmacists' training and supervised the screenings. Patients received education on osteoporosis and risk factors during the screening, and were stratified as Low, Moderate, or High Risk based on a T-score. Patients at risk were referred to their physician for further evaluation. Pharmacists telephoned patients at 3 and 6 months after screening to determine self-initiated or provider-initiated changes in their treatment plan. Data analysis will include descriptive population characteristics, proportion of patients screened at risk, multivariate analysis of the correlation between responses on the intake form and level of risk, and correlation between screening risks and DEXA results.
RESULTS: A total of 159 women were screened. Fifty-three percent were rated as moderate or high risk and referred to their physicians. Three- and 6-month follow-up results are pending and will reveal self-initiated or provider-initiated lifestyle or medication changes.
CONCLUSIONS: The majority of women > 60 who attended a community pharmacy osteoporosis screening were at moderate or high risk for osteoporosis. A fee-for-service model has been created for community pharmacists to improve recognition and treatment of patients at risk. A "toolkit" will be created for pharmacists to promote their role in improving the bone health of our older patients.

315. Development of Korean clinical trial guideline in elderly patients. *Sunsil Lee, Ph.D.*[1], Hunjoo Ha, Ph.D.[1], Jung Mi Oh, Pharm.D.[2], Wan Gyoon Shin, Pharm.D., Ph.D.[2]; (1)College of Pharmacy, Ewha Womans University, Seoul, South Korea; (2)College of Pharmacy, Research Institute of Pharmaceutical Sciences, Seoul National University, Seoul, South Korea.

PURPOSE: Aging and ethical issues in geriatric patients resulted in poor representation in clinical trials (CTs). Thus, the specific guideline is required for geriatric CTs. The International Conference on Harmonization (ICH) developed the guidance to ensure the CTs in geriatric patients, but it is not yet in Korea. The objective of this study was to develop a Korean geriatric CT guideline with detailed contents and procedures in accordance with Korean Good Clinical Practice (KGCP) and pharmaceutical affairs law on the basis of ICH guideline.
METHODS: The international and domestic regulations, pharmaceutical affairs laws, and the previous reports on geriatric CTs were assessed and investigated. Existing Korean CT guidelines were investigated with respect to the purposes, general principles, applicable scope, the definition of the population, and study-methodology. The specific ethical issues in geriatric patients were considered.
RESULTS: This Korean guideline developed for geriatric CT was composed of two parts, the principles and the discussions. The principles included the purposes, definition of elderly patients, applicable scope, legal issues, ethics committee, and the outlines of CT. The discussions included the application of geriatric CT protocol, geriatric CT design and analysis, geriatric pharmacokinetics and pharmacodynamics, drug interactions, study-methodology, statistical analysis, informed consent for geriatric patients, compensation to subjects, selection of subjects, case report forms, monitoring, multiple-center CT, safety and efficacy evaluation, and reporting of trial results. This guideline highlighted various mental and physical dysfunctions by aging and related ethics.
CONCLUSIONS: The Korean guideline for geriatric CT was developed and agreed with KGCP and domestic laws on the basis of ICH guideline. This would provide the basis for accomplishing standardization and internalization of geriatric CTs in Korea.

316. Do we need to routinely monitor serum level of theophylline in elderly patients? *Hui-Feng Cheng, M.Sc.*, Chia-Hui Lee, B.P. Shu-Min Lin, M.D., Han-Pin Kuo, Ph.D., Shin-Tarng Deng, B.P.; Chang Gung Memorial Hospital, Taipei, Taiwan.

PURPOSE: Theophylline is a potentially toxic drug with a narrow therapeutic window. Its metabolism, especially in old age, may be affected by several confounding factors leading to an unexpectedly high serum level, which sometimes is lethal. Thus, monitoring of the theophylline serum level is routinely required. The purpose of this study is to obtain a cut-off dose of theophylline that can be administered safely without routine monitoring serum level.
METHODS: Data of theophylline serum level of hospitalized patients over 60 years old were consecutively collected for 1 year from Jan. 1, 2005, to Dec. 31, 2005. The characteristics of patients, daily dose, sampling time, and drug interactions were reviewed. Correlation of dose with serum level was analyzed by linear regression. The cut-off dose was analyzed by ROC curve.
RESULTS: A total of 604 elderly patients (413 men and 191 women) were included with a mean age of 77.5 ± 7.7 years. Among them, 81 were smokers (13%), 118 with COPD (20%), 30 with de-compensated cardiac function (5%), and 157 patients were taking interacting drugs concomitantly (26%). There was a correlation between the dose and the steady state serum level ($r=0.6$, $p<0.0001$) for the total 604 patients as well as each subgroup. ROC curve analysis shows that the daily dose of theophylline under 255 mg in elderly patients is expected to attain a serum level of below 5 mg/L (AUC 0.835, sensitivity 0.740, specificity 0.856), while a daily dose over 918 mg would certainly attain a serum level of above 15 mg/L (AUC 0.780, sensitivity 1.000, specificity 0.998).
CONCLUSIONS: Our results indicate that routine serum level of theophylline even with other confounding factors might not be necessary in elderly patients with a daily dose less than 255 mg. In contrast, close monitoring serum level is warranted in elderly patients with a daily dose higher than 918 mg.

317. Prescribing among Dutch elderly patients in residential homes. *Clementine CM Stuijt, pharmacist*; Onze Lieve Vrouwe Gasthuis, Amsterdam, Netherlands.

PURPOSE: Elderly patients are at risk from inappropriate prescribing due to the higher amount of drug intake as a result of a higher disease burden, unsuitable choice of drug, dose or duration of treatment, or from inadequate monitoring. The risk of falling increases with the amount of cardiovascular and psychotropic drugs used. Drug distribution and metabolism are affected by a number of physical changes, which may predispose elderly patients to adverse drug reactions to drugs. The objective was to determine the influence of a monthly patient review among healthcare professionals (general practitioner, pharmacist, and nurse) on appropriateness of prescribing and health outcomes.
METHODS: Single-blind, controlled trial. Setting: Two residential homes in Purmerend, the Netherlands, supplied by two separated community pharmacies are included. One of the houses, the Rusthoeve (RH), was determined to be the intervention arm; the Jaap van Praaghuis (JVP) received usual care. The intervention group consisted of 54, the controls of 31 persons. Main Outcome Measures: To measure the influence on the outcomes, medical histories of all participants are analysed with special attention on the use of PPI, benzodiazepine, and ACE inhibitors. Appropriateness of prescribing was judged with the Medication appropriateness Index. Drug Therapy Problems are worked up according to Strand et all[1]. The cost of drugs are compared before and after intervention.
RESULTS:

	Not accepted	Accepted	Total
No indication	8	29	37
Start, under Tx	10	9	19
Switch drug	6	7	13
Dose too low	2	7	9
ADR	3	15	18
Dose too high	8	11	19
Total	37	78	115

In the period of 1 month before and 1 month after intervention, no difference is noticed in the mean cost per day.

318. Development of a wellness clinic at a community health center. *Joshua Caballero, Pharm.D.*[1], Garry Souffrant, M.D.[2], Eileen Heffernan, R.N., M.S.N.[2]; (1)Nova Southeastern University, Ft. Lauderdale, FL; (2)Su Clinica Familiar, Harlingen, TX.

PURPOSE: The Lower Rio Grande Valley (LRGV) is located along the U.S.-Mexico border and is home to the poorest people in the U.S., with its major metropolitan areas ranking last in per capita income. The number of uninsured persons living in the LRGV is close to 35%. A large majority of

these patients seek community health centers for discounted or free medical services. Su Clinica Familiar (SCF) is a community health center that sees more than 30,000 patients a year. Among these, approximately 20% have a psychiatric disorder. Unfortunately, there are no specialty psychiatric services offered by the clinic.
METHODS: A collaborative effort was established between a psychiatric clinical pharmacist and SCF to consult on patients with mental health complications referred by their primary care provider. Clinical pharmacy consults were reviewed by the medical director and treatment plan initiated the same day. With Institutional Review Board approval, data collection was completed on all patients seen by the referral service (Wellness Clinic). Patient demographics were collected and cost savings were also evaluated.
RESULTS: Seventy-two of 96 predominantly Hispanic adult patients have attended the Wellness Clinic over the past 13 months. Sixty percent of patients have returned for follow-up. More than 95% of consult recommendations were accepted. The majority of referrals include depression (n=32) and cognitive impairment (n=28). The most common medications for depression and cognitive impairment include sertraline (dose range: 25–150 mg/day) and donepezil (dose range: 5–10 mg/day), respectively. Other referrals included anxiety, insomnia, and smoking cessation. Cost savings for patients and SCF was estimated at more than $3000 and $11,000, respectively.
CONCLUSIONS: The Wellness Clinic was the first clinical pharmaceutical service established at SCF. The services provided were able to evaluate and recommend psychiatric drug management for a predominantly underserved Hispanic population at no cost to patients. Significant cost savings were also realized.

319. Coordinating clinical services and increasing awareness of bisphosphonate-induced osteonecrosis of the jaw. Patrick Skeffington, Pharm.D., M.S.[1], Peggy Yu-Chen, D.M.D.[2], *Sam A. Merabi, D.M.D.*[3], Rosemarie A. Harrington, Pharm.D.[1], Marissa J. Pasqualetti, Pharm.D.[1]; (1)Cambridge Health Alliance, Cambridge, MA; (2)Director of Dental Services CHA, Cambridge, MA; (3)Cambridge Health Alliance Windsor Dental Clinic, Cambridge, MA.

PURPOSE: Use of bisphosphonates for advanced cancer has increased significantly. The association between bisphosphonates and osteonecrosis of the jaw is not widely known among health professionals. The project's purpose is to increase awareness of this association and coordinate prevention, diagnosis and treatment of osteonecrosis of the jaw. The purpose of this study is to assess the need for expanded preventive treatment for osteonecrosis of the jaw.
METHODS: All patients who received intravenous bisphosphonates at Cambridge Health Alliance's (CHA) Oncology Clinics between June 2005 and June 2006 were identified. Patient specific data were collected. These data were cross matched with Dental Clinic data. Twenty-four receiving bisphosphonate therapy during this time frame were identified. Three were concurrently enrolled at CHA's Dental Clinics. The concern is that the remainder have no follow-up dental care. Pharmacy, dentistry, and oncology need to design a system to alert practitioners and to coordinate care of this population. Draft plan includes: 1) weekly dental/bisphosphonate clinic; 2) Baseline screening (panorex x-ray, caries control, needed extractions, dental emergencies) for patients beginning bisphosphonate therapy; 3) Medical history screening to include questions of bisphosphonate treatment; 4) Medical history screening will be scheduled if patients have no dental care; 5) Monthly list of new bisphosphonate patients sent to dental clinic; 6) Patients with osteonecrosis of the jaw will have dental treatment stopped and be referred to oncology.
CONCLUSIONS: Dental care may not be a primary concern for bisphosphonate-treated cancer patients in light of their many medical needs. Coordinated and cooperative management of care between health providers is essential for this vulnerable population. This effort can provide early detection of osteonecrosis for patients currently receiving bisphosphonate treatment and provide completion of invasive dental care for patients prior to bisphosphonate treatment. This will allow for improved patient-centered care.

320. Comparison of a pharmacy and nurse managed anticoagulation service in patients on chronic warfarin therapy. *Samuel L. Ellis, Pharm.D.*, Heather Ulrich, Pharm.D., Marianne McCollum, Ph.D., R.Ph.; University of Colorado School of Pharmacy, Denver, CO.

PURPOSE: Advantages of anticoagulation monitoring services have been well documented in patients receiving warfarin therapy. Pharmacy-managed anticoagulation services have been shown to significantly improve the number of international normalized ratios (INRs) greater than 5.0, the time in therapeutic range, and number of significant adverse events. Data are lacking detailing differences between pharmacy-managed service (PMAS) compared with nurse-managed anticoagulation service (NMAS).
METHODS: After 5 years of operation, a university-affiliated PMAS was converted to a NMAS. Electronic medical records were reviewed between September 2003 and December 2005 for patients receiving chronic anticoagulation therapy. Pharmacy-managed services (9/1/03–8/31/04) were compared with nurse-managed services (1/1/05–12/31/05) for time in therapeutic range and percent of INRs out of range.
RESULTS: 238 patients (146 women) receiving chronic anticoagulation were included in the analysis. Mean age was 65.5 ± 14.4 years. The most common indications for chronic anticoagulation therapy included DVT/PE (43%), atrial fibrillation (34%), and artificial heart valve (8%). A total of 6,409 INRs (3,515 and 2,894 in the pharmacy and nursing service, respectively) were included in the analysis. The percent of INRs in the target range were 49.4% for the PMAS and 50.9% for the NMAS. The percentage of total INR values ≥ 4 were 4.8% vs. 7.9% [OR 0.58 (CI=0.478–0.721); p< 0.0001] for the pharmacy and nursing service, respectively. The PMAS also had significantly fewer INRs ≥ 5 compared with the NMAS [OR 0.52 (CI=0.358–0.755); p<0.0001)]. Time in therapeutic range for those patients with goal INRs of 2–3 were 58.6% in the PMAS compared with 62.5% for the NMAS.
CONCLUSIONS: A PMAS significantly reduced the number of supratherapeutic INRs when compared with a NMAS in patients on chronic warfarin therapy despite no difference in time in therapeutic range. Major bleeding and thromboembolic event rates are being evaluated.

321. Is the medication system in hospitals failing patients on HAART? *Ann M. Snyder, Pharm.D.*[1], Kenneth P. Klinker, Pharm.D., BCPS[2], Joanne J. Orrick, Pharm.D., BCPS[3], Jennifer Janelle, M.D.[4], Almut G. Winterstein, Ph.D.[5]; (1)Pharmacy Practice, University of Florida, Gainesville, FL; (2)Pharmacy Department, Shands at AGH, Gainesville, FL; (3)AETC/ University of Florida, Gainesville, FL; (4)VA Medical Center, Gainesville, FL; (5)Department of Pharmacy Health Care Administration, University of Florida, Gainesville, FL.

