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American College of Clinical Pharmacy
2006 Spring Practice and Research Forum
April 9–12 • 2006
Monterey • California

American College of Clinical Pharmacy

2006 Spring Practice and Research Forum

April 9–12, 2006
Monterey,CA

ORIGINAL RESEARCH

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

ADR/Drug Interactions

1. Drug-related hospitalization to a tertiary care internal medicine service: a prospective study. Leslie J Samoy, B.Sc.Pharm.[1], Peter J Zed, B.Sc., B.Sc.Pharm., ACPR, Pharm.D.[1], Robert M Balen, B.Sc.Pharm., ACPR, Pharm.D.[1], *Kerry Wilbur, B.Sc.Pharm., ACPR, Pharm.D.*[1], Riyad B. Abu-Laban, M.D.[2], J. Mark Roberts, M.D.[3]; (1)Vancouver General Hospital - CSU Pharmaceutical Sciences, Vancouver, BC, Canada; (2)Department of Emergency Medicine, Vancouver General Hospital, Vancouver, BC, Canada; (3)Department of Internal Medicine, Vancouver General Hospital, Vancouver, BC, Canada.

PURPOSE: Adverse drug-related events (ADREs) are defined as unfavorable medical events related to the use of medications. Several studies have estimated the incidence of drug-related hospitalization (DRH); however, few data are available for the DRH rate and characterization in Canada.
The objectives of this study were to determine the frequency, severity, preventability and classification of ADREs resulting in hospitalization in a large tertiary care Canadian hospital, and to evaluate patient, prescriber, drug, and system factors associated with these events.
METHODS: Consecutive adult patients admitted to a tertiary care internal medicine service were prospectively enrolled during a 12-week period in 2005. Hospitalization was defined as drug-related if it was directly related to one of the eight predefined classes defined by Hepler and Strand. Severity and preventability were also classified. Multivariate regression analysis was used to evaluate patient, prescriber, drug, and system factors associated with DRH.
RESULTS: During the study period 565 patients were enrolled. DRH was found to be 24.1% (95% CI 20.6-27.8%) of which 72.1% (95% CI 63.7-79.4%) were deemed preventable. Severity was classified as mild, moderate, severe, and fatal in 8.1% (95% CI 4.1-14.0%), 83.8% (95% CI 76.5-89.6%), 7.4% (95% CI 3.6-13.1%) and 0.7% (95% CI 0.0-4.0%), respectively. Adverse drug reactions 35.3% (95% CI 27.3-43.9%), wrong/suboptimal drug 17.6% (95% CI 11.6-25.1%), and non-compliance 16.2% (95% CI 10.4-23.5%) were the most common classes of DRH. No independent risk factors for DRH were identified.
CONCLUSION: Approximately one-quarter of patients in our study were admitted for a drug-related cause and more than 70% were deemed preventable. Drug-related hospitalization is a significant problem that merits further research and intervention.

2. Interaction between bupropion and warfarin: a report of four cases. *Katie M. Speidel, Pharm.D.*, Stephanie R. Maciejewski, Pharm.D., Daniel E. Hilleman, Pharm.D.; The Cardiac Center of Creighton University, Omaha, NE.

BACKGROUND: Warfarin (W) is predominantly metabolized by CYP450 3A4 and 2C9. Bupropion (B) is metabolized by CYP 2B6. B is only 84% bound to plasma proteins. An interaction between B and W seems unlikely. We report 4 cases of an interaction between B and W.
DESCRIPTION OF CASES: Four patients (pts) had been stable on W for 3.5 mos to 2 yrs with INRs in the accepted range. Indication for W was DVT in 3 pts and AF in 1 pt. B was added to therapy in 3 pts for smoking cessation and 1 pt for depression. One pt presented to ER with a hemorrhage in the elbow 7 days after initiating B. The PT/INR on B and W in this pt was 57.8/5.6. The other 3 pts did not have adverse events, but had PT/INR rechecked 6–8 days after initiating B. The resultant PT/INR were 50.7/5.93, 48.5/5.2, 33.5/3.98. All pts had B discontinued with normalization of PT/INR. W was restarted without further incident. In pts where B was used for smoking cessation, subjects had not yet stopped smoking at the time of the interaction. Two pts were not taking any medications other than B and W. The pt with AF was taking furosemide, digoxin and lisinopril. The pt with depression was taking metoprolol and HCTZ for hypertension.
CONCLUSION: We report 4 cases of substantial interaction between B and W. No readily apparent mechanism for the interaction was identified. One case resulted in a spontaneous hemorrhage requiring medical intervention. A prospective evaluation of potential pharmacokinetic/pharmacodynamic interaction between B and W is warranted.

Analgesia

3. Confidence vs. competence: comparing physicians' self-reported pain management comfort level with an objective knowledge assessment in a large urban academic medical center. *Mark A. Douglass, Pharm.D.*[1], Gail M. Burniske, Pharm.D.[2], Gail Wilkes, R.N.C., M.S., A.O.C.N.[2], Daniel P. Alford, M.D., M.P.H.[2], Jeffrey L. Greenwald, M.D.[2]; (1)Northeastern University Department of Pharmacy Practice/Boston Medical Center, Boston, MA; (2)Boston Medical Center, Boston, MA.

PURPOSE: Pain management practices at our medical center are less than optimal, despite the implementation of institutional pain management guidelines. We sought to compare physicians' self-reported comfort level in several pain management competencies with an objective assessment of their knowledge in these areas.
METHODS: New medical residents, senior residents, and attending physicians were asked to complete a questionnaire that assessed their comfort level with core pain management competencies (Table 1). We compared physicians' self-reported comfort level with an objective assessment of their knowledge using validated and standardized case vignettes. Physicians were also asked about their awareness of the hospital's pain management guidelines.
RESULTS: The questionnaire response rate was 30% (91/304). Only 23% (21/91) of those surveyed reported awareness of the pain management guidelines and only 48% (10/21) of those that were aware of the guidelines used them "rarely" or "never." An overall disparity between physician self-reported comfort level and case vignette performance was observed (Table 1). Attending physicians and senior residents often reported a greater degree of comfort than new medical residents, despite an overall low performance on the objective measures.

Table 1. Physicians' self-reported comfort level and corresponding knowledge assessment

Physician type	Chronic-continuou pain		Equianalgesic dose conversion		Breakthrough dosing	
	Comfortable	Correct	Comfortable	Correct	Comfortable	Correc
	(%)	(%)	(%)	(%)	(%)	(%)
New residents (n=34)	12	45	26	50	23	18
Senior residents (n=30)	69	23	62	33	53	27
Attending (n=27)	81	44	59	54	67	44

CONCLUSION: Educational initiatives are needed to address low physician competency in pain management. These initiatives must take into account the discrepancy between physician comfort and relatively low level of competency, irrespective of level of training. Although our institution has pain management guidelines as a means of ensuring optimal pain management, they were rarely used.

Cardiovascular

4. Poor absorption of amiodarone administered via nasogastric tube in patients following thorocoabdominal esophagectomy. *James E. Tisdale, Pharm.D.*[1], Heather A. Wroblewski, R.N., B.S.N., CCRN[1], Karen M. Rieger, M.D.[2], Zane Hammoud, M.D.[2], Jo Ann Brooks, R.N., DNS[2], Jerry Young, M.D.[2], Donna Wall, Pharm.D.[3], Kenneth A Kesler, M.D.[2]; (1)Purdue University, 1001 West 10th Street, Indianapolis, IN; (2)Indiana University School of Medicine, Inidianapolis, IN; (3)Clarian Health Partners, Indianapolis, IN.

PURPOSE: Atrial fibrillation (AF) occurs in up to 1/3 of patients following thoracoabdominal esophagectomy surgery (ES), and is associated with increased morbidity and mortality. While planning a study of amiodarone for AF prophylaxis, we considered it desirable to avoid prolonged intravenous (IV) administration due to the potential for adverse effects. However, few data exist regarding the gastrointestinal absorption of drugs following ES. This study was conducted to determine whether amiodarone administered via nasogastric (NG) tube is absorbed in patients following ES.
METHODS: Plasma amiodarone concentrations were determined in 14 patients that underwent ES and in 13 patients that underwent pulmonary resection (PR, control group). At induction of anesthesia, a continuous IV infusion of amiodarone was initiated and continued for 24 hours (total IV

dose 1050 mg), followed by 400 mg via NG tube every 12 hours for 6 days. Blood samples were obtained immediately following completion of the IV infusion [post-operative day (POD) #1], and prior to the 3rd (POD #2) and 7th (POD #4) NG doses.
RESULTS: Plasma amiodarone concentrations at the end of the IV infusion were not significantly different in the ES vs PR groups. Concentrations tended to be lower in the ES group on POD #2 and were significantly lower on POD #4 (Table). In addition, 33.3% of the ES patients had undetectable concentrations on POD #2, compared with 0% in the PR group (p=0.045). Similarly, 58% of the ES patients had undetectable concentrations on POD #4 compared to 0% in the PR group (p=0.006).
CONCLUSIONS: Amiodarone administered via NG tube following ES is poorly and inconsistently absorbed.

Table. Plasma Amiodarone Concentrations (mg/L)

	Esophagectomy	Lung Resection	p value
POD #1	0.62±; 0.31	0.88±; 0.19	0.132
POD #2	0.33±; 0.25	0.58±; 0.18	0.054
POD #4	0.30±; 0.32	0.74±; 0.11	0.025

5E. Serum creatinine elevations in patients receiving nesiritide are related to starting dose. *William T. Abraham, M.D.*; Ohio State University, Columbus, OH.

PURPOSE: An increased risk of SCr elevation with nesiritide (NES) has been reported in the literature using pooled data from 5 trials; 4 used higher than the currently recommended starting dose of 0.01 µg/kg/min.
OBJECTIVE: To evaluate the impact of NES starting dose on the risk of SCr elevation in patients treated for decompensated heart failure.
METHODS: Pooled data from 5 previous trials, which employed starting doses of 0.01, 0.015, and 0.03 µg/kg/min of NES, were analyzed. Dose-response was assessed by calculating the OR of SCr increases > 0.5 mg/dL at any time within 30 days of initiating NES therapy, for each of these starting doses relative to control.
RESULTS: Data from 760 nesiritide (0.01 µg/kg/min: n = 268; 0.015 µg/kg/min: n=249; 0.03 µg/kg/min: n=243) and 462 control subjects were evaluated. The OR of a SCr rise >0.5 was not significantly increased at the currently approved starting dose of NES; findings were similar for both the fixed (0.01 µg/kg/min; OR: 1.4; 95% CI: 0.92-2.24) and the adjustable (0.01-0.03 µg/kg/min; OR: 1.0; 95% CI: 0.47-2.12) NES groups. The risk of SCr increase appeared to parallel the rate of symptomatic hypotension; 5%, 13%, and 19% of subjects in the 0.01, 0.015, and 0.03 µg/kg/min starting-dose groups, respectively, developed symptomatic hypotension during study drug infusion or within 2 hours of stopping treatment, compared with 5% of subjects in the control groups. Whether this association represents a causal relationship is not known at present.