PURPOSE: It is recognized that antiretroviral patient compliance is critical for success in treating HIV/AIDS. Little information is available describing the incidence and nature of medication errors in hospitalized patients with HIV/AIDS. Understanding the cause of hospital medication system errors is necessary to avoid jeopardizing HIV/AIDS treatment success.
METHODS: A daily-automated antiretroviral report was used to prospectively evaluate adult patients with HIV admitted to a 618-bed teaching hospital between March 9, 2005, and May 25, 2005. Patients' charts, medication profiles, and medication administration records were reviewed upon admission, throughout hospitalization, and at discharge. Once a potential event was identified, event and cause were further investigated through provider interviews. Once information was collected, an interdisciplinary team reviewed each case to validate error, assess severity, and determine underlying causes.
RESULTS: Sixty-nine HAART- and OI-related medication errors were identified in 26 patients, a 77% rate of occurrence with 2.7 medication errors per patient. An HIV physician and pharmacy specialist randomly assessed 20% of included patients with an investigator error sensitivity rate of 81%. In our current system, 73% of the medication errors were severity C and D of the NCCMERP index for categorizing medication errors. We don't know whether these errors had long-term effects because patients weren't followed after discharge, but some errors were perpetuated or continued in discharge recommendations. The main identified causes were lack of knowledge, drug information resources, and outcome appreciation.
CONCLUSIONS: Prospectively investigating the causes of medication errors provided insight into the nature of HIV-related medication errors and potential preventive strategies. Our investigation showed that the major sources of errors were a lack of knowledge and appreciation for the impact of an incorrect regimen or missed dose. The error diversity and system complexity warrants the need for special attention during medication reconciliation for patients on HAART.

322. *Candida tropicalis* endocarditis successfully treated with liposomal amphotericin. *Colleen M. Terriff, Pharm.D.*[1], Lisa T. Kostelac, Pharm.D.[1], Mark W. Garrison, Pharm.D.[2]; (1)Deaconess Medical Center, Spokane, WA; (2)Washington State University College of Pharmacy, Spokane, WA.

PURPOSE: Published reports of *Candida tropicalis* endocarditis in adults are rare. Nonsurgical treatment of neonatal or pediatric fungal endocarditis has included amphotericin B alone or in combination with 5-FC, miconazole or liposomal amphotericin B (LAB). We describe the successful clearing of *C. tropicalis* in blood, line, and urine cultures plus resolution of native mitral valve endocarditis in an adult male treated with LAB and caspofungin after unsuccessful treatment with caspofungin alone.
METHODS: A 54-year-old male presents with fevers and a nonfunctioning Port-a-Cath, status post surgical resection and adjuvant chemotherapy for head and neck squamous cell carcinoma. Medical history includes type II diabetes, hypertension, hyperlipidemia, malnutrition, and renal insufficiency requiring dialysis. Multiple urine, blood, and line cultures subsequently grew *C. tropicalis*. Transthoracic echocardiograms (TTE) taken every 2 weeks documented vegetational changes in mitral valve.
RESULTS: Caspofungin IV 70 mg load followed by 50 mg daily was initiated

and unsuccessful at clearing *C. tropicalis* from blood after 4 weeks of therapy. TTEs displayed progressive changes in mitral regurgitation and presence of posterior leaflet vegetation. After switching to LAB IV 5 mg/kg q36h and re-adding caspofungin, blood cultures were negative and mitral valve vegetation cleared. Details on cultures, MIC's, antifungal therapy, successive echo-cardiograms, and hospital course will be shared. Although the patient's endocarditis clinically improved and fungal cultures cleared, his hospital course was complicated and prolonged.
CONCLUSIONS: Four weeks of caspofungin therapy alone did not effectively clear *C. tropicalis* blood cultures or prevent mitral valve thickening and vegetation. Subsequent initiation of LAB plus caspofungin therapy combined with line changes cleared the candidemia.

323. Evaluation of an automated dose check algorithm and pharmacist responses to alerts for inappropriate vancomycin dosing in a large academic medical center. *Peggy S. McKinnon, Pharm.D.*[1], Jeffrey R. Blunt, Pharm.D.[1], Richard Reichley, B.S. Pharm[1], Ed Casabar, Pharm.D.[1], Thomas C. Bailey, M.D.[2]; (1)Barnes-Jewish Hospital, St. Louis, MO; (2)Washington University, St. Louis, MO.

PURPOSE: Medical Informatics at BJC Healthcare and Washington University operates the pharmacy expert system DoseChecker at Barnes-Jewish Hospital (BJH) which examines medication orders and generates alerts to pharmacists for under and overdosing of medications.
METHODS: This study evaluated all DoseChecker alerts generated for vancomycin with estimated trough values < 5 µg/mL and > 23 µg/mL from December 2005 to May 2006. Pharmacist action and the disposition of the alert were recorded and evaluated based on predicted trough values.
RESULTS: Over 6 months, 2454 alerts for predicted trough values < 5 µg/mL or > 23 µg/mL were generated on 14,311 vancomycin orders. 13.4% alerts were for predicted trough < 5, 14.1% for trough 23–25, 22.7% for trough 26–30, 14.5% for trough 31–35, 9.9% for trough 36–40 and 23.1% for trough > 40. Pharmacists screened all alerts. In 22.4% alerts were no longer active at time of review or no alert disposition was recorded. Physicians were contacted in 14.8% of alerts; doses were changed in 91.1% of these cases. The number of alerts resulting in dose change was highest for predicted troughs < 5 µg/mL with 20.8% resulting in change. Dose change % also increased with higher predicted troughs: 4.2% of alerts for trough 23–25 resulted in change, 6.5% for trough 26–30, 12.0% for trough 31–35, 9.4% for trough 36–40, and 19.4% for trough > 40. The most common reasons for no dose change were continued monitoring by the pharmacist or pending vancomycin level (59.5%), adequate drug levels documented (16.6%), or assessment that the patient's condition warranted the current dose (16.5%).
CONCLUSIONS: Computer-assisted pharmacist alerting for vancomycin dosing facilitates appropriate dosing and results in dose change in about 15% of alerts. Increasing the upper threshold for an alert may decrease the number of unnecessary alerts and allow pharmacists more time to focus on patients with more extreme predicted high and subtherapeutic troughs.

324. Medication utilization evaluation of low molecular weight heparin: nadroparin and enoxaparin. *Serene Yeow, B.Sc., (Pharm)(Hons)*, Joy Tan, B.Sc., (Pharm)(Hons), Ian Wee, B.Sc., (Pharm)(Hons), Jonathan Seah, B.Sc., (Pharm)(Hons); Changi General Hospital, Singapore, Singapore.

PURPOSE: This study was carried out to determine (1) the prescribing pattern, drug interactions, and adverse events among inpatients prescribed with low molecular weight heparins (LMWH): nadroparin and enoxaparin; (2) the extent of adherence of clinical practice to the hospital's LMWH guidelines; and (3) recommendations of appropriate measures to encourage rational prescribing and monitoring of LMWH therapy within the hospital.
METHODS: A retrospective review of clinical case notes, laboratory data, and medication records for all inpatients prescribed with LMWH during June 2004 was carried out.
RESULTS: 107 patients who received either nadroparin or enoxaparin were identified. Nadroparin was most commonly prescribed for the prevention of deep vein thrombosis after a surgical procedure (54.1%). Enoxaparin was most commonly prescribed for the treatment of acute coronary syndrome (52.6%). Adverse events to LMWH therapy reported included elevated ALT/AST levels, hemorrhage, thrombocytopenia, hematoma and bruising. About half of the cases (50.9%) were prescribed with a dosage regimen that complied with the LMWH guidelines. Throughout LMWH therapy, 46.8% and 48.6% of the cases had their platelet and hemoglobin levels monitored respectively; however, the occult blood test was carried out in only 5.5% of the cases. Anti-Xa monitoring was not routinely done, even in cases where it was preferred or required.
CONCLUSIONS: Nadroparin and enoxaparin were generally prescribed for their registered indications. Compliance of LMWH dosing to the established guidelines should be advocated and the importance of dosage adjustment in renally impaired patients should also be emphasized. Although LMWH therapy was generally well-tolerated, routine monitoring of platelet and hemoglobin levels, and occult blood tests should be encouraged, especially in patients predisposed to bleeding. In conclusion, an increased awareness of the current LMWH guidelines should be advocated within the hospital.

325. Medication therapy management in a dispensing pharmacy: a case series of successes and challenges. *Anne M. Schullo-Feulner, Pharm.D.*, Mary Ann Kliethermes, Pharm.D., Shiyun Kim, Pharm.D., Jessica Tilton, Pharm.D., Annette Pellegrino, Pharm.D.; University of Illinois at Chicago, Chicago, IL.

PURPOSE: The Medicare Modernization Act (MMA) of 2003 presented a reimbursable means for qualified health care providers to offer cognitive drug utilization services designed to optimize therapeutic outcomes for individual patients. Who will provide these services, as well as how they are to be provided was left intentionally vague, with the goal of evaluating differing programs on cost effective outcome measurers in 2007. The Medication Therapy Management (MTM) program at the University of Illinois at Chicago (UIC) is a 5-year-old, outpatient pharmacy based clinic. It is staffed by four pharmacists, a clinic manager, and one full-time technician. Patients are referred by any UIC healthcare professional recognizing a patient (1) with multiple medications, disease states or providers; (2) having difficulty with medication self-management or adherence; or (3) with significant medical literacy deficits. The clinic's mission is consistent with the purpose of MTM described in the MMA: to optimize therapeutic outcomes while reducing the risk of adverse events. The poster will be an in-depth look at the relationships built with the clinic's primary customers: (1) our patients and their care givers, (2) UIC health care professionals, and (3) the out-patient pharmacy that provides us both medication re-fills and our current facility. Benefits the customers listed above receive from UIC's MTM program will be discussed as potential justifications for similar clinics in the ambulatory setting. The poster will examine therapeutic and economic successes and review challenges faced by the MTM clinic in a case series format.

326. Effects of medication error monitoring in female medical ward at Rajavithi Hospital. *Suratchada Kongsri, Doctor of Pharmacy*; Mahasarakham University, Mahasarakham, Thailand.

The objectives of this study were to measure incidences of medication errors, to identify contributing factors, and to measure effects of the monitoring and the solving of these medication errors by pharmacists in the female medical ward at Rajavithi Hospital. A prospective study was conducted from August 8, 2005, to September 20, 2005. A total of 26 patients who received oral medication were observed by the investigator. There were 29 medication errors identified in 13 patients (50.00%): prescribing errors (19, 1.04%), administration errors (6, 0.22%), and post-dispensing errors (4, 0.22%). Most were found in cardiovascular drugs (9, 47.40%). A major contributing factor was adjusting the prescription. Most physicians did not correct the prescription (52.60%) after they received the pharmacist's recommendation to complete dose or dosage regimen in the prescription. The effects of solution were no change to the patients (13, 68.38%). Most of the errors occurred because the lack of verifying drug with a medication sheet before giving to the patients (4, 66.66%). Half of medication administration errors found in cardiovascular drugs (3, 50.02%). The pharmacist corrected the medication administration error by directly consulting with responsible nurses (5, 83.33%). For post-dispensing error, the errors were found were wrong labeling of dosage regimen (2, 50.00%) and wrong amount of drug (2, 50.00%). Antibiotics were the major medication classes involved in this kind of error (2, 50.00%). All post-dispensing error were caused by human error (100%). Patients received correct medications (3, 75.00%) after intervention by changing drug label. Most severity of errors was category C; the medication errors occur, but have no harm to the patients. Overall, monitoring and solving of medication errors by hospital pharmacist significantly reduced the incidence of medication errors. Pharmacists' role in monitoring of error could help to solve and prevent errors, therefore ensuring that the patients are being provided with correct, safe, and effective drug therapy.

327E. Using failure modes and effects analysis to develop an insulin infusion protocol with a low risk of causing hypoglycemia. *Rick M. Baker, Pharm.D., BCNSP*; Mt. Carmel Regional Medical Center, Pittsburg, KS.

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328. Effects of pharmaceutical care in patients with cancer at Roi-et Hospital. *Boonsong Minphimai Sr., Doctor of Pharmacy*; Mahasarakham University, Mahasarakham, Thailand.

The study of pharmaceutical care for patients with cancer groups at the surgical wards of Roi-et Hospital was conducted during March 2005 to April 2005. The objective of this study was to determine the effects of drug-related problems (DRPs), knowledge about disease and treatment, adverse drug reactions(ADRs), medication errors, quality of life of patient with cancer who is taking chemotherapy. Sixty-four patients with cancer participated. The pharmacist detected 253 DRPs (3.95+1.53).The most common DRPs were

adverse drug reaction, 217 problems (85.78%). One hundred and four problems were resolved (41.10%) Analyzing the problems with medication errors according to the process of drug use, the errors in each step were found as follows: prescribing 8.39%, orders receiving 17.18%, dispensing 8.04%, and preparing 3.25%. Knowledge of scores was statistically significant in every aspect ($p<0.05$). The quality of life of patients with cancer was not different in each drug-used cycle. The pharmaceutical care in patients with cancer was satisfied because most DRPs and medication errors were found, resolved and prevented. In addition, patients have more knowledge of good health activities. The pharmaceutical program should be performed continuously to promote efficiency and the most safe drug used.

329. Annual assessment of risk points in medication management. *Julie M. Alizio, Pharm.D.*; McKesson Medication Management, Bridgewater, MA.

PURPOSE: Each health care facility needs to be proactive in its goal to improve patient safety. It involves identifying both potential and actual risks, determining the causes, and instituting changes.
METHODS: Bridgewater State Hospital selected a high-risk process for assessment utilizing the Failure Mode Effect Analysis. The medication-ordering flow process was analyzed. It required a time period of 8 months involving a multidisciplinary team. Each step of the process, starting with the physician's evaluation of the patient's condition and ending with the administration of the medication, was evaluated for potential or real risks, the causes, and potential solutions. A medication management risk assessment form was developed. Each process was rated for probability of high to no risk. Then the risk was categorized from life-threatening to low disruption. Finally a determination was made as to the state of preparedness. A final score was given to each process. Those areas that had scores of 10 or higher were identified as requiring immediate attention.
RESULTS: Three areas were identified: reconciliation of medications, after-hours pharmacist review of medication orders, and adverse drug reaction reporting. Multidisciplinary teams were created to work on these issues. Policies and procedures for each were developed and implemented. These changes were supported and coordinated by management and staff together, and are continually being reevaluated for improvement.
CONCLUSIONS: Although our facility may be unique from other healthcare facilities because it is a forensic state facility, it also has the distinction of being one of the few correctional sites in the country to have attained JCAHO accreditation. We recognize the importance of medication safety. This assessment tool will be used annually to identify potential problem areas.

330. Development of a structured, integrated medication-reconciliation strategy from hospital admission to discharge. *Jacqueline Wong, B.Sc.Phm.*[1], Olavo Fernandes, Pharm.D.[1], Jana Bajcar, M.Sc.Phm., Ed.D., FCSHP[2], Shabbir Alibhai, M.D.[1], Kelly Gomes, B.Sc.[1], Tim Tripp, B.Sc.MLIS[1], Gary Wong, B.Sc.Phm.[1], Annemarie Cesta, B.Sc.Phm.[1], Stephanie Ong, B.Sc.Phm.[1], Jin Huh, B.Sc.Phm.[1], Jeff Nagge, Pharm.D.[1]; (1)University Health Network, Toronto, ON, Canada; (2)University of Toronto, Toronto, ON, Canada.

PURPOSE: Medication discrepancies can occur frequently at hospital admission and discharge. These discrepancies are important as they may contribute to drug-related problems and adverse drug events. This study aims to develop a multidisciplinary, structured, integrated medication-reconciliation strategy from hospital admission to discharge.
METHODS: Key elements of the development were a baseline measurement of discharge medication discrepancies (n=149), a literature review, and a needs assessment. The needs assessment consisted of interviewing experienced pharmacists in the field of medication reconciliation (n=9) and consulting key stakeholders (n=7) who included physicians, nurses, and pharmacists. The combined information was used to create an optimal multidisciplinary practice model to reduce medication discrepancies.
RESULTS: The strategy consists of a synchronized electronic platform to support a multidisciplinary practice model that includes admission and discharge reconciliation. On discharge, an electronic medication information transfer system generates a computerized prescription, a letter used to communicate hospital medication information to community healthcare professionals, a patient medication grid, and a patient medication wallet card. The electronic system facilitates electronic collection and transfer of medication information from the time of admission to discharge to facilitate both admission medication reconciliation and discharge medication reconciliation. It also allows for coding of medication discrepancies.
CONCLUSIONS: Through the use of a baseline evaluation of discharge medication discrepancies, a literature review, and a needs assessment, a structured, integrated medication-reconciliation strategy was created. This synchronized strategy may reduce medication discrepancies. It is anticipated that this strategy can be adapted to other institutions.

331. Pharmacovigilance in space. *Vernie R. Daniels, M.S., R.Ph.*[1], Lakshmi Putcha, Ph.D.[2], Richard McCluskey, M.D.[2]; (1)Wyle Laboratories Life Sciences Group, Houston, TX; (2)NASA - Johnson Space Center, Houston, TX.

PURPOSE: Pharmacovigilance is the science of and activities relating to the detection, assessment, understanding, and prevention of drug-related problems. Over the past decade, pharmacovigilance activities have contributed to the development of numerous technological and conventional advances focused on medication safety and regulatory intervention. As our civilization continues to expand its frontiers of exploration and discovery into space, we are discovering a need to develop proactive countermeasures that address the conditions of everyday life in space. One goal or countermeasure of this research is to address how medications are prepared for space travel and monitored for safety.
METHODS: A NASA pharmaceutical research project was designed to examine stability of a selected group of medications with various therapeutic classifications, dosage forms, and delivery systems, exposed to the conditions of Space Shuttle flight and storage on the International Space Station. Preparation for this experiment revealed three areas in need of pharmacovigilance intervention: (1) medication packaging and containment, (2) regulatory and security concerns, and (3) dosage, efficacy, and medication safety.
RESULTS: Medication enclosures and pharmaceutical kits are designed to securely contain the medications and prevent astronaut injury. Operating procedural and regulatory documentation is customized to address the unique security concerns of transporting, storing, and handling prescription and controlled substance medications intended for space travel. Chemical analysis outcomes from the medications returned from space flight are compared with ground-controlled and ground simulation study outcomes. These data will determine if manufacturer label claims for dosage, efficacy, and stability are valid for medications exposed to the conditions of space.
CONCLUSIONS: The science of pharmacovigilance should begin to explore customized regulatory and pharmacy practice interventions that address the unique concerns of space travel and exploration. These interventions will be crucial in the development of a blueprint for the next frontier of pharmaceutical research and clinical practice.

332. Development of Korean guidance for pregnancy exposure registries. *Su Hee Kim, M.D.*[1], Jung Mi Oh, Pharm.D.[2], Wan Gyoon Shin, Pharm.D., Ph.D.[3]; (1)College of Pharmacy, Sookmyung Womans' University, Seoul, South Korea; (2)Graduate of school of pharmacy, Seoul National University, Seoul; (3)College of Pharmacy, Research Institute of Pharmaceutical Sciences, Seoul National University, Seoul, South Korea.

PURPOSE: During clinical development of new drugs, pregnant women are excluded from clinical trials. Therefore, at the time of drug's initial marketing, human data on the effects of the drug during pregnancy are rarely available. These problems can be overcome through the use of prospective pregnancy exposure registries that are recognized as one method for identifying major risks for a drug exposure during pregnancy. In America and Europe, the guidance for pregnancy exposure registries is being used, but it is not prepared yet in Korea. Therefore, the ultimate goal of this study is to develop the guideline for pregnancy exposure registries applicable to our country.
METHODS: The international guidances, regulations, and laws related to pregnancy exposure registries were investigated and assessed. Especially, the guidance of Food and Drug Administration in the United States, the European Medicines Agency, and the International Conference on Harmonization were focused in this study. We also researched Korean Post Marketing Surveillance guideline and pharmaceutical affairs law. Finally, a pharmaceutical company-based pregnancy registry program was referred to for our study.
RESULTS: This newly developed guidance for pregnancy exposure registries was composed of two parts, the principles and the discussion. The principles included the purpose, definition of "pregnancy exposure registries," and its necessity. In the discussion, the criteria for possible candidate drug were presented, and all potential sources of human pregnancy data and data quality and standardization were also reviewed. This guidance included research methods, the specific requirements for reporting data of pregnancy exposure, concrete contents included in the report form, and their actual examples were developed.
CONCLUSIONS: This guidance provided the ways to establish pregnancy exposure registries for monitoring the outcomes of drug exposed in pregnancies. It was the standardized and internationalized guideline that was also applicable in Korea.

333. Establishment of a pharmacy nephrology clinic within an ambulatory nephrology service at the Baltimore VA Medical Center. *Chanel Agness, Pharm.D., BCPS*; University of Maryland, School of Pharmacy, Baltimore, MD.
PURPOSE: Health People 2010 has designated chronic kidney disease (CKD) as a public health priority for the United States to focus on for the beginning of this century. Chronic kidney disease is largely an undermanaged disease state where pharmacists can have a significant impact in delaying disease progression by managing disease-related complications and risk factors. The purpose of this pharmacy clinic is to partner with the ambulatory nephrology service at the Baltimore VA Medical Center to optimize the care of patients with CKD through pharmacologic and nonpharmacologic interventions. The

service provides support to improve drug therapy management in patients with CKD. Some of the pharmaceutical care services include medication and lifestyle education, and optimization of medication regimens relating to kidney disease in accordance with national guidelines.
CLINIC DESCRIPTION: Between August 2005 and December 2005 the clinic was established. A scope of practice was discussed with and approved by the Chief of Nephrology as a part of the Baltimore VA's credentialing process. The scope of practice allows the clinical pharmacist to perform a comprehensive medication review, conduct a physical exam, order laboratory data, and initiate, adjust, or discontinue medications with the attending nephrologist's approval. The pharmacy clinic is a part of the nephrology service which is supervised by the Chief of Nephrology. The clinic is supervised by one clinical pharmacist and the current clinic schedule includes one-half day of clinic per week. The clinic accepts only referrals from other nephrology clinic providers within the service at this time. The clinic also serves as a teaching site for University of Maryland doctor of pharmacy students and pharmacy residents to develop skills managing patients with CKD.
PATIENT POPULATION: The patient population served includes pre-dialysis patients with a documented diagnosis of kidney disease who have previously been evaluated by nephrology clinic providers.

334. A comparison of estimated creatinine clearance via Cockcroft-Gault equation and estimated glomerular filtration rate via Modified Diet in Renal Disease equation as a method of estimating renal function to determine dosage modification in renal impairment. *Becky J. Szymanski, Pharm.D.*, Erin R. Scruggs, Pharm.D. Candidate; NorthEast Medical Center, Concord, NC.

PURPOSE: Many medications are renally eliminated and require dosage modification (DM) for impaired renal function (RF). The usual measure of reduced RF for DM is creatinine clearance (CrCl). There are numerous methods to determine estimated CrCl. The most common is Cockcroft-Gault (CG). Reportedly, glomerular filtration rate (GFR) via Modified Diet in Renal Disease (MDRD) equation is a better estimate of RF. Northeast Medical Center's lab calculates GFR via MDRD for all patients. This study compares CrCl to GFR to determine whether a difference exists that would change the DM and whether the pharmacy protocol could use GFR for making DMs.
METHODS: Patients with assessments based on the pharmacy department's renal DM protocol between March 13 and June 7, 2006, were chosen. Patients with insufficient data were excluded. Data includes gender, age, height, actual weight, ideal body weight (IBW), serum creatinine (SCr), GFR, medication, dose ordered, and DM. Clinical relevance of the DM was determined by comparing the action taken based on CrCl and what the action would have been if GFR were used.
RESULTS: Of 164 patients, 55 were male and 109 were female. Average age, IBW, and SCr were 75, 59 kg, and 1.79 mg/dL respectively. Antibiotics were most frequently adjusted. The use of GFR would have led to a different DM 27% of the time. Patients with significant differences between GFR and CrCl had an average age of 84, average IBW of 54 kg, and average SCr of 1.27 mg/dL.
CONCLUSIONS: The use of GFR to determine DMs is acceptable the majority of the time. We recommend pharmacists use GFR provided by the lab and clinical judgment to make assessments of RF for DMs. Additionally, alternative methods for estimating RF may be necessary for patients greater than 80 years of age with low IBW and relatively normal SCr.

335. Parenteral nutrition prescribing trends in a community hospital setting: an opportunity for clinical intervention. *Jennifer L. Ash, Pharm.D.*[1], Randolph Cole, M.D.[2], Rochelle Alexander, R.D.[2]; (1)Rutgers, The State University of New Jersey, Ernest Mario School of Pharmacy, Piscataway, NJ; (2)Holy Name Hospital, Teaneck, NJ.

PURPOSE: There is a lack of literature detailing physician prescribing of parenteral nutrition (PN) in a community hospital setting. The objective of this observational study was to evaluate PN-prescribing habits of physicians in a 351-bed suburban community hospital to identify areas for clinical intervention and education, and to assess the need for a nutrition support team (NST).
METHODS: Data collected included appropriateness of PN using ASPEN criteria, use of concurrent oral medications/oral diet/tube feedings, duration of prescribed PN, and frequency of laboratory monitoring. The PN prescription for individual patients was evaluated for calories (kcal/kg/day), protein (g/kg/day), and lipid administration.
RESULTS: Data were collected on all patients receiving PN over a 2-week study period, representing 74 patient-days of PN. The majority of PN was prescribed in the intensive care unit (39.2%) or in the postoperative unit (36.5%). Indications for PN were: dysphagia (30.8%), small bowel resection (15.4%), cancer (15.4%), pancreatitis (15.4%), and others (23.1%). Only 46.2% of patients had an ASPEN-identified clinical indication appropriate for PN. 15.4% of the patients had a trial of enteral nutrition prior to PN, while 62.2% of patients had a concurrent oral diet or enteral feedings. In evaluating the appropriateness of nutrient delivery, 39.2% of patients were prescribed PN meeting recommended nutrient intake goals (20–35 kcal/kg/day, dependent on clinical status). 33.8% of the PN orders provided a caloric intake above recommended goals representing overfeeding (42.9 ± 6.1 kcal/kg/day), and 27.0% provided a caloric intake below recommended goals suggesting underfeeding (13.0 ± 4.1 kcal/kg/day).
CONCLUSIONS: The majority of patients received PN for inappropriate indications and were fed suboptimally. As a result, a NST was formed consisting of a physician, a registered dietician, and a clinical pharmacist to provide education and clinical interventions. Evaluation of the impact of this newly formed team in a community hospital is ongoing.

336. Parenteral nutrition use in a surgical unit: factors associated with inappropriate use. *Maria H. Duarte, DR*; Garcia de Orta' Hospital, Almada, Portugal.