SCr Increase >0.5 mg/dL

Nesiritide Starting Dose	N	Odds Ratio (95% CI)	*P*-value
0.01 µg/kg/min	268	1.35 (0.88-2.06)	0.17
0.015 µg/kg/min	248	1.90 (1.02-3.54)	0.02
0.03 µg/kg/min	243	2.58 (1.40-4.74)	0.001

CONCLUSIONS: The risk of SCr elevation with NES may be directly related to starting dose used. It is not significantly increased at the currently approved dose.
Published in Circulation 2005;112(17, suppl II):II-589.

6E. Nesiritide does not increase 30-day or 6-month mortality risk. *William T. Abraham, M.D.*; Ohio State University, Columbus, OH.

PURPOSE: Baseline differences in mortality risk factors may significantly influence mortality rates in clinical trials not powered to assess mortality. Objective: To determine mortality risk for nesiritide (NES) vs control (CON) after adjusting for baseline differences.
METHODS: Mortality data were analyzed from all NES trials with 30-day (7 trials) and 6-month (4 trials) mortality results; 30-day mortality was also analyzed excluding the FUSION study (6 trials). The mortality effect of all variables with ≥ 3% absolute baseline differences between NES and CON groups was assessed using univariate Cox regression. Significant predictors identified were then evaluated using multivariate Cox regression with a stepwise criterion of $P<0.05$ for entry and $P<0.10$ for retention in the model. These multivariate models were used to adjust mortality HR (95% CI) for NES vs CON.
RESULTS: Baseline creatinine clearance ≤ 60 mL/min, baseline SBP ≤ 100 mm Hg, prior dopamine/dobutamine use, ventricular tachycardia, and NYHA class IV HF were significant predictors of mortality. Adjusted and unadjusted 30-day mortality HR (95% CI) for 7 trials (N=1717), 6 trials (N=1507), and 6-month mortality HR (95% CI) for 4 trials (N=1167) are reported in the table.

Mortality Risk: Pooled Nesiritide Data

	Hazard Ratio (95% CI)	*P*-value
30-Day (7 trials)		
Unadjusted	1.27 (0.81-2.01)	0.30
Adjusted	1.12 (0.71-1.78)	0.63
30-Day (6 trials)		
Unadjusted	1.34 (0.84-2.15)	0.22
Adjusted	1.18 (0.74-1.90)	0.49
6-Month (4 trials)		
Unadjusted	1.05 (0.81-1.36)	0.73
Adjusted	0.98 (0.75-1.26)	0.85

CONCLUSION: In 3 pooled analyses NES did not increase mortality risk significantly vs CON; adjustment for baseline differences in mortality predictors reduced any trend toward higher risk.
Published in Circulation 2005;112(17, suppl II):II-676.

7E. Combining nesiritide (NES) with high-dose diuretics may increase the risk of increased serum creatinine. *J. Thomas Heywood, M.D.*; Scripps Clinic, La Jolla, CA.

INTRODUCTION: In acute decompensated heart failure (ADHF), addition of NES to standard therapy more rapidly lowers filling pressures and improves symptoms. It is unclear whether the diuretic dose or regimen should be modified when NES is added to therapy for ADHF.
OBJECTIVE: To determine the relative risk of increased SCr for NES vs nitroglycerin (NTG) in HF patients receiving high-dose diuretics.
METHODS: Data from the Vasodilation in the Management of Acute Congestive HF (VMAC) trial, a multicenter, double-blind, randomized evaluation of NES vs NTG therapy in subjects with ADHF, were retrospectively analyzed. The rates of SCr increases >0.5 mg/dL from baseline through study day 30 were calculated in patients who received high-dose diuretics and in patients who received low- or moderate-dose diuretics. The RR and 95% CI of SCr increase for NES vs NTG were based on the Mantel-Haenszel estimate. High-dose diuretic use was defined as a maximum daily dose of furosemide ≥ 160 mg, bumetanide ≥ 4 mg, torsemide ≥ 80 mg, metolazone ≥ 10 mg, chlorothiazide ≥ 1000 mg, or hydrochlorothiazide ≥ 50 mg or concurrent treatment with 2 or more of these diuretics regardless of dose.
RESULTS: Overall, 480/489 VMAC subjects (98%) had evaluable SCr data (NES: n=268; NTG: n=212). Of these, 149 NES (56%) and 131 NTG (62%; $P=0.19$) subjects received high-dose diuretics. The risk of SCr increase >0.5 mg/dL was unaffected by vasodilator type in the low- to moderate-dose diuretic group but was significantly increased by NES in the high-dose diuretic group.

	SCr Increase >0.5 mg/dL, n/total (%)		RR (95% CI)	*P*-value
Diuretics	NES	NTG	NES/NTG	
Low/Mod-Dose	24/119 (20.2%)	17/81 (21.0%)	0.96 (0.55-1.66)	0.975
High-Dose	49/149 (32.9%)	28/131 (21.4%)	1.50 (1.00-2.25)	0.044

CONCLUSIONS: Patients who received NES plus high-dose diuretics may have an increased risk of SCr increases >0.5 mg/dL. Prospective evaluations to determine optimal use of NES plus diuretics are warranted.
Published in Circulation 2005;112(17, suppl II):II-451–II-452.

8E. Temporal characteristics of serum creatinine elevations in patients receiving nesiritide (NES) and nitroglycerin (NTG). *J. Thomas Heywood, M.D.*; Scripps Clinic, La Jolla, CA.

INTRODUCTION: In patients admitted for decompensated HF, an acute rise in SCr has been associated with increased mortality. However, late SCr increases may reflect worsening clinical status during a prolonged hospitalization, whereas early increases likely reflect temporary but correctable volume depletion. Objective: To determine the prevalence, onset time, and persistence of SCr elevations in hospitalized HF patients receiving NES and NTG.
METHODS: SCr data from the Vasodilation in the Management of Acute Congestive HF (VMAC) trial, a randomized evaluation of NES vs NTG therapy in subjects hospitalized for decompensated HF, were analyzed retrospectively. The prevalence of SCr elevations >0.5mg/dL from baseline during study drug infusion, within 72 hours of study drug discontinuation, and during the remainder of the hospitalization were compared for the 2 treatments. SCr elevations were classified as persistent if the elevation was still present on study day 30.
RESULTS: During hospitalization, 38/268 NES (14%) and 25/212 NTG (12%; $P=.50$) subjects developed an acute SCr elevation. The onset time of these elevations was similar for both treatments. Persistent elevations were rare (see Table).

Prevalence of Serum Creatinine Elevation >0.5 mg/dL

		P-value	Persistent
During infusion			
Nesiritide	1.5% (4/268)	0.74	n=1
Nitroglycerin	1.9% (4/212)		n=0
<72 hrs after discontinuing infusion			
Nesiritide	6.7% (18/268)	0.57	n=2
Nitroglycerin	5.2% (11/212)		n=1
≥72 hrs after discontinuing infusion through hospital discharge			
Nesiritide	6.0% (16/268)	0.69	n=1
Nitroglycerin	4.7% (10/212)		n=1

CONCLUSIONS: The prevalence, onset time, and resolution of SCr elevations occurring during hospitalization for decompensated HF were similar in patients receiving NES and NTG treatment. Only 1%–2% of patients developed an acute SCr elevation during infusion of their vasodilator, and 40%–42% of the elevations occurred ≥ 72 hours after discontinuation of vasodilator therapy. Persistent renal dysfunction was rare in both groups.
Published in Circulation 2005;112(17, suppl II):II-590.

9E. Clinical predictors of worsening renal function (WRF) in patients hospitalized for heart failure. *Andrew J. Burger, M.D.*; Beth Israel Deaconess Medical Center, Boston, MA.

INTRODUCTION: In patients hospitalized for acute HF, renal insufficiency and WRF have been associated with increased morbidity and mortality. Objective: To identify clinical predictors of WRF for acute HF in the Vasodilation in the Management of Acute Congestive (VMAC) HF trial.
METHODS: VMAC was a prospective, multicenter evaluation of 489 subjects hospitalized for decompensated HF. Subjects were randomized to standard care plus nesiritide (NES), nitroglycerin (NTG), or placebo for the first 3 hours. Placebo subjects were then crossed over to 1 of the other 2 groups. Treatment was maintained for at least 24 hours; study drug was stopped in 94% of patients within 3 days. 22 baseline clinical, demographic, and treatment characteristics (potential risk factors for HF) were analyzed using a logistic regression model with a backward selection criterion of a=0.10 for retention. WRF was defined as a >0.5mg/dL increase in SCr within 7 or 30 days of enrollment.
RESULTS: Patients: 62±14 yr old; 69% male. Mean EF: 27±14; 49% had ischemic etiology of HF. Baseline SCr: 1.6±1.0 mg/dL; 42% of patients were NYHA class III, 42% class IV. Overall, 40/480 subjects (8.3%) with available SCr data developed WRF within 7 days; 118 subjects (25%) within 30 days. Significant predictors of WRF within 7 days: ACS in the 7 days prior to initiation of study drug (OR: 2.80, 95% CI: 1.23–5.97) and NYHA Class IV (OR: 1.74; 95% CI: 0.9-3.4). Significant predictors of WRF at 30 days: ischemic etiology (OR: 1.98; 95% CI: 1.28-3.06), baseline CrCl ≤60mL/min (OR: 1.71; 95% CI: 1.11-2.65), and NYHA Class IV (OR: 1.51; 95% CI: 0.98-2.31). Vasoactive treatment assignment (NES vs NTG) did not correlate with WRF at 7 or 30 days.
CONCLUSIONS: In VMAC, recent ACS, ischemic etiology, NYHA class IV, and baseline CrCl (but not NES or NTG) were independent predictors of WRF.
Published in Circulation 2005;112(17, suppl II):II-589–II-590.

10E. Effect of atorvastatin on leukocyte production of matrix metalloproteinase-8 and -9 in patients without dyslipidemia. *Issam Zineh, Pharm.D.*[1], Christopher B. Arant, M.D.[2], Timothy R. Wessel, M.D.[2], 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.

PURPOSE: Leukocytes are important in initiation of cardiovascular disease (CVD). One detrimental effect of leukocytes is secretion of matrix metalloproteinases (MMPs), which are implicated in pathological tissue remodeling. Statins may reduce MMP concentrations in hypercholesterolemia and acute coronary syndromes. No study has examined the effect of statins on MMP production from leukocytes in patients without overt dyslipidemia.
METHODS: Normocholesterolemic adult men and women without CVD or CVD risk equivalents were eligible. Patients using lipid-lowering or anti-inflammatory medications at baseline were excluded. After a two-week run-in period, subjects received atorvastatin 80 mg daily. Leukocyte cultures were prepared at baseline and after 4 weeks of therapy from subjects' buffy coat samples. Cells were incubated at 37°C with 5% CO_2, and after 24 hours culture media were collected and stored at -90°C until measurement of MMP-8 and MMP-9 by flow-based immunofluorescence detection. Samples were assayed in duplicate. Analyses were by paired t-test with significance set at p<0.05.
RESULTS: Ten subjects were studied with average age, total cholesterol, LDL, HDL, and triglycerides of 28±10 years, 187±41 mg/dl, 100±36 mg/dl, 65±20 mg/dl, and 109±51 mg/dl, respectively. After 4 weeks of atorvastatin, MMP-8 was reduced by 38% from 5767 pg/ml to 3548 pg/ml (p=0.02). MMP-9 was reduced by 9% from 26,636 pg/ml to 24,257 pg/ml (p=0.1).
CONCLUSIONS: Atorvastatin significantly reduced leukocyte production of MMP-8 in individuals without dyslipidemia or manifest CVD after four weeks. There was a non-significant reduction in MMP-9 concentrations. These data suggest a potential benefit of atorvastatin in individuals without high-risk for CVD and should be studied further.
Presented at the Annual Meeting of the American Society for Clinical Pharmacology and Therapeutics, Baltimore, M.D., March 2006.

11. Effects of national guideline and evidence-based medicine on thiazide diuretic prescribing in an outpatient resident clinic. *Ericka B. Ridgeway, Pharm.D.*[1], Sarah V. Muench, Pharm.D.[1], Sandor Shoichet, M.D.[1], Megan B. Bestul, Pharm.D.[2]; (1)William Beaumont Hospital, Royal Oak, MI; (2)William Beaumont Hospital, Wayne State University, Royal Oak, MI.

PURPOSE: Results of the ALLHAT demonstrate that thiazide-type diuretics are as or more effective at lowering blood pressure and reducing clinical events compared to other antihypertensive agents. Based on these outcomes JNC-VII recommends thiazide diuretics as first-line agents for the treatment of hypertension. The purpose of this study was to assess the effect of ALLHAT and JNC-VII on prescribing practices for the treatment of hypertension and assess the number of patients at goal blood pressure before and after publication of ALLHAT and JNC-VII.
METHODS: This was a retrospective chart review of patients with diagnosed hypertension treated at an internal medicine outpatient resident clinic. Thiazide prescribing rates were compared during five-month time periods, pre-ALLHAT/JNC-VII and post-ALLHAT/JNC-VII publication. Patient visits were assessed for blood pressure goal achievement based on national guideline recommendations.
RESULTS: One hundred seventeen patients were eligible for pre-ALLHAT/JNC-VII group, 112 patients for post-ALLHAT group, and 94 patients for post-JNC-VII group. There were no significant demographic differences between groups. Thiazides were prescribed in 14 patients (12%) in pre-ALLHAT/JNC-VII group, 17 (15%) in post-ALLHAT group, and 12 (13%) in post-JNC-VII group (p>0.05 for comparison of pre- and post-groups). During 80% of patient visits, 26 patients (22%) were at goal blood pressure in pre-ALLHAT/JNC-VII group compared with 37 (33%) in post-ALLHAT group and 23 (24%) in post-JNC-VII group (p=0.08, 0.74, respectively, for comparison between pre- and post-groups).
CONCLUSIONS: There were no significant differences in prescribing of thiazide diuretics between groups. Goal blood pressure, for the majority of patient visits, was not achieved in each group evaluated. Results from this study demonstrate the need to reinforce evidence-based medicine data and national guideline recommendations for the treatment of hypertension.

12. Characteristics of patients admitted to the hospital for amiodarone toxicity. *Katie M. Speidel, Pharm.D.*, Stephanie R. Maciejewski, Pharm.D., Daniel E. Hilleman, Pharm.D.; The Cardiac Center of Creighton University, Omaha, NE.

PURPOSE: Amiodarone (AMIO) remains the most commonly prescribed antiarrhythmic agent in the US. The FDA recently mandated that pharmacists provide a medication guide with any prescription for AMIO, presumably due to increasing prevalence of drug-related toxicity. We evaluated our hospital admissions for AMIO-related toxicity.
METHODS: Medical records of pts admitted to the hospital for AMIO-related toxicity were identified and reviewed. Demographic and clinical characteristics and the type and severity of AMIO toxicity were evaluated.
RESULTS: Admissions for AMIO toxicity by year were: 2001 n = 2; 2002 n = 8; 2003 n = 7; and 2004 n = 20. Demographics of patients were: 74.7±8.2 yrs; 23M/14W; indication for AMIO: AF = 24; ICD = 9; AF+ICD = 4; duration of AMIO therapy: ≤ 3 mos = 7; > 3 ≤ 6 mos = 4; > 6 ≤ 12 mos = 8; >12 ≤ 24 mos = 11; and > 24 mos = 7. Daily AMIO doses: 800 mg in 1 pt and 1200 mg in 1 pt (both still loading); 100 mg = 1; 200 mg = 13, and 400 mg = 18. Toxicity included: peripheral neuropathy = 1; tremor = 1; GI = 2 (both during loading); hepatic =3; dermatologic = 2; AV block/bradycardia = 2; pulmonary/AV block/bradycardia =1; hyperthyroid/pulmonary = 1; hypothyroid/pulmonary = 2; hyperthyroid = 7; hypothyroid = 7; pulmonary = 8. Thirty-two pts discontinued AMIO permanently with 5 restarting and continuing AMIO. Five pts expired during hospitalization.
CONCLUSION: At our institution, the number of pts admitted due to AMIO toxicity appears to be increasing. The vast majority of pts admitted with AMIO toxicity have pulmonary or thyroid toxicity. Hyper- and hypothyroidism occur with equal frequency. Whether outpatient monitoring can identify or prevent pulmonary and thyroid toxicities and potentially avoid hospital admissions needs to be evaluated.

13. Comparative efficacy and safety of LotrelÆ (amlodipine/benazepril) and TarkaÆ (trandolapril/verapamil): a meta-analytic evaluation. *Katie M. Speidel, Pharm.D.*, Tammy Burns, Pharm.D., Stephanie R. Maciejewski, Pharm.D., Michele A. Faulkner, Pharm.D., Daniel E. Hilleman, Pharm.D.; The Cardiac Center of Creighton University, Omaha, NE.

PURPOSE: The most commonly prescribed fixed dose combinations of angiotensin converting enzyme inhibitors (ACEI) and calcium channel blockers (CCBs) are LotrelÆ (amlodipine/benazepril) and TarkaÆ (trandolapril/verapamil). There are currently no published comparative data evaluating the efficacy and safety of LotrelÆ (L) and TarkaÆ (T). This study is a meta-analysis of published randomized controlled trials that included a treatment cohort with either L or T.
METHODS: A literature search (Medline, Embase) using the key terms L, T, amlodipine, benazepril, trandolapril, verapamil, and randomized controlled trial was conducted for 1990 through 2005. Randomized, double-blind, and placebo or active controlled studies were included. Data abstracted from each study included the absolute change in systolic and diastolic BP, percentage of responders, percentage of patients with adverse effects (AE), and percentage of patients discontinuing therapy due to an adverse effect (DC AE). Outcomes were pooled using standard meta-analytic software and compared statistically using the "t" test.
RESULTS: L was used in 16 cohorts including 7828 patients and T was used in 24 cohorts including 1630 patients. Systolic BP was reduced by 15.8±6.8 mm Hg with L and 18.3±8.7 mm Hg with T (p=0.02). Diastolic BP was reduced by 11.7±5.7 mm Hg with L and 12.9±7.0 mm Hg with T (p=NS). Percentage of patients with BP response was 69% (95% CI 58%-80%) with L and 72% (95% CI 64%-80%) with T (p=NS). AE rate was 16.7±13.6% with L and 19.7±12.5% with T (p=NS). DC AE rate was 5.6±3.1% with L and 3.2±1.8% with T (p=0.01).
CONCLUSIONS: T is associated with a significantly greater reduction in systolic BP and a significantly lower rate of discontinuation due to AEs than L. This meta-analysis suggests that a prospective comparison of L and T is needed to compare the relative efficacy and safety of these two fixed-dose combinations of ACEI and CCBs.

14. Evaluation of therapeutic options for patients who fail to reach low density lipoprotein cholesterol goal on simvastatin monotherapy. *Julie S. Altman, Pharm.D.*, Christina C. Piro, Pharm.D.Candidate, C. Gene Reeder, Ph.D.; South Carolina College of Pharmacy, Columbia, SC.