PURPOSE: Parenteral Nutrition (PN) is an important therapy for critically ill patients who have nonfunctioning gut. The aim of our study was to determine the appropriateness of the prescription/pharmacist's recommendations of Parenteral Nutrition in our surgical unit based on the American Society for Parenteral and Enteral Nutrition (ASPEN) 2002 Guidelines. The authors wanted to identify the factors associated with the inappropriate use and find some solutions.
SETTING: Surgical and Pharmacy Department in a general Hospital.
METHODS: A retrospective review of adult patients prescribed with PN in 2004/2005 was undertaken. Data on patient demographics, diagnoses, indications, and duration were collected. Clinical pharmacists determined the total daily calories need using a previous developed software based on the Harris Benedict Equation (Main Outcome Measures, Number of PN prescribed, Return to oral feeding, Duration of administration (days), Diagnoses).
RESULTS: Data on 110 patients receiving PN were collected, 57 in 2004 and 53 in 2005. The average length was 11.6 and 13.2 days(2004/2005). The surgical patients (82.5% and 73.6%) received it for postsurgical complications and 42.1%/54.7% had malignancies. PN was prescribed for less than 7 days in 28.1%/39.6% of the patients and was considered inappropriate. We considered the prescription appropriate in 42.1% in 2004 and 41.5% in 2005 based on the above guidelines.
CONCLUSIONS: Inappropriate prescriptions were attributed to the insufficient number of jejunal tube feeding in uncomplicated surgical procedures or obscure indications for support such as cachexia in oncological patients. The authors decided to create a Nutrition Support Team for the management of the PN in the surgical unit.

337. Promoting patient safety: relationship between hospital and community pharmacy. *Maria H. Duarte, DR*, Armando S. Alcobia, DR; Garcia de Orta' Hospital, Almada, Portugal.

PURPOSE: Hospitalization is a great opportunity to improve patients' medication use. The objectives of this study were to identify and solve Drug Related Problems (DRP) in elderly patients (more than 65 years) fully awake and oriented of a Medicine Ward and write a reference letter to the community pharmacist.
METHODS: Prospective Study (4 months). A Clinical Pharmacist interviewed patients or a member of his family, using a previous validated questionnaire (1 month pilot study). Identification and classification of DRP using the Second Granada Consensus. Written recommendations were established informing of the DRP and drug prescriptions after the patient's discharge. This study was validated by the ethical committee.
RESULTS: This study included 34 patients. Data from the interview group were as follows: average age 74.5 years; mean hospital stay 8.47 days; mean number of drugs per patient at admittance was 5.2 and during hospitalization 6.8. Arterial Hypertension was the most common diagnose (88.2%), followed by Diabetes Mellitus II (44.1%), Cardiac Insufficiency (32.4%), Renal Failure and Asthma both with 8.8%. The average number of diagnostics per patient was 3.7, and 67.6 % of the patients were usual customers of the same community pharmacy. In the interview group were found 68 DRP: 52.9% related to need, 13.2% concerning effectiveness, and 33.9% safety problems. 32.4% of the DRP were admission's motive. Pharmacists' interventions (58) were distributed over two categories: 55.2% prescribing related and 44.8% patient related. Only four of the 20 pharmacies reported to us the pharmacotherapy follow up of our patients.
CONCLUSIONS: The applied questionnaire provides sufficient information to identify, prevent, and solve DRP. Only 4 of the 68 DRP were not solved at discharge. We are using this study as a model for Clinical Practice and to interact with Community Pharmacy.

338E. A retrospective analysis of the impact of erythropoeitic growth factor utilization on transfusion requirements in patients with AL amyloidosis undergoing autologous SCT. *David M. Baribeault, B.S., BCOP*, Bhavesh Shah, B.S., Finn Kathleen, R.N., M.S.N., RNP, Seldin David, M.D., Quillen Karen,

M.D., Sanchorawala Vaishali, M.D.; Boston Medical Center, Boston, MA.

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339. Implementation of a pharmacist-directed research and clinical program at a medical oncology private practice office. *Siu-Fun Wong, Pharm.D.*; Western University of Health Sciences, College of Pharmacy and Hematology Oncology Medical Group of Orange County, Inc., Pomona, CA.

PURPOSE: Currently, few pharmacists work in a physician-owned practice office. In oncology practice, the success of a practice is highly dependent on providing efficient patient care, particularly with cutbacks in MediCare reimbursements. The practice model of a pharmacist-directed research and clinical program is described to demonstrate the cost-effectiveness of an oncology pharmacist in a private practice office.
METHODS: The private practice group consists of 8 medical oncologists and 3 nurse practitioners. A full-time pharmacy faculty initiated a clinical research program at the office in 2002 with 60% FTE effort. Responsibilities included serving as principal investigator, protocol selection/development/activation, regulatory documentation, contract negotiation, patient accrual/enrollment/management/assessment, and data management. Additional clinical and administrative services were provided as needed. Research funding serves as the sole source of salary reimbursement.
RESULTS: A total of 24 protocols have been activated, including 6 pharmacist principal investigator-initiated trials with 113 patients enrolled so far. An extended research program with the affiliated hospital cancer center was established, resulting in membership of several disease-management groups, development of clinical trials in these groups, and initiation of a co-funded pharmacy research fellowship. Additional accomplishments included standardization of chemotherapy orders, administrative analyses leading to personnel justification for pharmacy technician and data managers, and medical economic analysis to optimize drug therapy for major cancer types. The pharmacist actively engages in patient education and support groups and provides direct patient care activities including pharmacotherapy consultation and education. The site provides a progressive practice environment for teaching activities. Cost evaluations concluded a benefit to the practice.
CONCLUSIONS: A trained oncology pharmacist in a private practice office is a great enhancement to benefit the patients, health care providers, administrators and the practice. Furthermore, the economic assessment showed that an oncology pharmacist in a private practice office is cost effective.

340. Development of Korean clinical trial guideline in the pediatric patients. *Jee Hyun Suh, Ph.D..Candidate*[1], Jung Mi Oh, Pharm.D.[2], Wan Gyoon Shin, Pharm.D., Ph.D.[3]; (1)Graduate of School of Pharmacy, Seoul National University, Seoul; (2)College of Pharmacy Seoul National University, Seoul; (3)College of Pharmacy, Research Institute of Pharmaceutical Sciences, Seoul National University, Seoul, South Korea.

PURPOSE: The procedures for drug development through clinical trials in pediatric patients have been widespread and rely on past experiences. Even if the FDA has tried to find ways to provide more specific information for drug development in pediatric patients, their ways are too limited to cover complete procedures and to apply to the Korean clinical trials. In order to overcome such limits, we established a new guideline that includes detailed contents and procedure for the pediatric clinical trials based on Korean Good Clinical Practice (KGCP) and pharmaceutical affairs law on the basis of the ICH guideline.
METHODS: The international and domestic regulations, laws, guidelines, such as guidances of FDA and ICH, KGCP, and articles related to the pediatric clinical trials were investigated and assessed. Several Korean guidelines for the clinical trials were also investigated for the purposes, general principles, study-methodology, and ethical issues.
RESULTS: Our newly developed guideline consisted of two parts, the introduction and the discussion. The introduction consisted of the purposes, general subjects, pediatric patients classified by age, and the outline of clinical trials. The discussion included the pediatric-specific plans and procedures for clinical trials, pediatric pharmacokinetics and pharmacodynamics, study-methodology, selection of subjects and criteria for inclusion and exclusion, monitoring, case report format, quality and management of data, multiple-center trial, safety and efficacy evaluation, reporting of trial results, the statistical analysis and monitorings, which were specific for the pediatric patients. Indispensable contents such as pediatric-specific end points, description of amount of blood (on mL/kg or percentage of total blood volume basis), and number of venipunctures were established. The guideline included ethical issues for vulnerable pediatric patients, providing legal recruitment, informed consent, minimizing risk, and minimizing distress.
CONCLUSIONS: The Korean Clinical Trial Guideline in the Pediatric Patients, which is suitable for the Korean clinical environment while harmonizing with international standards, was established.

341. Development of a preprinted pediatric discharge prescription form. *Elisabeth M. Mouw, Pharm.D.*, Sandra S. Garner, Pharm.D., Gautham Suresh, MD; Medical University of South Carolina, Charleston, SC.

PURPOSE: Pediatric prescribing errors are common in inpatient and outpatient settings. Although preprinted medication order forms are reported to reduce prescribing errors, they have not been studied for hospital discharge prescriptions. The purpose of this study was to develop a preprinted discharge prescription form and assess its acceptance by prescribers.
METHODS: The components and format of an ideal pediatric prescription as recommended by experts, including the Institute for Safe Medication Practices, were used to design a preprinted prescription form. The form includes prompts for patient weight, indication, allergies, dosage form, dose, route, frequency, dose calculation, and refills. It also has preprinted decimal points, field restrictions, and forcing functions to ensure accurate prescribing. Ten prescribers (residents and nurse practitioners) used the preprinted form to complete discharge prescriptions for 5 mock patients. Prescribers then rated the form's ease of use, readability, and potential to decrease errors on a survey using a Likert scale. Additional suggestions were also requested.
RESULTS: Of the 10 prescribers studied, 8 agreed or somewhat agreed that the preprinted prescription form was easy to understand and use; 9 agreed or somewhat agreed that the form was easy to read; and 9 agreed or somewhat agreed that the form would decrease prescribing and dispensing errors. However, only 4 agreed or somewhat agreed that the form would reduce the time required to write prescriptions, while 5 agreed or somewhat agreed that they preferred the form to the traditional prescription blank.
CONCLUSIONS: Overall, prescribers reported positive opinions regarding the preprinted pediatric discharge prescription form's ease of use and potential to reduce errors. However, as with any new process, they were concerned about the increased time requirement. Design of new prescription methods should ideally include an evaluation of user acceptance and utility.

342. Applying benchmarks to aprotinin utilization. *Blane Schilling, M.D.*[1], K. Alicia Brand, Pharm.D.[2]; (1)Aspen Healthcare Metrics, Englewood, CO; (2)MedAssets, Bridgeton, MO.

PURPOSE: Marketing efforts and placebo-comparison trials fostered a belief that use of aprotinin, which costs approximately $1000 per case, reduces rates of stroke and bleeding in patients undergoing coronary artery bypass graft surgery (CABG) more so than other less costly agents. However, there is a lack of current comparison trials against less costly agents looking at these same outcomes. The objective of this study was to determine if there is a cost benefit in decreasing aprotinin use without compromising safety.
METHODS: Based on evaluation of available literature, it was determined that aminocaproic acid (ACA) offers similar benefits in reduced bleeding complications with no increased risk. A benchmarking analysis, based on diagnosis-related group (DRG) codes 107 and 109 representing coronary bypass with and without cardiac catheterization, respectively, was conducted using available data from 53 acute care facilities. The analysis was used to compare utilization rates of aprotinin and ACA within these DRGs, as well as rates of hemorrhages complicating procedure and iatrogenic stroke within the two drug groups.
RESULTS: The available data represented a total of 7672 patients. Within DRG 107, aprotinin was used in 18% of patients and ACA was used in 45%. Rates of hemorrhages complicating procedure were 3% and 4%, respectively; rates of iatrogenic stroke were 2% and 1%, respectively. Within DRG 109, aprotinin was used in 16% of patients and ACA was used in 48%. Rates of hemorrhages complicating procedure were 4% and 2%, respectively; rates of iatrogenic stroke were 1% in both groups.
CONCLUSIONS: Aminocaproic acid offers similar benefits to aprotinin at a lower cost, and utilization of ACA could be approximately three times that of aprotinin within the two DRGs included. Initiation of appropriate practice guidelines, as well as recent articles questioning its safety, will assist in reducing utilization and expenditure of aprotinin.

343. Linezolid: a well-used or a misused resource? *Branca Teixeira, Pharm.D.*, Teresa Cunha, Pharm.D., M.Sc., Bárbara Santos, Pharm.D., Gustavo Dias, Pharm.D., José das Neves, Pharm.D., Jorge Brochado, Pharm.D.; Pharmacy Department St Antonio General Hospital, Porto, Portugal.

PURPOSE: Determine the evolution of linezolid use since its prescription was first authorised in St. Antonio General Hospital. Identify and characterize the patients' population treated with linezolid. Establish the economical impact of linezolid use inpatients and outpatients in St. Antonio General Hospital. Establish guidelines on the pharmacist's role in ensuring the best use of linezolid in the treatment of serious Gram positive infections.
METHODS: Retrospective analysis of pharmaceutical records of inpatients and outpatients treated with linezolid between September 2004 and June 2006 in St. Antonio General Hospital. Analysis of clinical data and pharmacotherapeutic follow up of 22 inpatients treated with linezolid between April 2006 and June 2006. Literature review.
RESULTS: Since linezolid prescription was first authorized in September

2004 until June 2006, 934 inner and 127 outpatients have been treated with this oxazolidinone, 601 of them in the last 6 months with a direct cost of 319,945.50 . When comparing the total number of patients treated with linezolide in 2005 and 2006, we observed a raise of 404%, which was associated with a raise in costs of 137% (15,601.62 monthly). Of the 22 patients observed, 5 had a confirmed infection caused by methicillin-resistent *S. aureus*, and 3 by methicillin-sensitive *S. aureus*; in no case resistance to vancomycine was demonstrated, and 7 patients had impaired renal function.
CONCLUSIONS: Pharmacists have a role in ensuring the best use of linezolid in the treatment of serious Gram positive infections. For these patients linezolid is an effective and well-tolerated therapeutic option; nevertheless, the high acquisition cost of linezolid must be taken into account when selecting between drugs. Clinical pharmacists are responsible for the quality of care and the efficient use of resources.

344. Economic evaluation of bivalirudin or glycoprotein IIb/IIIa inhibitors plus heparin for percutaneous coronary intervention. Divya A. Abraham, Pharm.D., M.S., *Kerry Pickworth, Pharm.D.*, Danielle M. Blais, Pharm.D.; The Ohio State University Medical Center, Columbus, OH.