PURPOSE: Low density lipoprotein cholesterol (LDL-C) reduction is associated with reduced cardiovascular morbidity and mortality. Treatment with the statin drugs simvastatin 80mg and atorvastatin 40mg can reduce LDL-C 48% and 51% respectively. Ezetimibe, an absorption inhibitor, can reduce LDL-C 18% as monotherapy and an additional 25% when added to a statin. The purpose of this study was to compare percentage LDL-C reduction in patients changed from simvastatin 80 mg daily monotherapy to simvastatin 80 mg plus ezetimibe 10 mg daily or atorvastatin 40 mg daily monotherapy, two common occurrences in the Veterans Affairs Medical Center for patients who fail to reach LDL-C goal on maximal simvastatin monotherapy.
METHODS: Sixteen patients were identified to have been prescribed ezetimibe as add-on therapy to simvastatin 80 mg daily. To serve as comparators, 16 patients who had been switched from simvastatin 80 mg to atorvastatin 40 mg were randomly selected. A retrospective chart review was conducted to collect patient demographic information, information concerning lipid lowering therapy, lipid parameters prior to and after lipid lowering therapy change, concomitant lipid lowering medications, and presence of adverse effects following change in lipid lowering therapy.
RESULTS: Patient demographics were similar between groups. The average LDL-C prior to therapy change was 144 mg/dL in the simvastatin/ezetimibe group and 139 mg/dL in the atorvastatin group. Six months following the switch, LDL-C was reduced 19.8% in the simvastatin/ezetimibe group versus 11.8% in the atorvastatin group. The average LDL-C value 6 months following the switch in therapy was 107 mg/dL in the simvastatin/ezetimibe group and 119 mg/dL in the atorvastatin group. No adverse events were reported related to a change in lipid lowering therapy in either group.
CONCLUSIONS: Patients switched to simvastatin 80 mg plus ezetimibe 10 mg had a greater reduction in LDL-C than those switched to atorvastatin 40 mg monotherapy.

15E. Diminishing rates of return in reducing coronary heart disease event rates with progressive LDL cholesterol lowering: linear vs inhibitory maximum effect modeling. *Scott L. Charland, Pharm.D.*, Eric J. Stanek, Pharm.D., Mark E McGovern, M.D.; Kos Pharmaceuticals, Inc, Cranbury, NJ.

BACKGROUND: The relationship between LDL-C and CHD event rates during statin prevention trials is commonly reported to be linear and extrapolated to result in zero CHD events at LDL-C ~40 mg/dL. We sought to explore this relationship further through maximum effect modeling.
METHODS: Linear and nonlinear inhibitory maximum effect (iEmax) models were used to evaluate the LDL-C versus absolute CHD event rate relationship from 5 published long-term (4-6 years) secondary-prevention statin trials. Goodness of fit was calculated for both models and compared (Akaike Information Criteria and F-test) Additionally, the incremental number needed to treat (iNNT) and potential treatment cost (statin AWP) to prevent one CHD event for each 10 mg/dl LDL-C lowering below 100 mg/dl was determined.
RESULTS: The LDL-C versus CHD event rate plot was fit significantly better by the iEmax model (F=11.15, p=0.0046), indicating a closer approximation of the true relationship. Whereas the linear model yielded an unchanging NNT, the iEmax model yielded increasing iNNTs for lowering LDL-C from 100 mg/dL to 90 mg/dL, 90 mg/dL to 80 mg/dL, and 80 mg/dL to 70 mg/dL of 154, 182 and 666, respectively. Based upon the iNNT, the incremental annual statin cost associated with the iEmax model ranged from $212,5200 to $1,238,760 for each 10 mg/dL decrease in LDL-C.
CONCLUSION: The relationship between LDL-C lowering and CHD events is better fit with a nonlinear maximum effect iEmax model, and should not be assumed to be linear. Additionally, there is a marked diminishing rate of return at progressively lower LDL-C levels leading to increasing annual costs. Greater event reduction once LDL-C is <100 mg/dL may require aggressive concomitant modification of other cardiovascular risk factors, such as HDL-C, triglycerides, and blood pressure, as opposed to exclusive focus on further LDL-C lowering
Published in Circulation 2005;112:II-816.

16. The healthy at heart evaluation study: 4-month interim results. *David Vlahov, Ph.D.*[1], Sandro Galea, M.D.[1], Tinka Markham Piper, M.P.H.[1], Pamella Thomas, M.D.[2], Debra Parsow, .[3], Erik Kuntze, M.D.[4], Tracy Mayne, Ph.D.[5]; (1)New York Academy of Medicine, New York, NY; (2)Lockheed Martin Aeronautics, Marietta, GA; (3)ConAgra Foods, Omaha, NE; (4)Pfizer Global Pharmaceuticals, New York, NY; (5)Pfizer, New York, NY.

INTRODUCTION: The Healthy at Heart program (H@H) uses patient and physician education and learning techniques to reduce/prevent cardiovascular-related risk-producing behavior within an employer setting.
OBJECTIVE: Measure 4-month change in treatment initiation (diet and exercise, medicine), blood pressure and LDL-C between participants in both arms: current sample =20% of total.
METHODS: This multi-center, controlled intervention study compares the impact of the H@H disease management program versus control in employees at Lockheed Martin Aeronautics and ConAgra Foods at 4 and 12 months. Participants were screened at health fairs. Eligible employees were assigned to receive the H@H Program or control in a 4:1 ratio.
RESULTS:

Table 1. Baseline and 4-month follow-up

	Intervention (N= 318)		Control (N=95)		Time p-value	Group* p-value
	BL	4-Mo	BL	4-Mo		
Cholesterol						
Seeing a physician for Chol	7%	20%	13%	15%	<0.01	0.61
Now taking chol meds	11%	25%	15%	19%	<0.01	0.88
At ATP-III LDL-C goal	36%	63%	50%	67%	<0.01	0.04
Mean LDL - C	143	113	128	109	<0.01	0.55
Hypertension						
Seeing a physician for HTN	33%	42%	22%	45%	<0.01	0.22
Now taking HTN meds	28%	34%	31%	41%	0.02	0.33
At JNC-7 BP goal	53%	50%	36%	66%	0.11	0.32
Systolic blood pressure	135	130	141	131	<0.01	0.35
Diastolic blood pressure	82	80	85	80	<0.01	0.37
Diet						
Has changed diet	78%	90%	79%	88%	<0.01	0.05
Exercise						
More active	52%	70%	58%	70%	<0.01	0.55
BMI (M,SD)	31	31	33	32	0.24	0.68
Smokers	37%	34%	40%	34%	0.83	0.78

*Differences at 4-months controlling for baseline value

CONCLUSIONS: In these early analyses, nearly all cardiovascular health measures improved over time, but the incremental benefit of the H@H intervention was primarily significant for the percentage of employees reaching ATP-III LDL-C goal.

17E. Nesiritide-associated increase in serum creatinine does not increase early mortality in patients with decompensated heart failure. *Uri Elkayam, M.D.*[1], J. Thomas Heywood, M.D.[2]; (1)University of Southern California Medical Center, Los Angeles, CA; (2)Scripps Clinic, La Jolla, CA.

PURPOSE: The use of nesiritide (NES) has been associated with an increased risk of serum creatinine (SCr) elevations in some patients. SCr increases during hospitalization for heart failure has been associated with an increased risk of mortality. However, SCr may be influenced by a wide variety of factors such as baseline renal function, hemodynamic status, comorbid conditions, and concomitant medications such as diuretics and ACE inhibitors. The effect of NES-associated SCr increases on mortality is unknown. Objective: To evaluate the effect of NES-associated SCr increases on mortality.
METHODS: Pooled data from 5 randomized NES trials were analyzed. Mortality was assessed at 30 days in patients who had SCr increases >0.5

mg/dL within 30 days. The hazard ratio (HR) and 95% CI of death associated with SCr increases >0.5 mg/dL were compared for subjects in the NES and control groups. Control agents included inotropes, nitroglycerin, and/or diuretics.
RESULTS: In total, 214 of 1248 subjects (17%) had SCr increases >0.5 mg/dL (NES: 151 of 786 subjects [19%]; control: 63 of 462 subjects [14%]). A SCr increase >0.5 mg/dL was associated with a 1.1-fold increase in 30-day mortality risk in NES subjects compared with a 3.4-fold increase in 30-day mortality risk in control subjects.

Kaplan-Meier Mortality Rates Patients With SCr Increase at Any Time Through Study Day 30

	SCr Increase vs No Increase			
	SCr Increase >0.5 mg/dL*	No SCr Increase	HR (95% CI)	*P* value
30-Day Mortality				
NES	7.3 (11/151)	5.9 (37/635)	1.1 (0.6, 2.2)	0.722
Control	13.0 (8/63)	4.3 (17/399)	3.4 (1.4, 8.3)	0.005

*Number of deaths/number of patients with SCr increase >0.5 mg/dL.

CONCLUSIONS: These data suggest that SCr increases in patients treated with nesiritide are not associated with an increased risk of mortality at 30 days. Prospective studies designed to evaluate the effects of nesiritide on renal endpoints are needed.
Published in Circulation 2005;112:(17, suppl II):II-675–II-676.

18E. Intensive lipid lowering with atorvastatin in patients with metabolic syndrome and stable coronary disease. *Prakash Deedwania, M.D.*[1], James Shepherd, M.D.[2], Philip Barter, M.D.[3], Steve Haffner, M.D.[4], Rafael Carmena, M.D.[5]; (1)UCSF Fresno, Fresno, CA; (2)Royal Infirmary, Glasgow, United Kingdom; (3)The Heart Institute, Camperdown, Australia; (4)University of Texas Health Science Center at San Antonio, San Antonio, TX; (5)Hospital Clinico Universitario, Valencia, Spain.

PURPOSE: The TNT study showed that intensive lipid-lowering therapy with atorvastatin 80 mg/day provides significant clinical benefit beyond that afforded by treatment with atorvastatin 10 mg/day in patients with stable CHD. The current post hoc analysis investigates whether similar benefits of high-dose intensive atorvastatin therapy can be achieved in patients with CHD and metabolic syndrome.
METHODS: A total of 3477 patients with metabolic syndrome and clinically evident CHD, with LDL-C levels of <130 mg/dL (3.4 mmol/L) (following an 8-week open-label run-in period with atorvastatin 10 mg) were randomized to double-blind therapy with either atorvastatin 10 mg/day (n=1771) or 80 mg/day (n=1706). Metabolic syndrome was defined based on NCEP ATP III criteria (body mass index >30 kg/m^2). Patients with diabetes mellitus were not excluded and comprised 30% of the subgroup. The primary end point was the occurrence of a first major cardiovascular event, defined as death from CHD, nonfatal non-procedure-related myocardial infarction, resuscitated cardiac arrest, or fatal or nonfatal stroke.
RESULTS: Mean on-treatment LDL-C levels at 3 months were 100.0 mg/dL (2.6 mmol/L) with atorvastatin 10 mg, and 73.3 mg/dL (1.9 mmol/L) with atorvastatin 80 mg. After mean follow up of 5.0 years, a primary event occurred in 252 patients (14.2%) receiving atorvastatin 10 mg, compared with 175 patients (10.3%) receiving atorvastatin 80 mg (HR=0.71; 95% CI 0.58-0.86, P=0.0005). Secondary measures of efficacy were consistent with those in the overall study population. There was no clinically important difference in the rates of adverse events between the two treatment arms. LFT elevations were reported in 0.9% of patients on atorvastatin 80mg, and in 0.2% of patients on atorvastatin 10mg.
CONCLUSION: Intensive therapy with atorvastatin 80 mg significantly reduced the rate of major cardiovascular events by 29% compared with atorvastatin 10 mg in patients with clinically evident CHD and metabolic syndrome.
Presented at the American Heart Association Scientific Sessions 2005, Dallas, TX, November 13-16, 2005.

19E. Safety and efficacy of atorvastatin at very low LDL-C levels: a post-hoc analysis of the TNT study. *John C. LaRosa, M.D.*[1], John J. Kastelein, M.D.[2], John B. Kostis, M.D.[3]; (1)SUNY Downstate Medical Center, Brooklyn, NY; (2)University of Amsterdam, Amsterdam, Netherlands; (3)Robert Wood Johnson Medical School, New Brunswick, NJ.

INTRODUCTION: The TNT study showed that intensive lipid-lowering (atorvastatin 80mg) to an LDL-C of 77 mg/dL (2.0 mmol/L) provides significant additional clinical benefit in stable CHD patients. Observational studies have raised concern about the safety of lowering LDL-C well beyond levels recommended in current guidelines.
METHODS: A total of 10,001 patients with clinically evident CHD and LDL-C levels <130 mg/dL (3.4 mmol/L) were randomized to double-blind therapy with either atorvastatin 10 or 80 mg/day. The primary end point was the occurrence of a first major cardiovascular event. Patients were stratified by on-treatment LDL values into quintiles.
RESULTS: Baseline characteristics were similar across quintiles. There was a significant reduction in the rate of major cardiovascular events with lower levels of on-treatment LDL-C (p<0.0001). Death due to any cause, due to cardiovascular causes and due to non-cardiovascular causes was lowest in the quintile with the lowest on-treatment LDL-C levels. There were no clinically important differences in adverse event rates across quintiles.
CONCLUSIONS: Results confirm the safety and incremental clinical benefit of reducing LDL-C to very low levels (≤ 64mg/dL [1.7 mmol/L]) with atorvastatin in patients with stable CHD.

	Quintile 1 N=1836 1722/114*	Quintile 2 N=1932 1403/529*	Quintile 3 N=1987 968/1019*	Quintile 4 N=2030 515/1515*	Quintile 5 N=1984 266/1718*
LDL-C†(mg/dL)	≤ 64	>64-77	>77-90	>90-106	>106
LDL-C†(mg/dL)	53.9	70.3	83.0	97.1	121.9
Major CVE, %	7.7	8.2	9.2	11.1	11.9
Major CVE (80 mg), %	7.5	7.8	9.6	10.5	10.5
Major CVE (10 mg), %	11.4	9.3	8.7	11.3	12.1
All-cause mortality, n (%)	83 (4.5)	106 (5.5)	114 (5.7)	124 (6.1)	104 (5.2)
CV deaths, n (%)	43 (2.3)	43 (2.2)	56 (2.8)	62 (3.1)	51 (2.6)
Non-CV deaths, n (%)	40 (2.2)	63 (3.3)	58 (2.9)	62 (3.1)	53 (2.7)

*N/N - atorvastatin 80 mg/atorvastatin 10 mg; †On-treatment LDL-C; CVE = cardiovascular events
Presented at the American Heart Association Scientific Sessions 2005, Dallas, TX, November 13-16, 2005.

20E. Effects of intensive lipid lowering with atorvastatin on cerebrovascular events in patients with stable coronary disease: a treating to new targets (TNT) substudy. *David Waters, M.D.*[1], John C. LaRosa, M.D.[2], Philip Barter, M.D.[3]; (1)San Francisco General Hospital, 1001 Potero Avenue, San Francisco, CA; (2)SUNY Downstate Medical Center, Brooklyn, NY; (3)The Heart Institute, Camperdown, Australia.

PURPOSE: The cerebrovascular benefits of treating patients with stable CHD to LDL-C levels substantially below 100 mg/dL (2.6 mmol/L) have not been previously investigated. We describe a post hoc analysis of cerebrovascular events in TNT.
METHODS: Clinical endpoints analyzed were time to first cerebrovascular event (fatal or non-fatal stroke, or transient ischemic attack [TIA]), time to first stroke and time to first TIA. Cerebrovascular events, stroke of any etiology, and hemorrhagic stroke were stratified and compared by quintile of achieved LDL-C.
RESULTS: Mean on-treatment LDL-C levels were 101 mg/dL (2.6 mmol/L) with atorvastatin 10 mg and 77 mg/dL (2.0 mmol/L) with atorvastatin 80 mg. In addition to the reduction in major cardiovascular events (hazard ratio [HR]=0.78, 95% confidence intervals [CI]=0.69-0.89, P=0.0002), patients in the atorvastatin 80mg arm achieved significant reduction in the risk of cerebrovascular events (HR=0.77, 95% CI=0.64-0.93, P=0.007) and stroke (HR=0.75, 95% CI=0.59-0.96, P=0.020). There was a reduction in the incidence of TIA in patients receiving atorvastatin 80mg that did not reach statistical significance (HR=0.79, 95% CI=0.60-1.05, P=0.098). Cerebrovascular events and stroke occurred at a lower rate in the lowest quintile of achieved LDL-C compared with the highest quintile (3.6% vs 5.4%, and 2.1% vs 2.8% for cerebrovascular events and stroke, respectively). The incidence of hemorrhagic stroke did not differ significantly between patients in the two treatment groups (16 vs 17 events in the atorvastatin 80mg and 10mg groups, respectively, P=NS), or across quintiles of achieved LDL-C (6, 5, 6, 9, and 7 events from lowest to highest quintile, P=NS).
CONCLUSION: Significant reduction in cerebrovascular morbidity was observed in the group treated intensively with atorvastatin 80 mg. These data show that the reduction of LDL-C substantially below 100 mg/dL (2.6 mmol/L) with atorvastatin produces important clinical benefit beyond the coronary vasculature.
Presented at the American Heart Association Scientific Sessions 2005, Dallas, TX, November 13-16, 2005.

21E. Effect of atorvastatin on stroke in the collaborative atorvastatin diabetes study (CARDS): factors predictive of the risk of stroke. *Connie Newman, M.D.*[1], H. Andrew Neil, DSc[2], Graham A. Hitman, M.D.[3], Helen M. Colhoun, M.D.[4], D. John Betteridge, B.Sc., MBBS, M.D., Ph.D.[5], Paul N. Durrington, M.D.[6], Shona J. Livingstone, M.Sc.[5]; (1)Pfizer Human Health, New York; (2)University of Oxford, Oxford, United Kingdom; (3)Barts and the London, Queen Mary's School of Medicine and Dentistry, London, United Kingdom; (4)University College Dublin, Dublin, Ireland; (5)University College London, London, United Kingdom; (6)University of Manchester, Manchester, United Kingdom.

PURPOSE: Patients with diabetes are at increased risk of stroke; however, tools for predicting risk of primary stroke are limited. In CARDS, 2838 patients with type 2 diabetes, with no history of CHD or macrovascular disease, were randomized to atorvastatin 10 mg or placebo and followed for a median of 3.9 yr. Strokes were classified based upon neurological deficits and

MRI or CT scans. Treatment groups were compared on time to first stroke by a Cox regression model.
RESULTS: Of 60 strokes [8 fatal (1 atv, 7 pbo), 52 nonfatal (20 atv, 32 pbo)], 41were classified as ischemic (13 atv, 28 pbo), 1 hemorrhagic (1 atv, 0 pbo), 18 indeterminate (7 atv, 11 pbo). Atv was associated with a 48% RRR for all stroke (p=0.016) and a 55% RRR for ischemic stroke (p=0.017). Adjusted for treatment, factors associated with a higher risk of stroke were: older age (HR for 10 y=2.19, p<0.001), longer duration of diabetes (HR for 10 y= 1.49, p=0.020), higher SBP (HR for 10 mmHg=1.17, p=0.044), HbA1c > 10% (HR=2.35, p=0.019), male gender (HR=3.12, p=0.003), albumin:creatinine ratio (ACR) > 2.5 mg/mmol (HR=2.40, p<0.001), and history of retinopathy (HR=1.72, p=0.038). When treatment and the significant baseline covariates were entered in a single model, treatment was associated with a 50% RRR (p=0.011), and age, gender, ACR > 2.5 mg/mmol and HbA1c > 10% remained significant (all p<0.05).
CONCLUSIONS: In CARDS diabetes-specific variables ACR and HbA1c were important predictors of stroke independent of treatment. Despite the lack of association between baseline LDL-C and stroke, there was a significant reduction in the risk of stroke associated with atorvastatin treatment. These observations underscore the need for diabetes-specific risk engines for estimating risk of stroke and for intensive management of modifiable risk factors in patients with type 2 diabetes.
Presented at the American Heart Association Scientific Sessions 2005, Dallas, TX, November 13-16, 2005.

22E. Efficacy and safety of high dose atorvastatin therapy in CHD patients ≥65 years of age in the aggressive lipid lowering abates new cardiac events (ALLIANCE) study. *Michael Koren, M.D.*[1], Robert Mendes, M.D.[2], Don Luo, Ph.D.[3]; (1)Jacksonville Center for Clinical Research, Jacksonville, FL; (2)Pfizer Global Pharmaceuticals, New York, NY; (3)Pfizer Inc, New York, NY.