PURPOSE: The primary objective of this study is to compare estimated in-hospital costs for patients receiving bivalirudin to those receiving heparin plus glycoprotein IIb/IIIa inhibitors for PCI. The secondary objective is to determine the impact of bleeding complications on the cost of PCI.
METHODS: A retrospective review of hospital billing data, from January to June 2004, was performed in patients who received bivalirudin compared with glycoprotein IIb/IIIa inhibitors plus heparin for PCI. Data collected for each group included: total hospital costs and costs associated with bleeding complications including additional laboratory tests, room charge for extended length of stay, transfusion costs, and use of therapeutic agents. Hospital costs were determined by applying the institution's specific cost-to-charge ratio in 2004. Statistical analysis was performed by chi-squared analysis.
RESULTS: A total of 285 patients were included. There were statistically fewer bleeding complications in the bivalirudin group (14%) compared with the glycoprotein IIb/IIIa inhibitor plus heparin group (27%, $p < 0.05$). The average total cost per admission for patients who received bivalirudin compared with glycoprotein IIb/IIIa inhibitor plus heparin and who experienced a bleed was $24,971 and $37,482, respectively. The average total cost per admission for a patient who did not experience a bleed between the groups was $11,448 and $15,785, respectively. The average bleeding complication cost per admission for a patient who received bivalirudin compared with glycoprotein IIb/IIIa inhibitor plus heparin was $5,352 and $6,393, respectively. The difference between the groups can be attributed to the increased use of transfusions and hemostatic medications within the glycoprotein IIb/IIIa inhibitors plus heparin group.
CONCLUSIONS: Use of bivalirudin was associated with cost-savings for PCI. Additionally, the economic impact of a bleeding complication is $5,352–$6,393, per procedure depending on antithrombotic agent used.

345E. Impact of a cost-savings initiative for the treatment of hyperlipidemia. *Marile Santamarina, M.S., Pharm., D.*, Julie A. Chapman, Pharm.D., CDE, Cherylyn Beckey, Pharm.D., CDE; Veterans Affairs Medical Center, West Palm Beach, Florida, West Palm Beach, FL.

Presented at the Midyear Clinical Meeting of the American Society Health-System Pharmacists, Las Vegas, NV, December 7, 2005.

346. Cost-effectiveness analysis of chronic obstructive pulmonary disease pharmacotherapy: a comparison of ipratropium and tiotropium. *Alicia M. Reese, Pharm.D., M.S.*[1], Laurajo Ryan, Pharm.D.[2]; (1)University of the Sciences in Philadelphia, Philadelphia College of Pharmacy, Philadelphia, PA; (2)University of Texas at Austin, University of Texas Health Science Center, San Antonio, TX.

PURPOSE: COPD is the fourth leading cause of death in the United States. In 2004, the cost of medical care for COPD in the U.S. was $37.2 billion, not accounting for indirect costs or lost work days. It is projected that 10 years from now the annual healthcare costs will have risen to $389 billion. The goal of this study was to determine the cost effectiveness of tiotropium to treat COPD compared with ipratropium. Tiotropium is an inhaled anticholinergic agent approved for once-daily use in COPD. Prior to its approval, ipratropium was the only anticholinergic agent approved for bronchodilation in COPD.
METHODS: We analyzed the results of a large randomized, double-blind, active-controlled trial, which assessed the effects of usual COPD pharmacotherapy combined with either tiotropium or ipratropium. Outcome statistics and resource utilization data were modeled using decision tree analysis. Cost of drug therapy was based on average wholesale price (AWP) of tiotropium, ipratropium and albuterol. Other drug costs were assumed to be equivalent and were therefore not included in the analysis. Cost differences were calculated using exacerbations per treatment arm, unscheduled office visits, and hospitalizations. Costs were adjusted to 2006 dollars using the medical component of the Consumer Price Index. Sensitivity analyses were performed to determine the variables with the greatest impact on the cost.
RESULTS: The average cost in this study to treat one patient for a year with tiotropium was $2068.11 compared with $2429.74 for ipratropium. This demonstrates a cost savings of $0.10 per exacerbation avoided to treat a patient with tiotropium versus ipratropium over the course of a year.

347. Bioequivalence study of injectable famotidine between novel solution E1170 and conventional freeze-dried form. *Hidetoshi Furuie, M.D., Ph.D., FACP*[1], Yutaka Atsuta, Manager[2], Mayuko Kanda, CRC[1], Satoko Imazuya, Pharmacist[1], Kyoko Matsuguma, M.D.[1], Shin Irie, M.D.[1]; (1)Medical Co.LTA Kyushu Clinical Pharmacology Research Clinic, Fukuoka, Japan; (2)Astellas Pharma Inc., Tokyo, Japan.

PURPOSE: E1170 is a novel solution of injectable Famotidine under development. Famotidine intravenous injection is indicated in gastrointestinal hemorrhage, Zollinger-Ellison syndrome, and prevention of gastrointestinal hemorrhage caused by invasive operation. The conventional freeze-dried form needs to be dissolved in sterile water or normal saline at the time of injection. E1170, which does not require dissolution, has been long desired in emergency medicine field. The primary objective was to evaluate the bioequivalence between E1170 and conventional freeze-dried form by intramuscularly injection of 20 mg Famotidine. The secondary objective was to evaluate the safety of these agents.
METHODS: This trial was conducted by a 2-way, crossover, open-label design. One vial of E1170 contains slightly more than 2.0 mL solution, which involves 20 mg Famotidine in 2.0 mL. We took 2.0 mL of E1170 from vial to syringe. One vial of conventional freeze-dried form contains exactly 20 mg of Famotidine. We dissolved conventional freeze-dried form with 1.5 mL of sterile water and moved all solution from vial to syringe with meticulous care. E1170 and conventional freeze-dried form were injected intramuscularly in 18 healthy Japanese male adults at the dose of 20 mg in order to study bioequivalence and safety.
RESULTS: The 90% confidence interval of geometric mean ratio of Cmax and AUCt was 0.86–1.00 and 0.98–1.04 respectively. They implement the criteria of bioequivalence. Adverse event was only one case and was mild increase of serum total bilirubin.
CONCLUSIONS: The novel injectable Famotidine solution E1170 and the conventional freeze-dried form were safe and considered to be bioequivalent.

348. Development of Korean clinical trial guideline in hepatic-impaired patients. *Seunghee Kim, M.S.candidate*, Jung Mi Oh, Pharm.D., Wan Gyoon Shin, Pharm.D., Ph.D.; College of Pharmacy, Research Institute of Pharmaceutical Sciences, Seoul National University, Seoul, South Korea.

PURPOSE: The clinical trials in hepatically impaired patients (HIPs) should consider the changes of the pharmacokinetics (PK) and pharmacodynamics (PD) caused by impaired hepatic function. Although Food and Drug Administration (FDA) and European Medicines Agency (EMEA) have developed PK study guidance in HIPs, it is limited to PK studies and not suitable for Korean environment. This study was to develop the Korean clinical trial guideline specific for HIPs, providing the detailed contents and procedures in all aspects of clinical trial, in accordance with Korean Good Clinical Practice, Pharmaceutical affair laws, and International Conference on Harmonization.
METHODS: The international and domestic regulations, laws, and guidelines related to clinical trials such as guidance of FDA and EMEA for HIP, ICH, and KGCP were evaluated for the development of the HIP specific clinical trial guideline that can be utilized in Korea.
RESULTS: Our newly developed guideline consisted of two sections, the introduction and the discussion. The introduction section included the purposes, classification of HIP, and the outline of clinical trials. The discussion section included detailed plans and procedures of clinical trials that are specific for HIPs. Issues such as the study-methodology for the PK and PD studies, selection of subjects, and inclusion and exclusion, monitoring, case report format, quality and management of data, multiple-center trial, safety and efficacy evaluation, reporting of trial results, monitoring the statistical analysis and ethical issues that should be considered specifically for the HIPs were included in the discussion section of the guideline. In addition, ethical issues such as legal recruitment, informed consent, and risk and distress minimization specific for HIP were emphasized.
CONCLUSIONS: The guideline on the evaluation of the clinical trials of drugs in HIP was developed in this study. This guideline can be applied to standardization and internationalization of Korean clinical trials in HIPs.

349. Extended interval gentamicin dosing in neonates: a new approach. *Roger W. Wyssman, B.S., Pharm*[1], Colleen M. Terriff, Pharm.D.[2]; (1)Deaconess Medical Center, Spokane, WA; (2)Washington State University College of Pharmacy, Spokane, WA.

PURPOSE: Our neonatal intensive care interdisciplinary team developed a

protocol for extended interval administration of gentamicin that should lead to therapeutic peak levels 5–10 µg/mL, and trough levels below 2 µg/mL.
METHODS: Gentamicin is dosed at 4 mg/kg IV every 24 hours with peak and trough levels drawn around the fourth dose for neonates expected to have normal renal function (method I). When inadequate renal function is anticipated, administration frequency is based on a neonate's clearance by drawing a level 20 hours after the first dose (method II). The following algorithm determines dosing frequency based on the 20-hour level: 1) Less than 1.7 µg/mL, continue 4 mg/kg gentamicin every 24 hours; 2) Between 1.7 and 2.3 µg/mL, continue 4 mg/kg gentamicin every 36 hours; 3) Greater than 2.3 µg/mL, hold gentamicin, and take another level in 24 hours; 4) Continue gentamicin 4 mg/kg every 48 hours if second level is less than 0.7 µg/mL. Physician to evaluate level if above 0.7 µg/mL.
RESULTS: Over 6 months 87 neonates were dosed by method I. Steady state peak and trough levels were drawn on 50 patients. Ten peak levels were above 10 µg/mL (2 were above 12 µg/mL), and two were below 5 µg/mL. One trough level was above 2 µg/mL. Using method II, dosing was continued every 24 hours for 27 neonates and every 36 hours for 24 neonates. Ten neonates required the second level with three continuing every 48 hours. Steady state peak and trough levels were drawn on 31 patients. Peak levels were above 10 µg/mL in 3 patients, and below 5 µg/mL in 3 patients. Two trough levels were above 2 µg/mL.
CONCLUSIONS: This gentamicin extended interval protocol was successful in assigning the proper dosing frequency to the majority of neonates.

350. Implementation of a patient-oriented pharmacy services model in a community hospital. *Tanya D. Gordon, Pharm.D.*, Laura H. Waite, Pharm.D.; Florida Hospital Orlando, Orlando, FL.

Pharmacy departments in community-based hospitals struggle to develop a realistic process for implementing clinical services. Previously at Florida Hospital Orlando, clinical pharmacy services were provided upon physician consultation only. In an effort to expand services in the internal medicine units, we designed the patient-oriented pharmacy services (POPS) model. Our model extends the role of the clinical pharmacist to encompass medication administration record (MAR) reconciliation, home medication reconciliation, and evaluation of medication appropriateness for all patients in addition to physician-initiated consults. Prior to implementation, we developed objective evaluation tools, competency assessments, an extensive training manual detailing pharmacy-specific procedures, a training program syllabus outlining expectations and responsibilities of the POPS pharmacists, and a customized clinical intervention documentation system. Each candidate must undergo a formalized interview, including a presentation, to allow unbiased evaluation of the candidate's communication skills and clinical knowledge. Selection of candidates is based on predetermined eligibility criteria addressing clinical acumen, prior clinical training and experience, and communication skills. Once chosen, the candidate enters an intensive training program that includes: 1) multiple baseline competency exams reviewing commonly encountered disease states; 2) a thorough review of pertinent literature and current guidelines; 2) extensive chart review, MAR reconciliation, and home medication evaluation and reconciliation; 3) utilization of appropriate communication techniques; and 4) successful completion of a case-based competency exam. Upon completion of training, each POPS pharmacist independently provides clinical services on a 40-bed nursing unit and prioritizes daily patient care activities based on the presence of medication-related problems. Activities are documented in a Web-based software program that captures interventions, physician acceptance, and associated cost savings. Currently, POPS pharmacists provide clinical services on four internal medicine nursing units. Expansion to three oncology units is expected by the end of 2006, and further expansion throughout the hospital is anticipated.

351. Implementing a pharmacist privileging process at a university medical center. *Christopher R. Fortier, Pharm.D.*[1], Melissa M. Blair, Pharm.D., FCCP, BCPS, CDE[2], Joseph E. Mazur, Pharm.D., BCPS, BCNSP[1]; (1)Medical University of South Carolina, Charleston, SC; (2)North Carolina Coastal Area Health Education Center, Wilmington, NC.

PURPOSE: Privileging is the method by which a healthcare organization authorizes a practitioner to perform a scope of patient care services according to the facility's standard of care. To better recognize pharmacists as providers within the organization, document clinical competencies, and be consistent with other healthcare providers, a voluntary pharmacist privileging program was created and implemented at a university medical center.
METHODS: A task force was formed, consisting of members from the various aspects of pharmacy services. The task force established a credentialing and privileging policy, which was approved by the state Board of Pharmacy, the medical center Credentials Committee, and pharmacy and hospital administration. Candidates complete an application listing their qualifications and outlining requested clinical activities to be performed under a collaborative protocol. Credentials including postgraduate training, certification, and professional experience are verified using supporting documentation. Applicants are recommended for approval by a Pharmacy Credentials Committee, consisting of pharmacists from various department divisions. Final approval is granted by the Director of Pharmacy Services. Once approved, the applicants submit collaborative practice agreements and protocols, which require review and approval by the Pharmacy Credentials Committee and pharmacy and medical administration.
RESULTS: To date, a total of eight pharmacists from the ambulatory care division have been privileged using five collaborative drug therapy management protocols.
CONCLUSIONS: A pharmacist privileging system is a proficient way to recognize pharmacists as patient care providers within a hospital setting. Barriers for this system may include perceived need from medical and pharmacy staff and the time commitment necessary to submit and verify information.

352. Development of an electronic pharmacy patient profiling system in the era of computerized physician order entry. *Ada Seto, B.Sc.Phm., ACPR*[1], Jin Huh, B.Sc.Phm., ACPR[1], Manhim Chau, B.Com.[2]; (1)University Health Network, Toronto, ON, Canada; (2)University Health Network, Toronto, ON, Canada.