PURPOSE: High-dose statin therapy may be underutilized in the elderly due to safety concerns and doubts about efficacy in the aged.
METHODS: We examined outcomes and safety in patients ≥ 65 years of age in the ALLIANCE study, a "real world" trial that compared the effects of an aggressive atorvastatin regimen with usual care in stable coronary heart disease (CHD) patients. Of 2442 patients with dyslipidemia randomized to either aggressive treatment (LDL-C titration goal of <80 mg/dL or maximum 80 mg/day of atorvastatin) or usual care (continuation of baseline lipid-lowering therapy, with changes/laboratory analyses directed by treating physicians), 1001 (41%) were aged ≥ 65 years. The composite primary endpoint was time to first cardiovascular event. Mean dose of atorvastatin was 40 mg/day; 45% used 80 mg/day for an average of 3.6 years.
RESULTS: In the older cohort, mean age was 69.6 ± 3.2 years, with no difference in age, gender, smoking status, baseline lipids, or cardiovascular history between atorvastatin and usual care groups. Older patients randomized to aggressive therapy with atorvastatin realized greater benefit than those assigned usual care, experiencing relative risk reductions of 27% for the primary composite endpoint (HR=0.73, 95% CI=0.57-0.94, P=0.016). Similarly, greater risk reductions were observed with atorvastatin in patients aged ≥ 65 years for nonfatal MI (HR=0.48, 95% CI=0.32-0.72, P=0.001) and the composite endpoint of CHD death and nonfatal MI (HR=0.43, 95% CI=0.23-0.79, P=0.006). A trend in the reduction of nonfatal stroke (HR=0.74, 95%CI=0.39-1.40, P=0.358) was also observed. The rate of significant liver transaminase elevations in atorvastatin-treated patients was low; there were no differences between older and younger patients. Rates of serious adverse events leading to discontinuation were higher in older subjects, but were similar between atorvastatin and usual care.
CONCLUSIONS: Our data support the efficacy and safety of aggressive lipid management in older CHD patients.
Presented at the American Heart Association Scientific Sessions 2005, Dallas, TX, November 13-16, 2005.

23E. Adherence to evidence-based, multi-drug regimens in older persons' post-myocardial infarction. *Cynthia A. Jackevicius, B.Sc.Phm., M.Sc., Pharm.D., BCPS, FCSHP*[1], Gary Naglie, M.D.[2], Kathy Sykora, M.Sc.[3], Muhammad Mamdani, Pharm.D.[3], Nadja Gunraj, M.Sc.[3], Geoffrey M. Anderson, M.D., Ph.D.[3]; (1)Western University of Health Sciences, Pomona, CA; (2)Toronto Rehabilitation Institute, Toronto, ON, Canada; (3)Institute for Clinical Evaluative Sciences, Toronto, ON.

PURPOSE: Strong evidence supports the routine use of multi-drug regimens, including angiotensin-converting-enzyme inhibitors (ACEI), beta-blockers (BB), and statins, in post-acute myocardial infarction (AMI) patients. Adherence to individual drugs is known to be low. The objectives of this study were to describe levels and predictors of adherence in AMI patients dispensed one, two or three drugs of proven benefit (ACEI, BB, statins).
METHODS: This cohort study using linked population-based administrative data included all patients aged 66 years and older, discharged from hospital post-AMI April 1997 to March 2002. Patients were categorized according to the number and type of target medication dispensed within 30 days post-AMI. Adherence to individual and multiple drugs within the multi-drug regimen, controlling for patient and provider characteristics, was estimated using time-to-event analysis.
RESULTS: 8,157 patients discharged with AMI were evaluated. Medication adherence to each specific drug increased with the number of post-AMI medications dispensed. For example, 1-year adherence to ACEI alone was 54%, but increased to 64–66% when combined with a BB, a statin or both. However, adherence to all drugs in a multi-drug regimen was lower with two- and three-drug regimens than with single-drug regimens. For example, at one year, 48% of patients were adherent to both drugs in two-drug regimens while only 38% were adherent to all three drugs in three-drug regimens.
CONCLUSIONS: Adherence with an individual evidence-based medication post-AMI increases as more evidence-based medications are dispensed. However, overall levels of adherence for multiple secondary prevention drugs post-AMI remain lower than optimal in order to maximize the benefits of these efficacious therapies.
Published in Can J Cardiol 2004(abstr);20(Suppl D):140D.

24. Retrospective cohort validation of enoxaparin versus heparin with revascularization and glycoprotein IIbIIIa inhibition for efficacy and safety (REVERIFY). Adam B. Pesaturo, Pharm.D.[1], Heath R. Jennings, Pharm.D.[2], *Stacy A. Voils, Pharm.D.*[1], Kevin L. Poe, Pharm.D.[1], Bill Harris, M.D.[3]; (1)Saint Joseph HealthCare, Inc., Lexington, KY; (2)Saint Joseph HealthCare, Lexington, KY; (3)Cardiology Associates of Kentucky, Lexington, KY.

PURPOSE: ACC/AHA recommends enoxaparin over heparin (UFH) for patients with unstable angina (UA) or non-ST-segment myocardial infarction (NSTEMI). SYNERGY trial has since demonstrated enoxaparin to be neither superior nor inferior to UFH but noted increased risk of bleeding with enoxaparin. Lack of real world appraisal concerning outcomes with these agents combined with the questionable impact of anticoagulant crossover noted in SYNERGY complicates clinical decisions regarding enoxaparin and UFH.
METHODS: This retrospective cohort study evaluated and stratified reperfusion for acute coronary syndromes according to anticoagulant therapy, between 2/1/02 and 7/31/05. Antiplatelet treatment occurred per physician discretion and institution protocol. Further stratification occurred by glycoprotein IIb/IIIa inhibitor use and NSTEMI/UA versus ST-segment elevated myocardial infarction (STEMI). Anticoagulant crossover treatment was also evaluated. Primary outcomes were efficacy (triple composite of death, recurrent ischemia, urgent revascularization), safety (TIMI major bleeding), and safety-efficacy combined. Power analysis (90%) demonstrated 1053 patients (527 per group) required to detect a 10% difference in the primary endpoints (SD = 50, alpha = 0.05).
RESULTS: Total of 2108 patients were included for analysis. Due to small sample size, evaluation of crossover was not possible (n = 76). Enoxaparin demonstrated increased incidence in TIMI major bleeding (13.1 % vs. 8.2%, p<0.01) and in combined safety-efficacy endpoint (19.3% vs. 13.3%, p<0.01; RR = 1.44, 95%CI 1.17, 2.05) for NSTEMI/UA. Non-significant differences were noted in the efficacy endpoint for both NSTEMI/UA and STEMI. Subset analysis revealed increased incidence in efficacy (14.8% vs. 2.3%, p<0.01) and combined safety-efficacy endpoints (24.4% vs. 9.3%, p=0.01) for enoxaparin + eptifibatide versus enoxaparin + abciximab for STEMI patients.
CONCLUSIONS: Results of this study reflect outcomes noted in SYNERGY and suggest that patients treated with enoxaparin for NSTEMI/UA may be at increased risk for bleeding regardless of anticoagulant crossover prior to PCI.

25. Evaluation of regionally administered analgesia versus conventional pain management in post-operative cardiothoracic surgery patients. Kimberly A. Deady, Pharm.D., *Stacy A. Voils, Pharm.D.*, Heath R. Jennings, Pharm.D., BCPS, Kevin L. Poe, Pharm.D., BCPS; Saint Joseph HealthCare, Inc., Lexington, KY.

PURPOSE: Compare the effects of intraincisional analgesia (IA) to conventional analgesia (CA) on opiate requirements following cardiothoracic surgery.
METHODS: Retrospective pilot study in a cardiothoracic ICU. Following cardiothoracic surgery with median sternotomy, patients receiving IA were matched by age, gender, procedure, and number of risk factors for increased length of stay (LOS). Treatment group patients received IA with bupivacaine or ropivacaine via elastomeric pump for 72 hours. Primary endpoint: morphine equivalents (ME) received at 72 hours. Secondary endpoints: ME at 24, 48, and 96 hours; daily incidence of pain (pain score > 2 on a 0–10 scale); time to extubation and ambulation; and LOS.
RESULTS: n=49 (IA = 25, CA = 24). Mean ME utilized at 72 hours in control vs. treatment groups were 55.2 mg (95% CI, 47.4-63.0mg) vs. 50.7mg (95% CI, 42.7-58.8mg) respectively. Mean ME at 24, 48 and 96 hours in control vs. treatment groups were 25.0 mg (95% CI, 19.5-30.5 mg) vs. 21.7 mg (95% CI, 16.4-26.9 mg), 43.6 mg (95% CI, 36.8-50.4 mg) vs. 40.0 mg (95% CI, 34.1-45.9), and 62.0 mg (95% CI, 54.2–69.8 mg) vs. 57.9 mg ME (95% CI, 48.6-

67.2mg) respectively. Incidence of pain in control vs. treatment at 24, 48, 72 and 96 hours was 62.5% vs. 56.0% (p=0.65), 62.5% vs. 52.5% (p=0.47), 54.2% vs. 44.0% (p=0.49), and 58.3% vs. 44.0% (p=0.33) respectively. Treatment group relative risk for ambulation in < 48 hours and extubation in < 12 hours was 0.96 (95% CI, 0.23–3.8) and 1.78 (95% CI, 0.60–7.7) respectively. Median LOS for control vs. treatment groups was 6 days vs. 7 days respectively (p=0.69).
CONCLUSION: IA via elastomeric pump non-significantly decreased opiate requirements through 72 hours. A trend towards fewer patients experiencing pain in the IA group was identified. No significant effect was observed on time to extubation, ambulation, or LOS.

26. Evaluation of hypertensive emergency management within a large teaching institution. *Dipti Patel, Pharm.D.*[1], Laura P. Muller, Pharm.D.[2]; (1)Southern Regional Health System, Riverdale, GA; (2)Grady Health System, Atlanta, GA.

PURPOSE: Hypertensive emergency (HTNE) requires immediate blood pressure (BP) reduction to limit end-organ damage. Optimal management affects morbidity and length of hospital and intensive care unit (ICU) stay. The primary objectives were to evaluate the appropriateness of drug therapy selection and to determine if BP control was achieved within desired time frame. The secondary objectives were to determine the percentage of diagnoses of HTNE that did not fulfill the criteria of manifesting end-organ damage and to develop a HTNE management guideline.
METHODS: Patients were evaluated retrospectively (n=30) as well as prospectively (n=11). Exclusion criteria were age less than 18 years, pregnancy/lactation, intracranial hemorrhage (ICH), admission to neurology or neurosurgery service, and inadequate documentation of end-organ damage during the retrospective phase. Outcome measures that were evaluated include type and appropriateness of drug therapy, time to achieve goal mean arterial pressure (MAP), time until initiation of intravenous (IV) and oral therapy, ICU length of stay (LOS), and adverse events of bradycardia and hypotension.
RESULTS: A total of 41 patients were evaluated. Seventy-six percent of patients were started on inappropriate drug therapy. Seventy percent of patients started on continuous IV drug therapy did not reach goal BP within 6 hours. Seven percent of patients were inappropriately diagnosed as having HTNE.
CONCLUSIONS: The evaluation of HTNE management provides valuable information to improve the management of patients with HTNE.

Critical Care

27. Educational program for the prevention of ventilator-associated pneumonia in adult patients admitted to the intensive care unit. *Rajae Omrane, B.Pharm., M.Sc.*[1], Jihane Eid, B.Pharm., M.Sc.[1], Marc M. Perreault, Pharm.D., BCPS[1], Hala Yazbeck, B.Pharm, M.Sc.[2], Ashvini Gursahaney, M.D., FRCPC[2], Nancy Fong, RT[2], Luc Lortie, R.N.[2], Yola Moride, Ph.D.[1]; (1)Université de Montréal, Montreal, QC, Canada; (2)Montreal General Hospital, Montreal, QC, Canada.

PURPOSE: Ventilator-associated pneumonia (VAP) is the most common infection among patients receiving mechanical ventilation (MV). VAP is associated with increased mortality and morbidity. Several interventions are effective in reducing the incidence of VAP, but their implementation into clinical practice is not yet a standard in our hospital. The objective is to determine whether a protocol incorporating evidence-based measures shown to reduce the frequency of VAP could decrease rates of VAP in the ICU of a tertiary care adult teaching hospital.
METHODS: This pre- and post-intervention observational study included mechanically ventilated patients admitted to our ICU (MICU/SICU/Trauma) between November 8, 2003, and May 8, 2004 (pre-intervention), and between November 8, 2004, and May 8, 2005 (post-intervention). A multidisciplinary protocol and education program was developed and implemented, and posters reinforcing adherence were placed in the ICU. Rates of VAP per 1,000 ventilator days were calculated before and after the implementation of the protocol for all patients, for those with early onset VAP (EOVAP) and those with late onset VAP (LOVAP).
RESULTS: Twenty three episodes of VAP occurred in 921 ventilator days (25.00 per 1,000 ventilator-days) during the 6 month pre-intervention period. Following implementation, the rate of VAP decreased to 22 episodes in 989 ventilator days (22.40 VAP per 1,000 ventilator days), a relative reduction rate of 10.4% (p<0.001). The incidence of EOVAP decreased from 25.58 to 19.56 VAP per 1,000 ventilator-days (p< 0.001) while the incidence of LOVAP remained stable (from 24.48 to 24.14 VAP per 1,000 ventilator-days).
CONCLUSION: Implementation of an educational program for VAP prevention significantly reduced the overall incidence of VAP, and specifically that of EOVAP.

28. Does adjunctive dexmedetomidine therapy impact sedation/analgesia requirements to facilitate extubation?. *Laurel Forrest, B.S.*, Tyree Kiser, Pharm.D., Robert MacLaren, Pharm.D.; University of Colorado School of Pharmacy, Denver, CO.
PURPOSE: To determine if adjunctive dexmedetomidine (dex) administration alters sedation/analgesia requirements and levels of sedation/analgesia to facilitate tracheal extubation.
METHODS: Retrospective assessment of 40 ICU patients ≥ 18 yo with dex initiated while receiving propofol, lorazepam and/or fentanyl infusions. Data collected included demographics, sedative/analgesic requirements, levels of sedation/analgesia (Riker/PABS), hemodynamics, and ventilator parameters. Statistical analyses included repeated-measures analysis of variance and chi-square test.
RESULTS: Patients were 48±15 yo with APACHE II scores of 22±7, most in the surgical ICU (n=33). Four patients received a dex bolus. The initial dex rate of 0.4±0.25 µg/kg/hr changed minimally through 47.4±61.1 hours of infusion. Within three hours of initiating dex, 9 of 12 patients had propofol stopped resulting in reduced hourly rate (54.4±19.9 at hr-1 to 26.7±5.8 µg/kg/min at hr+3, p=0.02) and total daily dose (4072±3222 at day-1 vs. 1334±870 mg at day0 p=0.01). Within 24 hours of initiating dex, 4 of 14 patients had lorazepam stopped and 7 of 26 patients had fentanyl stopped but hourly rates and total daily doses varied minimally. Within 24 hours before and after initiating dex, 64.6% and 47.9% of assessments represented adequate sedation (Riker of 3-4), respectively (p<0.001). Four and 12 patients had severe agitation before and after, respectively (p=0.006). One and 12 patients had severe pain before and after, respectively, (p<0.001). Seven patients experienced hypotension/bradycardia requiring dex discontinuation, 22 patients were extubated within 24 hours after stopping dex with dex the final sedative, 5 patients self extubated within 24 hours of dex initiation, and 7 patients required sedation/analgesia escalation. CONCLUSION: Adjunctive dex reduces propofol requirements but does not alter lorazepam or fentanyl requirements, possibly due to differences in the clinical application of these sedatives/analgesics. Transitioning to dex in an effort to reduce other sedatives/analgesics may worsen sedation/analgesia but potentially serves as a bridge to extubation.

29. Retrospective surveillance of antimicrobial usage for the treatment of pneumonia in a medical intensive care unit. *Emily J. Young, Pharm.D.*[1], Steven E. Pass, Pharm.D., BCPS, FCCM[2]; (1)The University Hospital, Cincinnati, OH; (2)University of Houston College of Pharmacy, Houston, TX.

PURPOSE: This study was conducted to identify trends in empiric antimicrobial selection for the treatment of pneumonia in a MICU at a large academic medical institution and to determine whether the empiric therapy was adequate based upon final culture results.
METHODS: A retrospective chart review was conducted of all patients greater than or equal to 18 years of age admitted to the MICU from April 2004 through September 2004 that were treated for pneumonia. Patient demographics, type of pneumonia, antimicrobial agents utilized, pertinent laboratory data, microbial culture results, clinical signs and symptoms of pneumonia, ventilator days, hospital and ICU LOS, and mortality data were collected from computerized patient records and patient charts. Descriptive statistics were utilized to analyze the data.
RESULTS: A total of 88 patients with 96 cases of pneumonia were reviewed. The mean age was 57 ± 16 years and 62% (n=55) of patients were female. Based upon final microbial culture results from 32 patients, empiric therapy was considered adequate in 65% of cases (n=21). Initial empiric therapy was considered appropriate based upon national guidelines in only 32% of cases (n=31). The most common pathogen isolated from respiratory cultures was methicillin resistant *Staphylococcus aureus* (n=12), followed by *Pseudomonas aeruginosa* (n=5), and *Stenotrophomonas maltophilia* (n=5).
CONCLUSION: In this retrospective chart review of patients admitted to a MICU, empiric therapy was adequate in 65% of cases of microbiologically confirmed pneumonia. Initial empiric therapy was appropriate based upon national guidelines in 32% of cases. Educational initiatives and a pneumonia treatment protocol are being implemented in order to improve both the adequacy and appropriateness of empiric regimens for the treatment of pneumonia at our institution.

30. Comparison of darbepoetin alfa and epoetin alfa for anemia of critical illness. *Stacy A. Voils, Pharm.D.*, Spencer E. Harpe, Ph.D., Pharm.D., M.P.H., Gretchen M. Brophy, Pharm.D., BCPS; Virginia Commonwealth University, Medical College of Virginia Campus, Richmond, VA.

PURPOSE: Studies have shown that recombinant human erythropoietin (rHuEPO) may decrease blood transfusions in critically ill patients. However, no published data exists to support or refute use of darbepoetin alfa (DPA) for anemia of critical illness. The purpose of this study is to compare the effectiveness of DPA to rHuEPO at achieving transfusion independence and increasing hemoglobin levels in critically ill patients.
METHODS: This was a retrospective, descriptive study in a 72-bed ICU at a level I trauma center. Cardiothoracic, medical or surgery/trauma ICU patients who received at least one dose of DPA or rHuEPO were screened for study inclusion. Patients received rHuEPO 40,000 units or DPA 100 micrograms

administered subcutaneously every 7 days. Data was collected for up to 28 days following the first dose of study drug.
RESULTS: Seventy-two patients were included in the study (DPA, n=39; rHuEPO, n=33). Patients in both groups received an average of 4 doses of drug beginning a median of 10 days after ICU admission. The average hemoglobin level at which treatment with DPA or rHuEPO was initiated was 8 g/dL and 8.2 g/dL, respectively (p=0.4). Transfusion independence was achieved in 44% of patients in the DPA group versus 36% of patients in the rHuEPO group (p=0.96). Patients in both groups received an average of 2.7 units of packed red blood cells during the 28-day study. The mean hemoglobin change from baseline at 7, 14, 21, and 28 days was not statistically significant between groups at any time point (p=0.25).
CONCLUSION: Patients receiving DPA or rHuEPO for anemia of critical illness achieved similar rates of transfusion independence and increases in hemoglobin levels from baseline at 28 days. In a "real world" setting, erythropoietic agents are administered late in the course of critical illness in response to low hemoglobin values.

31. Recombinant human activated protein C in patients with sepsis at a tertiary care institution: impact on outcome. *Brandi M. Beyhan, Pharm.D.*[1], Aimee C. LeClaire, Pharm.D.[1], Kenneth P. Klinker, Pharm.D., BCPS[2], A. Joseph Layon, M.D., FACP[3]; (1)Pharmacy Department, Shands at the University of Florida, Gainesville, FL; (2)Pharmacy Department, Shands at AGH, Gainesville, FL; (3)Division of Critical Care Medicine, Shands at the University of Florida and the University of Florida College of Medicine, Gainesville, FL.