PURPOSE: Pharmacists have relied on paper-based notes to convey clinical and operational issues to their colleagues. Communication on paper has several limitations including: nonstandardized template for communication, frequent loss of information, limited accessibility, and inability to easily retrieve and analyze data. Computerized Physician Order Entry was implemented in February 2005. With the advent of this new technology, the development of a computer-based pharmacy documentation system was needed to improve communication.
METHODS: Pharmacy Clinical Intervention Report and Track (P-CIRT) was developed using Microsoft Access 2000 and was piloted at our institution in July 2005 with the following objectives: 1) overcoming barriers to effective communication with paper-based methods of transferring information; 2) standardizing methods of documentation of pharmacy interventions; 3) providing accessibility to documented information in a central location for all pharmacists without breaching confidentiality and 4) facilitating data collection for analysis of clinical and workload statistics.
RESULTS: Between July 2005 and May 2006, 6021 patients and 15530 issues were profiled by staff pharmacists, pharmacy residents, and casual pharmacists using a standardized template on P-CIRT. Communication was improved as evident by 6812 (44%) issues accessed by more than one pharmacist. Clinical data and workload statistics were easily retrieved by using database queries. The most common issues documented in general medicine and ER are pneumonia (277), urinary tract infections (252), hypertension (204), and acute renal failure (200). A total of 26631 therapeutic interventions were accepted during this period.
CONCLUSIONS: P-CIRT has been in use for 10 months with great success in improving communication amongst pharmacists. It has allowed for improved tracking of workload statistics and interventions. P-CIRT began as a departmental project with limited technical support. As a result of its success, the project has now been accepted as an institution-wide Information Technology project in collaboration with pharmacy for further technical enhancements.

353. Justification of a patient-oriented pharmacy services model in a community hospital. *Tanya D. Gordon, Pharm.D.*, Laura H. Waite, Pharm.D.; Florida Hospital Orlando, Orlando, FL.

Implementing a novel process for the provision of clinical pharmacy services is challenging in a community-based hospital where justification of those services is primarily financial in nature. The potential benefit of expanding clinical services must offset the cost of additional staff and resources. At Florida Hospital Orlando, the patient-oriented pharmacy services (POPS) model was initiated requiring a transition from 6 clinical pharmacists per day providing consultative services only for the adult population (~32 nursing units) to a clinical pharmacist dedicated to each nursing unit to provide consultative services as well as medication reconciliation and evaluation of medication appropriateness. This model was approved for initiation based on two assumptions: cost avoidance and improved patient safety. We have maintained administrative support by demonstrating an increase in medication event prevention, as well as overall cost savings, through POPS pharmacist intervention documentation. Initially, we designed an Excel spreadsheet to capture intervention data, physician acceptance, and medication events. Unfortunately, we were unable to attribute direct cost savings to individual interventions. To further facilitate data collection and analysis, we converted to the Web-based software program Quantifi. Once we customized this software for our health system, it provided a more user friendly and comprehensive database for documentation and reporting, allowed more sophisticated manipulation of intervention records, and incorporated figures for intervention-specific cost savings. Three full-time pharmacists from January through May 2006, with the addition of a fourth

full-time pharmacist in April, documented 4137 interventions, which correspond to $120,000 in cost savings. Although cost avoidance related to medication event prevention is not represented in this figure, to date the actions of the POPS pharmacists have precluded the occurrence of 649 medication events. We anticipate that the data generated from the POPS model will continue to justify the expansion of clinical pharmacy services at our institution.

354. Two-year results of a telephonic diabetes disease management program in a community-based primary care medical group. *Dawn Fuke, Pharm.D.*, Pape Ginger, Pharm.D., Hunt Jacquelyn, Pharm.D., M.S., Siemienczuk Joseph, M.D.; Providence Medical Group, Milwaukie, OR.

PURPOSE: Despite annually updated guidelines from the American Diabetes Association (ADA) and effective medications, data demonstrate low rates of guideline-recommended goal achievement. The purpose of our program is to determine whether the addition of a collaborative, telephonic diabetes program improves key diabetic parameters beyond clinic-based disease management patient-tracking software.
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 9 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. Randomization occurred at the clinic level. All clinics received CareManager, a Web-based disease management tool, at study start. Clinics in the 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 (LDL-C) 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 mm Hg) and aspirin use, patient and physician/staff satisfaction scores, as well as healthcare utilization during the study period.
RESULTS: One-year interim results showed more patients at LDL-C goal in the intervention group (65% intervention versus 47% control, $p<0.05$). Furthermore, patients in the intervention group were more likely to be prescribed a statin medication (65% intervention versus 47% control, $p<0.05$). Final 2-year results with cost analysis will be presented.

355. Treatment of chronic heart failure in an academic primary care clinic for low-income patients. *Amy B. Riley, Pharm.D.*, Theresa R. Prosser, Pharm.D.; St Louis College of Pharmacy, St Louis, MO.

PURPOSE: To determine whether appropriate drugs and target doses are prescribed for systolic heart failure as recommended by the 2005 ACC/AHA chronic heart failure update (i.e. angiotensin converting enzyme inhibitors [ACEI] or angiotensin receptor blockers [ARB] and beta blockers [BB]).
METHODS: Charts with ICD-9 Heart Failure (HF) codes (428.0, 428.1, 402.91) were retrospectively reviewed at a primary care clinic for uninsured patients managed by academic Internal Medicine physicians with collaboration by clinical pharmacists. Most recent ejection fraction (EF) results were used to identify systolic heart failure (EF < 40%). Target indicators addressed: (1) percent hospitalized for HF in 2005, (2) percent on an ACEI, ARB, or BB, (3) and percent receiving target doses of each medication.
RESULTS: Of the 72 charts available, 22 (31%) had documented systolic HF. Of those with systolic HF, 95% were prescribed ACEI therapy (86% at target dose), 91% were prescribed a recommended BB (14% at target dose), and 5% were prescribed ARB therapy (none at target dose). All patients were prescribed one of the recommended drugs (ACEI or ARB or BB) and 91% were prescribed both an ACEI/ARB and a BB. Of all patients, 24 (33%) were hospitalized for HF, including 8 (36%) of those with systolic HF. Drug data for diastolic dysfunction (EF > 40%) will also be presented.
CONCLUSIONS: Based on an initial screen, most patients were prescribed target dose ACEI therapy for HF and dual therapy with ACEI plus BB. Further study would be needed to determine the cause for the lower percentage of patients prescribed target dose BB therapy. No conclusions can be made about the diastolic HF data because current ACC/AHA diastolic HF guidelines only targets control of co-morbid disease states. Due to the relatively high percentage of hospitalizations, patient education interventions to prevent rehospitalizations will be explored.

356. The effect of clinical pharmacy services on diabetes care outcomes in a primary care clinic for low-income patients. *Amy B. Riley, Pharm.D.*[1], Amanda Milstead, M.D.[2], Theresa R. Prosser, Pharm.D.[1]; (1)St Louis College of Pharmacy, St Louis, MO; (2)St John's Mercy Medical Center, St Louis, MO.

PURPOSE: To compare the American Diabetes Association/National Committee for Quality Assurance (ADA/NCQA) indicators for diabetes (DM) care between 2 similar clinics (i.e., eligibility, physicians, and benefits) for uninsured patients. Determine whether indicators from a clinic with clinical pharmacy collaborative/quality assurance services (MPHC) are significantly different from the clinic without (JFK).
METHODS: Over 5 months, data were collected at DM appointments for ADA/NCQA indicators. Data of both clinics were compared with NCQA recommended percentages and to each other.
RESULTS: Total of 367 charts were assessed; half from each clinic. Both clinics met NCQA standards for the percentage of charts with HbA1c > 9% (≤ 20%), LDL < 100 (≥ 36%), and LDL < 130 (≥ 63%). Neither clinic met standards for annual dietitian visits, diabetes education, or microalbumin checks. JFK blood pressures met NCQA standards < 130/80 (≥ 35%) and < 140/90 (≥ 65%). MPHC met standards for A1c < 7% (≥ 40%), annual tobacco counseling (≥ 80%), HbA1c checks (≥ 93%), foot exams (≥ 80%), and eye exams (≥ 60%). More ($p < 0.05$) JFK blood pressures were < 130/80 (42% vs 29%) and < 140/90 (73% vs 55%). No differences ($p>0.05$) were noted between clinics for: A1c < 7 (43% vs 39%), A1c > 9% (20% vs 18%), LDL < 100 (64% vs 58%), or LDL <130 (86% vs 79%). More MPHC charts ($p<0.05$) met indicators for annual: HbA1c checks (98% vs 90%), eye exams (61% vs 38%), foot exams (90% vs 55%), tobacco status/counseling (93% vs 55%), dietician visits (37% vs 15%), diabetes education (68% vs 2%) and microalbumin checks (52% vs 47%).
CONCLUSIONS: Although similar values were seen for lipids and HbA1c, JFK blood pressures were significantly lower. However, clinical pharmacy services may have helped MPHC meet overall more NCQA standards for process indicators. Methods to further improve DM care should continue to be explored.

357. Pharmaceutical intensive treatment of type 2 diabetes mellitus (PITT-DM pilot). *Deanne L. Hall, Pharm.D., CDE*, Wishwa N. Kapoor, M.D., M.P.H., Gary Fischer, M.D., Linda L. Fevrier, R.N., CDE, Deborah M Simak, R.N., M.N.Ed.; University of Pittsburgh Medical Center, Pittsburgh, PA.

PURPOSE: To evaluate whether intensive diabetes management delivered by a pharmacist following protocol will improve glycemic control, reduce cardiovascular risk factors (LDL cholesterol and BP), and improve patient and provider knowledge of diabetes treatment as compared with usual care in patients with uncontrolled type 2 diabetes.
METHODS: Consenting patients within a university hospital based medicine clinic with uncontrolled type 2 diabetes (HbA1c > 7%) were randomized to intervention (INT) or usual care (UC) for 12 months. Glycemic control evaluated by HbA1c, cardiovascular risk reduction evaluated by LDL and BP, and patient diabetes knowledge assessed at baseline, 6 and 12 months. Hypoglycemic events assessed every 3 months. Quality-of-life (SF-36), ADA markers for standard of care, and provider knowledge assessed at baseline and 12 months.
RESULTS: Ninety-four subjects were randomized, resulting in 78 evaluable subjects (35 INT, 40 UC) at 6 months. Baseline average HbA1c, BP and LDL were similar between groups. At month 6 for INT and UC respectively, there were no differences in average HbA1c (8.1% vs 7.9%) or proportion of patients at goal HbA1c (25.7% vs 27.5%), BP (systolic, 50% vs 35.7%; diastolic 52.8% vs 50%) or LDL (47.2 % vs 47.6%). Hypoglycemic episodes were similar between groups. Evaluation of 12-month data and questionnaires in progress.
CONCLUSIONS: Six-month analysis reveals similar outcomes between study groups. This is possibly due to quality improvement measures implemented within the clinic just prior to and during the study. Analysis of current data may assist in identifying patient and physician characteristics that may benefit from pharmacist managed diabetes treatment and education.

358. A crossover study of eszopiclone in the treatment of primary insomnia: a subset analysis by baseline wake time after sleep onset (WASO). Milton Erman, M.D.[1], *Robert Rubens, M.D.*[2], Kendyl Schaefer, M.S.[2], Holly Huang, M.S.[2]; (1)Pacific Sleep Medicine Services, San Diego, CA; (2)Sepracor Inc., Marlborough, MA.

PURPOSE: To evaluate the effect of eszopiclone treatment on patients with moderate degrees of sleep-maintenance problems.
METHODS: Multicenter, double-blind, placebo-controlled, 6-way Williams-design crossover study. Patients (n=65) received 2 nights' treatment with placebo, eszopiclone 1, 2, 2.5, and 3 mg, or zolpidem 10 mg in a random order. Visits were separated by a 3–7 day washout. This analysis evaluated sleep end points in a subset of patients who met the PSG maintenance study entry criteria of WASO > 20 minutes (n=59).
RESULTS: Analysis of objective WASO in patients who met WASO entry criteria (baseline WASO > 20 minutes) revealed that eszopiclone 2.5 mg ($p=0.01$) and 3 mg ($p=0.002$), but not zolpidem 10 mg ($p=0.19$), were associated with improvements in WASO vs placebo, with statistical trends ($p=0.065$) when eszopiclone 3 mg and zolpidem 10 mg were compared. Eszopiclone 2, 2.5 and 3 mg, as well as zolpidem 10 mg, significantly reduced patient-reported (subjective) WASO ($p<0.009$ vs placebo), but treatment with

eszopiclone 3 mg was associated with significant improvements vs zolpidem 10 mg (p=0.04).
CONCLUSIONS: Eszopiclone 2.5 mg and 3 mg significantly improved both objective and subjective WASO in subjects with baseline WASO > 20 minutes vs placebo, and eszopiclone 3 mg was associated with greater improvements in subjective WASO relative to zolpidem 10 mg.

359. Pharmacist-managed tuberculosis program in a student health service. *Donna G. Beall, Pharm.D.*, Jean T. Carter, Ph.D.; The University of Montana, Missoula, MT.

PURPOSE: Screening and treating latent tuberculosis infection (LTBI) are key components of the national strategy for tuberculosis (TB) elimination. The Centers for Disease Control and Prevention (CDC) recommends targeted tuberculin testing. At the University of Montana, students targeted for tuberculin testing include those who major in education or healthcare disciplines, are foreign-born, or traveled to countries with endemic TB within the past 3 years. Originally, the student monitoring of LTBI was housed in the local health department. When the funding for the position was lost, the responsibility was shifted to the student health service pharmacy personnel. The opportunity to create a pharmacy-based public health service was immediately embraced.
METHODS: In 2005, the campus-based service was developed. Development required: 1) writing the screening and management protocol for latent TB infections; 2) writing policies and procedures to outline the responsibilities of the clinical pharmacist, providers, and lab personnel; 3) developing written information for patients and translating the information into the 8 most common languages seen in our foreign students, and 4) presenting the proposed program to the clinic staff. Students with a positive PPD, as defined by CDC guidelines, are now referred to the pharmacy service. During the initial encounter, the pharmacist discusses positive PPD test issues (e.g., specificity, sensitivity), latent versus active infections, and recommendations. Ambulatory care APPE students are actively involved. Evaluation of the service focused on success in following students with LTBI and their antibiotic therapy completion rates.
RESULTS: The pharmacy service had a 62 percent completion rate compared with rates of 40%–60% and 13%–45% found in literature and the health department, respectively. The APPE student evaluations have been positive.
CONCLUSIONS: Pharmacists can successfully manage patients with LTBI. Such programs provide a wonderful learning opportunity for APPE students and promote pharmacy involvement in critical public health initiatives.

360E. A pharmacoeconomic analysis of liver transplant charges at a single institution over 11 years. *Timothy M. Clifford, Pharm.D.*[1], Thomas D. Johnston, M.D.[2], Hoonbae Jeon, M.D.[2], Dinesh Ranjan, M.D.[2]; (1)University of Kentucky Chandler Medical Center, Lexington, KY; (2)University of Kentucky Department of Surgery, Section of Transplantation, Lexington, KY.

Presented at 2006 World Transplant Congress of the American Society of Transplantation, Boston, MA, July 24, 2006.

361E. New onset diabetes after transplantation (NODAT) in early corticosteroid withdrawal regimens: an analysis using multiple definitions with multivariate analyses of risk factors for each definition. *Adele H. Rike, Pharm.D.*, Rita R. Alloway, Pharm.D., Michael Cardi, M.D., Gautham Mogilishetty, M.D., Paul Succop, Ph.D., E. Steve Woodle, M.D.; University of Cincinnati, Cincinnati, OH.

Presented at the World Transplant Congress of the American Society of Transplantation, Boston, MA, July 24, 2006.

362E. Liver failure etiology. *Tiffany E. Kaiser, Pharm.D.*, G. Mogilishetty, M.D., P Roy-Chaudhury, M.D., N Weimert, Pharm.D., V Zacharias, M.S., PA-C, N Kemmer, M.D., R Alloway, Pharm.D., A Tevar, M.D., J Martin, Pharm.D., G Neff, MD; University of Cincinnati, Cincinnati, OH.

Presented at the World Transplant Congress of the American Society of Transplantation, Boston, MA, July 24, 2006.

363. Weekly outpatient administration of 17 alpha-hydroxyprogesterone caproate in obstetrical patients at high risk for preterm birth. *Roger B. Williams, M.S.*[1], Beverly S. Palmer, B.S.[1], Robert W. Rossi, B.S.[1], Deborah A. Delph, B.S.[2], Niki B. Istwan, R.N.[1], Debbie J. Rhea, M.P.H.[1], Gary J. Stanziano, M.D.[1]; (1)Matria Healthcare, Marietta, GA; (2)PharMerica, Indianapolis, IN.

PURPOSE: We describe our experience with weekly outpatient administration of intramuscular (IM) injections of 17 alpha-hydroxyprogesterone caproate (17P), a compounded medication shown to reduce the incidence of recurrent preterm birth (PTB) in singleton gestations. Our experience is compared with data from a recent Level I study conducted by the National Institutes of Health (NIH) and published in 2003 supporting the use of 17P for this indication.
METHODS: Patients with current singleton pregnancies and a history of previous spontaneous PTB were prescribed weekly IM injections of 250 mg of 17P by their physician, initiated between 16–20 weeks' gestation, and continued until 36 weeks' gestation or PTB. After screening of patient criteria for acceptance to the Matria 17P administration service by clinical pharmacists and nurses, 17P was compounded for individual patients by a contracted pharmacy utilizing US Pharmacopeia chapter <797> specifications. Weekly 17P injection and patient assessment were performed by specialized obstetrical nurses in the patient's home, and 24/7 telephonic access to nursing education and support was available.
RESULTS: Outcomes of 320 pregnancies receiving 17P were collected and analyzed. Compliance with the outpatient protocol was 97.9%, and each patient received an average of 16.5 weekly injections. The incidences of spontaneous PTB at < 37 weeks, < 35 weeks, and < 32 weeks were 32.5%, 18.1%, and 7.5%, respectively, which compared favorably to the NIH 2003 trial. Compared to published controls, a cost analysis showed a net savings of $943,940 in the 320 patients, or $2,950 per pregnancy, based on a reduction in NICU utilization and nursery length of stay resulting from a reduced number of preterm births.
CONCLUSIONS: 17P administered within a structured clinical protocol, including weekly injections and obstetrical assessments in the home, resulted in delivery outcomes comparable to those reported in a recent Level I study conducted by the NIH.

RESIDENTS AND FELLOWS RESEARCH IN PROGRESS

These papers describe original research by 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* online; the full abstract will be published in the meeting program book.

364. An in-vitro analysis of drug-drug interactions between voriconazole and immunosuppressants (sirolimus, tacrolimus, and cyclosporine). *Yasar O. Tasnif, Pharm.D.*, Mary F. Hebert, Pharm.D., FCCP, Justina C. Calamia, B.S., Kenneth E. Thummel, Ph.D.; University of Washington, Seattle, WA.

365. Evaluation of the effectiveness of insulin infusion protocols in cardiothoracic patients. *Jessica T. Peng, Pharm.D.*[1], Sheryl L. Chow, Pharm.D., BCPS[1], Anandi V. Law, Ph.D.[2], Etie Moghissi, M.D.[3]; (1)Western University of Health Sciences, College of Pharmacy and Centinela Freeman Regional Medical Center, Pomona, CA, Inglewood, CA; (2)Western University of Health Sciences, Pomona, CA; (3)Centinela Freeman Regional Medical Center, Inglewood, CA.

366. Lack of a correlation between A_{1c} and glycemic burden using a glycemic medication potency value. *Joel C. Marrs, Pharm.D.*, Joseph J. Saseen, Pharm.D., Laura B. Hansen, Pharm.D., Kavita V. Nair, Ph.D.; University of Colorado at Denver and Health Sciences Center, Denver, CO.

367. Thiazolidinediones and the risk of edema: a meta-analysis. *Helen D. Berlie, B.Sc., Pharm.D.*, James Kalus, Pharm.D., BCPS, Linda A. Jaber, Pharm.D.; Wayne State University, Detroit, MI.

368. Enoxaparin dosing and incidence of bleeding in patients with renal dysfunction. *Lauren G. Veltry, Pharm.D.*, Deanne L. Hall, Pharm.D., Kristine E. Schonder, Pharm.D.; University of Pittsburgh Medical Center, Pittsburgh, PA.

369. High frequency of HIV-related medication errors and associated risk factors found in hospitalized patients. *Sonak D. Pastakia, Pharm.D., BCPS*, Amanda H. Corbett, Pharm.D., BCPS, Ralph H. Raasch, Pharm.D., FCCP, BCPS, Sonia Napravnik, Ph.D., Todd A. Correll, Pharm.D., BCPS; University of North Carolina Hospitals, Chapel Hill, NC.

370. Physician adherence to national HIV treatment guidelines in antiretroviral naive patients. *Sonia Vibhakar, Pharm.D.*, Mariela Diaz-Linares, Pharm.D.; University of Illinois at Chicago, Chicago, IL.

371. Impact of pharmacist-related outcomes: vital effect in diabetes (IMPROVED). *Daniel M. Riche, Pharm.D.*[1], Gloria R. Grice, Pharm.D.[1], James Deckert, M.D.[2]; (1)St. Louis College of Pharmacy, St. Louis, MO; (2)Saint Louis University, St. Louis, MO.

372. The impact of hospitalization on inappropriate medication use in elderly patients. *Shawna E. King, Pharm.D.*, Krystal K. Haase, Pharm.D., Ann E. Canales, Pharm.D.; Texas Tech University Health Sciences Center School of Pharmacy, Amarillo, TX.

373. Evaluation of thrice-weekly vancomyin dosing in high-flux hemodialysis. *Scott J. Bergman, Pharm.D.*[1], Douglas Slain, Pharm.D.[1], Justin Hare, Pharm.D.[2]; (1)West Virginia University, Clinical Pharmacy Dept, Morgantown, WV; (2)West Virginia University Hospitals, Morgantown, WV.

374. Suicidality as measured by Beck Depression Inventory and adverse events during initiation and withdrawal of low-dose, controlled-release paroxetine in 10 non-depressed subjects. *Nicholas B. Norgard, Pharm.D.*[1], Andrea R. Phillips, Pharm.D.[2], Stephen F. Hamilton, Pharm.D., FCCP[1]; (1)University of Oklahoma Health Sciences Center, College of Pharmacy, Oklahoma City, OK; (2)Norman Regional Hospital, Norman, OK.

375. The impact of antipsychotics on lipid levels: an assessment of lipid measurements at an acute care psychiatric facility. *Robin N. Hieber, Pharm.D.*[1], Rafia S. Rasu, Ph.D.[2], Valerie L Ruehter, Pharm.D.[1]; (1)Western Missouri Mental Health Center, Kansas City, MO; (2)University of Missouri Kansas City School of Pharmacy, Kansas City, MO.

STUDENT SUBMISSIONS

These papers describe original research by students in therapeutics, pharmacokinetics, pharmacodynamics, pharmacoeconomics, and pharmacoepidemiology. The abstract title and authors are published in *Pharmacotherapy* online; the full abstract will be published in the meeting program book.

376. The effects of pharmacist interventions on patients with polypharmacy. *Elinor Chumney, MS*, Leslie C. Robinson, Pharm.D. Candidate; Medical University of South Carolina, Charleston, SC.

377. Elevation of liver enzymes with use of Atorvastatin and Black Cohosh. *Ramona M. Derkits, Pharm.D.*, Nima M. Patel, Pharm.D., BCPS; Temple University School of Pharmacy, Philadelphia, PA.

378. Evaluation of compliance with clopidogrel therapy post PCI in a VA hospital. *Ambreen Ali, Pharm.D.*[1], Adhir Shroff, M.D., M.P.H.[2], Todd Lee, Pharm.D.[3], Vicki L. Groo, Pharm.D.[4]; (1)University of Illinois at Chicago, College of Pharmacy, Chicago, IL; (2)University of Illinois at Chicago, Department of Medicine, Chicago, IL; (3)Hines VA Hospital, Hines, IL; (4)University of Illinois at Chicago, College of Pharmacy and Medicine, Chicago, IL.

379. Ultrafiltration vs. IV diuretics for patients hospitalized for acute decompensated congestive heart failure: a prospective randomized clinical trial. *Hobart L. Rogers Jr., Pharm.D*[1], Thomas C. Dowling, Pharm.D, Ph.D.[1], Joanne Marshall, R.N.[2], Stephen S. Gottlieb, M.D.[2]; (1)University of Maryland, School of Pharmacy, Baltimore, MD; (2)University of Maryland, School of Medicine, Baltimore, MD.

380. Pharmacodynamics of cangrelor when administered alone or in combination with clopidogrel. *Julie H. Oestreich, Pharm.D.*, Steven R. Steinhubl, M.D., Suellen P. Ferraris, Ph.D., Jennifer J. Oh, Pharm.D., Adam C. Locklar, B.S., Mary Wethington, R.N., B.S.N., Wendell S. Akers, Pharm.D., Ph.D.; University of Kentucky, Lexington, KY.

381. Influence of anti-hypertensive choice on the achievement of intensive blood pressure control in a subset of patients from the ongoing secondary prevention of small subcortical strokes (SPS3) clinical trial. *Nicolas A. Forcade, B.A., Pharm.D., candidate*[1], Christopher R. Frei, Pharm.D., M.Sc.[2], Jason M. Cota, Pharm.D.[3], Oscar R. Benavente, M.D.[4], Pablo E. Pergola, M.D.[4], Ana M. Roldan, MD[4], Robert L. Talbert, Pharm.D.[2]; (1)The University of Texas at Austin College of Pharmacy, Austin, TX; (2)The University of Texas at Austin College of Pharmacy and The University of Texas Health Science Center at San Antonio, San Antonio, TX; (3)University of Texas at Austin, San Antonio, TX; (4)The University of Texas Health Science Center at San Antonio, San Antonio, TX.

382. Effects of paroxetine on immediate-release and sustained-release metoprolol beta-blockade: evaluation of heart rate response. *Stacey Kuboske, Pharm.D., student*[1], Judith Soberman, M.D.[2], Robert B. Parker, Pharm.D.[3]; (1)University of Tennessee College of Pharmacy, Memphis, TN; (2)University of Tennessee Division of Cardiovascular Diseases, Memphis, TN; (3)University of Tennessee Dept of Pharmacy, Memphis, TN.

383. Effects of paroxetine on immediate-release and sustained-release metoprolol beta-blockade: evaluation of systolic blood pressure response. *Stacey Kuboske, Pharm.D., student*[1], Judith Soberman, M.D.[2], Robert B. Parker, Pharm.D.[3]; (1)University of Tennessee College of Pharmacy, Memphis, TN; (2)University of Tennessee Division of Cardiovascular Diseases, Memphis, TN; (3)University of Tennessee Dept of Pharmacy, Memphis, TN.

384. Influence of experimental sleep apnea on myocardial P-glycoprotein expression. *Scott W. Mueller, Pharm.D., Candidate*[1], John M. Dopp, Pharm.D.[1], Nicholas A. Wiegert, B.S.[1], Nicole J. Abel, B.S., Candidate[1], John J. Moran, B.S.[1], E. Burt Olson, Ph.D.[2], J. Jason Sims, Pharm.D.[3]; (1)University of Wisconsin School of Pharmacy, Madison, WI; (2)University of Wisconsin School of Medicine and Public Health, Madison, WI; (3)Cardiac Rhythm Disease Management, Medtronic, Inc., Minneapolis, MN.

385. Development of Korean clinical trial guideline in patients with impaired renal function. *Mi Young Kim, B.S.*, Wan Gyoon Shin, Pharm.D., Ph.D., Jung Mi Oh, Pharm.D.; Seoul National University, Seoul, South Korea.

386. Survey of intensive care nurses on preferences for various sedative agents, ideal levels of sedation, and a nurse-initiated daily awakening protocol. *Lisa M. Bendz, Pharm.D., Candidate*[1], Shannon S. Carson, M.D.[2], Jo E. Rodgers, Pharm.D.[1]; (1)University of North Carolina School of Pharmacy, Chapel Hill, NC; (2)University of North Carolina School of Medicine, Chapel Hill, NC.

387. Evaluation of the clinical pharmacy project course. Daniel P. Healy, Pharm.D.[1], *Shane E. Lindsay, B.A.*[2], William K. Fant, Pharm.D.[3]; (1)University of Cincinnati, Cincinnati, OH; (2)University of Cincinnati College of Pharmacy, Loveland, OH; (3)University of Cincinnati College of Pharmacy, Cincinnati, OH.

388. The role of a pharmacy student in assessing a pharmacy elective course. *Marie E. Ganski, Pharm.D., Candidate*[1], Karen J. Kopacek, R.Ph.[1], Orly Vardeny, Pharm.D.[1], Anna Legreid Dopp, Pharm.D.[2]; (1)Pharmacy Practice Division, University of Wisconsin School of Pharmacy, Madison, WI; (2)Extension Services in Pharmacy, University of Wisconsin School of Pharmacy, Madison, WI.

389. Development of pharmaceutical services in a low-income free clinic. *Jon Edwards, Pharm.D.*[1], Marisa C Lopez, Pharm.D.[1], Joshua Caballero, Pharm.D.[2], Sandra Benavides, Pharm.D.[2]; (1)University of Texas, Austin College of Pharmacy, BROWNSVILLE, TX; (2)Nova Southeastern University, Ft. Lauderdale, FL.

390. Broad-spectrum antibacterial use in 22 U.S. university teaching hospitals from 2002-2005. *Ryan J. Leftwich, B.S.*[1], Amy L. Pakyz, Pharm.D./M.S.[1], Michael J. Oinonen, Pharm.D., M.P.H.[2], Ron E. Polk, Pharm.D.[1]; (1)Virginia Commonwealth University School of Pharmacy, Richmond, VA; (2)University HealthSystem Consortium, Oak Brook, IL.

391. Vancomycin use at university teaching hospitals and proportion of methicillin resistant *Staphylococcus aureus* over a 4-year period. *Ryan J. Leftwich, B.S.*[1], Amy L. Pakyz, Pharm.D./M.S.[1], Michael J. Oinonen, Pharm.D., M.P.H.[2], Ron E. Polk, Pharm.D.[1]; (1)Virginia Commonwealth University School of Pharmacy, Richmond, VA; (2)University HealthSystem Consortium, Oak Brook, IL.

392. Intracellular bacteria activate intestinal P-glycoprotein. *Jessica L. Rosson, M.S.*, Jayshree Mishra, Ph.D., Qiuye Zhang, M.D., Brien L. Neudeck, Pharm.D.; University of Tennessee College of Pharmacy, Memphis, TN.

393. Activity of tigecycline alone and in combination with gentamicin against *Staphylococcus aureus* in an in vitro pharmacodynamic model. *Kevin W. McConeghy, student*, Kerry L. LaPlante, Pharm.D.; University of Rhode Island and Veterans Affairs Medical Center, Providence, RI.

394. Vancomycin MICs and accessory gene regulator (agr) function in clinical *Staphylococcus aureus*. *Ryan Attwood, Pharm.D, Student*, Kerry L. LaPlante, Pharm.D.; University Of Rhode Island and Veterans Affairs Medical Center, Providence, RI.

395. Methods for assessing the potential severity of medication errors. *Katarina M. Gesser, Ph.D.-student, M.S.Pharm.*[1], Mette Rasmussen, Ph.D.[1], Trine Kart Sorensen, Ph.D.[2]; (1)The Danish University of Pharmaceutical Sciences, Department of Pharmacology and Pharmacotherapy, Copenhagen, Denmark; (2)Aalborg Hospital Pharmacy, Aalborg, Denmark.

396. Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers prescribing patterns and costs in chronic kidney disease patients. *Tonya L. Crawford, Pharm.D., Candidate*[1], Rafia S. Rasu, Ph.D.[1], Harold J. Manley, Pharm.D., BCPS[2]; (1)University of Missouri Kansas City School of Pharmacy, Kansas City, MO; (2)Albany College of Pharmacy, Albany, NY.

397. Renal protective effects of angiotensin converting enzyme inhibitors or angiotensin II receptor blockers in normotensive CKD patients. *Huang Chen-Huei, Master*[1], Yang Kao Yea-Huei, B.S.Pharm.[1], Wang Ming-Cheng, M.D.[2], Kao Shu-Min, Master[3]; (1)Institute of Clinical Pharmacy, Medicine, National Cheng Kung University, Tainan, Taiwan; (2)Department of Internal Medicine, Division of Nephrology, Cheng Kung University Medical Center, Tainan, Taiwan; (3)Department of Pharmacy, Cheng Kung University Medical Center, Tainan, Taiwan.

398. Are phenothiazines overused in cancer chemotherapy? *Salvatore A. Ferro, Pharm.D., candidate*[1], Leon E. Cosler, Ph.D., R.Ph.[1], Brian S. Myer, B.S., candidate[1], Sarah L. Scarpace, Pharm.D., BCOP[1], Eva Culakova, Ph.D.[2], Debra A. Wolff, M.S., P.C.N.P.[2], Marek S. Poniewierski, M.D., M.S.[2], Gary H. Lyman, M.D., M.P.H., FRCP[2]; (1)Albany College of Pharmacy, Albany, NY; (2)University of Rochester School of Medicine & Dentistry, Rochester, NY.

399. Enoxaparin use in the neonatal intensive care unit (NICU): experience over 7 years. *Janet I. Malowany, B.HSc.(Hons)*[1], David C. Knoppert, MSc.Phm., MSc[2], Anthony K. C. Chan, M.B.B.S., FRCPC[3], Dion Pepelassis, M.D., FRCPC[1], David S. C. Lee, M.B.B.S., FRCPC[1]; (1)Department of Paediatrics, Schulich School of Medicine & Dentistry, University of Western Ontario, London, ON, Canada; (2)Department of Pharmacy, St. Joseph's Health Centre, London, ON, Canada; (3)Department of Pediatrics, McMaster University, Hamilton, ON, Canada.

400. Comparison of drug utilization in hospital out-patients and primary care patients. *Soren Ilsoe-Kristensen, Ph.D.-student, M.S.Pharm.*[1], Mette Rasmussen, Ph.D.[1], Steffen Thirstrup, Ph.D., M.D.[2]; (1)The Danish University of Pharmaceutical Sciences, Department of Pharmacology and Pharmacotherapy, Copenhagen, Denmark; (2)The Danish Medicines Agency, Copenhagen, Denmark.

401. An IMPDH1 gene polymorphism is associated with leukopenia in liver transplant patients treated with mycophenolic acid. *Jacqueline Fu, B.S.*, Jian Wang, M.D., Adriana Zeevi, M.D., Steve Webber, M.D., Paula Phongsamran, Pharm D, Rick Selby, M.D., Ian V. Hutchinson, Ph.D, Gilbert J. Burckart, Pharm.D.; USC School of Pharmacy, Los Angeles, CA.

402. Association of CYP3A5 genotypes with sirolimus dosing and trough concentrations in renal transplant patients. *Lakshmi Potti, B.S.*[1], Christine Chamberlain, Pharm.D.[2], Su-Jun Lee, Ph.D.[3], Joyce Goldstein, Ph.D.[3], Douglas Hale, M.D.[4], Roslyn Mannon, M.D.[4], Allan Kirk, M.D., Ph.D.[4], Yuen Yi Hon, Pharm.D.[2]; (1)University of Maryland School of Pharmacy, Baltimore, MD; (2)NIH Clinical Center Pharmacy Department, Bethesda, MD; (3)NIH NIEHS, Research Triangle Park, NC; (4)NIH NIDDK Transplant Branch, Bethesda, MD.

403. Systemic cytokine balance differs between asthma patients with and without positive response to adenosine bronchoprovocation. *Courtney L. Mack,* Issam Zineh, Pharm.D., Leslie Hendeles, Pharm.D.; University of Florida College of Pharmacy, Department of Pharmacy Practice, Gainesville, FL.

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.

404. ACCP Career Development Research Award: Resource utilization associated with comorbid depression among people with diabetes. *Marianne McCollum, Ph.D., R.Ph.*[1], Lori Nichols[2], Weiming Zhang[2]; (1)University of Colorado School of Pharmacy, Denver, CO; (2)University of Colorado Department of Preventive Medicine, Denver, CO.

405. ACCP Frontiers Research Award: Optimizing the treatment of recurrent platinum-resistant ovarian cancer using a human xenograft mouse model. *Judith A. Smith, Pharm.D., BCOP*[1], Jiang Yu, M.D.[1], Robert Coleman, M.D.[2], Judith K. Wolf, M.D.[2]; (1)The University of Texas, M.D. Anderson Cancer Center, Houston, TX; (2)The University of Texas, M.D. Anderson Cancer Center-Dept of Gynecologic Oncology, Houston, TX.

406. ACCP Pharmacotherapy Investigator Development Research Award: Modulation of adiponectin in the metabolic syndrome. *Christina L. Aquilante, Pharm.D.*, Lisa A. Kosmiski, M.D., Lucille Capo Rome, N.P.; Department of Clinical Pharmacy, University of Colorado School of Pharmacy, Denver, CO.

407. ACCP-AstraZeneca Cardiovascular Investigators: Electrophysiological effects of sympathetically mediated I(Ks) activation during I(Kr) inhibition. *Brian R. Overholser, Pharm.D.*, Xiaomei Zheng, M.S., James E. Tisdale, Pharm.D.; Department of Pharmacy Practice, Purdue University School of Pharmacy and Pharmaceutical Sciences, Indianapolis, IN.

408. ACCP-Aventis Infectious Diseases Investigator Development Research Award: Pharmacokinetic comparison of two generic and trade formulations of lamivudine, stavudine, and nevirapine in HIV infected Malawian children: Triomune tablets vs generic liquids vs trade liquids. *Amanda H. Corbett, Pharm.D.*[1], Mina C. Hosseinipour, M.D.[1], Jean Nyirenda[2], Cecelia Kanyama, MBBS[2], Idah Mshali[2], Sarah Chinyama[2], Alison Lyke, Pharm.D.[1], Naser Rezk, M.S.[1], Irving Hoffman, P.A.[1], Angela D.M. Kashuba, Pharm.D.[1], Charles Mwansambo, M.B.Ch.B.[3], Ralf Weigel, M.D.[3], Peter N. Kazembe, M.B.Ch.B.[3]; (1)University of North Carolina Hospitals, Chapel Hill, NC; (2)UNC Project in Malawi, Lilongwe, Malawi; (3)Kamuza Central Hospital, Lilongwe, Malawi.

409. ACCP-TAP Pharmaceuticals GI Investigator Development Research Award: Alteration of intestinal P-glycoprotein function following toll-like receptor-4 activation. *Brien L. Neudeck, Pharm.D.*, Jayshree Mishra, Ph.D.; University of Tennesse College of Pharmacy, Memphis, TN.

410. Amgen Hematology/Oncology Investigator Development Research Award: Cyclophosphamide (CP), doxorubicin (Dox), and doxorubicinol (dox-ol) pharmacokinetics (PK) in women receiving adjuvant chemotherapy for breast cancer. *Robert DiCenzo, Pharm.D.*[1], Jennifer J. Griggs, MD, MPH[2], Alan Forrest, Pharm.D.[1]; (1)University at Buffalo, Buffalo, NY; (2)University of Rochester, Rochester, NY.

411. 2004 ACCP-Amgen Hematology/Oncology Investigators Development Research Award: Melphalan toxicity and genetic polymorphisms. *Scott A. McConnell, Pharm.D.*[1], Jarrett R. Amsden, Pharm.D.[2], Keith J. Christensen, Pharm.D.[2]; (1)Creighton University, Omaha, NE; (2)Butler University, Indianapolis, IN.

412. Bayer Infectious Diseases Investigator Development Research Award: Vancomycin activity in agr group II *Staphylococcus aureus*. Brent M. Booker, Pharm.D, Pamela Kelchlin, A.A., Muhaymin Kamal, B.S., *Patrick F. Smith, Pharm.D.*; University at Buffalo, Buffalo, NY.

413. Ortho-McNeil Infectious Diseases Fellowship: Evaluation of efflux pumps in multidrug-resistant *Pseudomonas aeruginosa*. *Tyree Kiser, Pharm.D.*, Marilee D. Obritsch, Pharm.D., BCPS, Douglas N. Fish, Pharm.D., BCPS, Robert MacLaren, Pharm.D., Rose Jung, Pharm.D., BCPS; University of Colorado School of Pharmacy, Denver, CO.

414. Sanofi-Aventis Infectious Diseases Investigator Development Award: Cell-wall integrity pathway mediated response of *Candida glabrata* to caspofungin challenge. *Jason M. Cota, Pharm.D.*[1], Christopher R. Frei, Pharm.D., M.S.[1], David S. Burgess, Pharm.D.[1], Jose L. Lopez-Ribot, Pharm.D., Ph.D.[2], Nathan P. Wiederhold, Pharm.D.[1]; (1)University of Texas at Austin College of Pharmacy, San Antonio, TX; (2)University of Texas at San Antonio, San Antonio, TX.

415. Sanofi-Aventis Infectious Diseases Investigator Development Award: Pharmacodynamics of itraconazole and voriconazole in combination with the histone deacetylase inhibitor trichostatin A against *Aspergillus fumigatus*. *Nathan P. Wiederhold, Pharm.D.*, Robert L. Talbert, Pharm.D.; University of Texas at Austin College of Pharmacy, San Antonio, TX.

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