PURPOSE: Improvements in resuscitation, antimicrobial timeliness, glucose control, and immunomodulation with rhAPC have led to significant reductions in sepsis-related mortality. Evidence-based guidelines support such initiatives and recommend implementation of a pathway.
METHODS: Outcomes of patients with sepsis treated with rhAPC were evaluated and compared to pertinent clinical trials. Retrospective review evaluating course and outcome for adult patients receiving rhAPC from 2001 through July 2004 was conducted. Primary outcome measure was 28 d mortality. Secondary outcomes included mortality correlations with time-to-administration of rhAPC from onset of organ dysfunction and glycemic control.
RESULTS: Study population mortality was significantly greater than reported in published trials. APACHE II and SOFA scores were 28.4 ± 7.3and 11.2 ± 3.2, respectively. Cancer, hypertension, liver disease, diabetes, transplant, and recent trauma were more prevalent in study patients. Patient mix was 71.1% surgical. All patients had more than one organ system failure. For patients receiving rhAPC within 24 hrs of organ dysfunction, 40% had died at 28 d compared to 59% of patients receiving rhAPC later (p=0.01). Tight glucose control was achieved in 61.2% of the population. Patients with intensive glucose control had a lower 28 d mortality rate (p=0.02).
CONCLUSIONS: Our institutional mortality for septic patients treated with rhAPC is greater than reported in clinical trials. The noted difference in mortality speaks to several issues: severity of illness, comorbidities, timeliness of drug administration, and glycemic control.

Measure	Overall	Inclusion	Exclusion	PROWESS	ENHANCE
28 d mortality (%)	50	39	53	25	26

Inclusion defined as meeting all criteria for enrollment in PROWESS. Given PROWESS criteria, 79% of study patients would have been excluded.

32. Comparison of darbepoetin alfa to epoetin alfa in anemia of critical illness. *Eric Wittbrodt, Pharm.D.*[1], Danielle Dalton, Pharm.D.[2], Anthony Chiefari, Pharm.D.[2]; (1)University of the Sciences in Philadelphia, Philadelphia, PA; (2)Hahnemann University Hospital, Philadelphia, PA.

PURPOSE: The purpose of this study was to compare the impact of darbepoetin alfa (D) and epoetin alfa (E) on selected clinical outcomes in patients with anemia of critical illness.
METHODS: This was a matched case-cohort study. Patients were included if they were >18 years of age, anemic upon ICU admission (hemoglobin < 11 g/dL), and had received at least one dose of either D 100 µg SC QW or E 40000 units SC QW in the ICU. Exclusion criteria included dialysis, antineoplastic therapy within 30 days of ICU admission, and chronic anemia. Selected demographic and clinical outcomes data were retrospectively collected for the first 30 days of admission or until discharge. Patients were matched 1:1 by APACHE II score (+/- 3 points). Continuous data were analyzed using Wilcoxon test, and proportions were compared using chi square.
RESULTS: The records of 30 patients were reviewed (15 D, 15 E). Baseline data were as follows: mean age was 62.1 y for D and 49.4 y for E, mean baseline hemoglobin was 9.3 g/dL for D and 8.3 g/dL for E, and mean APACHE II score was 14.2 for D and 18.3 for E. Outcomes data were as follows: mean ICU LOS was 15.8 days for D and 17.8 days for E (p=0.67), mean last recorded hemoglobin value was 10.4 g/dL for D and 10.6 g/dL for E (p=0.69), and mean units of red blood cells transfused per patient was 3.8 for D and 6.7 for E (p=0.27).
CONCLUSIONS: No significant differences emerged with respect to length of stay and red blood cell transfusion requirements in a small sample of matched critically ill patients. Both drugs appear to have a similar impact on selected clinical outcomes in the ICU.

33. Assessment of thrombotic events in a neurosciences critical care unit. Jason A. Hoffman, Pharm.D.[1], *John J. Lewin III, Pharm.D., BCPS*[1], Marek A. Mirski, M.D., Ph.D.[2]; (1)The Johns Hopkins Hospital, Baltimore, M.D.; (2)The Johns Hopkins Medical Institutions, Baltimore, M.D.

PURPOSE: Within the neurosurgical population, the incidence of venous thromboembolism (VTE) is high, with reports of VTE occurring in 6% of patients receiving prophylaxis, and VTE-related complications occurring in 19–54% of patients. The most commonly employed prophylaxis strategy in our Neuro-Critical Care Unit (NCCU) is Unfractionated Heparin (UFH) 5000 units SC BID plus mechanical methods. There is currently no uniformly accepted prophylactic regimen for this patient population. We propose that an assessment of thrombotic events in our NCCU would provide valuable information for optimizing our VTE prophylaxis strategy, and provide direction for the development of future studies to determine the risk factors for, and natural progression of, VTE in this patient population.
METHODS: Retrospective chart review of 42 patients admitted to the NCCU between 2001-2004 diagnosed with VTE.
RESULTS: Over the study time frame there were 1211 admission to the NCCU with an ICU stay > 48 hours. Overall incidence of VTE in these patients was 3.5%. The most common admitting diagnosis in patients developing VTE was tumor resection (23%) and hemorrhagic stroke (14%). Fifty percent of the patients that developed VTE had undergone a craniotomy. Compliance with mechanical and pharmacologic prophylaxis was high (97% and 96% respectively). Median hospital length of stay was 40 days (range 2–123). Ninety-five percent of patients had at least one major risk factor for VTE, and 74% had 3 or greater.
CONCLUSIONS: Incidence of VTE in the NCCU is consistent with that reported in the literature. Compliance with the existing prophylaxis regimen is high. Patients developing a VTE had long hospitalizations with numerous risk factors. Further evaluation of the risks vs. benefits of a more aggressive prophylactic regimen such as UFH 5000 units SC TID or Low Molecular Weight Heparin in patients with brain tumors, hemorrhagic strokes, and those undergoing craniotomies is warranted.

Education/Training

34. Development and implementation of an interprofessional course in patient safety: a case study. *Kimberly A. Galt, Pharm.D.*, Karen A. Paschal, PT, M.S., Richard O'Brien, M.D., Robert McQuillan, M.D., Barbara Harris, M.S.W., Janet Graves, R.N., Ph.D., Catherine Mahern, J.D., Bartholomew E Clark, Ph.D., James D. Bramble, Ph.D., Linda Scheirton, Ph.D., Keli Mu, Ph.D., OTR/L, Pat Hoidal, R.N., M.P.H., John M. Gleason, D.B.A., Ann Rule, Pharm.D., J. Chris Bradberry, Pharm.D., Roberta E. Sonnino, M.D., Debra Gerardi, R.N., M.P.H., JD; Creighton University, Omaha, NE.

PURPOSE: The purpose of this case study is to describe the development and implementation of an interprofessional course in patient safety offered to students across healthcare and health-related disciplines.
METHODS: A total of 17 faculty members representing 13 health professions or related disciplines accepted an invitation to participate. The team identified key issues to be addressed including content of current courses, the logistical demands of varying curricular delivery models on campus, student and program level considerations, faculty development and engagement, and course content, delivery and assessment. A two-credit elective course was developed based on expected student learning outcomes. Instructional design focused on active learning methods to engage students in interprofessional case-based discussion applying the basic principles and tenets of patient safety in a systems-based context. The course was first offered Spring Term 2005 to 31 students from nursing, occupational therapy, physical therapy, and pharmacy.
RESULTS: Overall student mastery of the content knowledge of patient safety science was demonstrated in a multiple choice examination and final examination case designed to evaluate the application of safety theory. Final course evaluations revealed that 87% of the students believe the material taught in the course is core knowledge and essential to be learned by all health professionals, and 74% believed this course should be required for all health professions students. Students achieved an application level of learning (77%) within the cognitive domain and the valuing level within the affective domain. Students agree (96%) that they can define and apply the basic principles and tenets of patient safety, including identification of tools needed to work effectively within the health system to improve safety, and 100% strongly agree or agree that they value patient safety as a professional practice framework.
CONCLUSION: The university-wide implementation case may offer important lessons to others nationally in healthcare education.

35. Implementing a classroom performance system in an introductory therapeutics course. *Jennifer Trujillo, Pharm.D.*, Michael Gonyeau, Pharm.D., Jennifer Kirwin, Pharm.D., Gerald Schumacher, Pharm.D., Ph.D.; Northeastern University School of Pharmacy, Boston, MA.

PURPOSE: Computer-based classroom performance systems (CPS) are interactive response systems that provide immediate student feedback while increasing active student participation. Strategies for effective implementation into a pharmacy curriculum are not available. Our purpose was to evaluate CPS implementation in a Therapeutics course.
METHODS: The 2005 Therapeutics 1 course was taught with CPS using three implementation strategies. The "early discovery" strategy used CPS to assess students' fundamental knowledge from pre-requisite coursework. The "immediate feedback" strategy used CPS to assess comprehension or application of content just taught. The "retention" strategy used CPS to assess retention of information at subsequent lectures. Study outcomes were student and faculty attitudes and examination scores. Students and faculty completed satisfaction surveys. 2005 exam scores were compared to 2004 scores.
RESULTS: CPS was used to pose 94 questions in 14 class periods (51 early discovery, 28 immediate feedback, 15 retention). Eighty-nine students (94%) and three faculty (100%) completed the satisfaction survey. Both groups rated the system positively. Eighty-seven percent of students enjoyed using the CPS technology. Eighty-four percent agreed that CPS encouraged active learning and allowed participation without fear of judgment. The majority of students agreed that each implementation strategy was effective (83% early discovery, 88% immediate feedback, 80% retention). All faculty agreed that each implementation strategy was effective. Assessment of 2004 and 2005 examinations yielded 22 similar questions for comparison. While there was not a statistically significant change observed in overall examination scores (p=0.093), one content area showed significant improvements (p=0.037).
CONCLUSIONS: Implementing CPS using three strategies was well received by both students and faculty. Students and faculty agreed that CPS encouraged participation and active learning. While overall examination scores did not improve significantly, certain content areas saw improvement. Due to positive feedback, utilization of this system has been implemented in subsequent Therapeutics courses.

36. Evaluation of antibacterial test performance of students after completing an antibacterial elective. *Paul P. Belliveau, Pharm.D.*[1], Ronald J. DeBellis, Pharm.D.[1], Gary R. Tataronis, M.S.[2], Courtney I. Jarvis, Pharm.D.[1], Michael Steinberg, Pharm.D.[1]; (1)Massachusetts College of Pharmacy and Health Sciences - Worcester, Worcester, MA; (2)Massachusetts College of Pharmacy and Health Sciences, Boston, MA.

PURPOSE: The purpose of this study is to determine whether there is a difference in test performance on information related to antibacterial pharmacotherapy for students who have and have not taken the elective Basic Concepts in Antibacterial Pharmacotherapy prior to entering Pharmacotherapeutics III at our institution.
METHODS: On day one of Pharmacotherapeutics III, before any lectures were given, students were administered an antibacterial exam (ABX) consisting of 24 questions addressing information related to the infectious diseases topics to be discussed during the first few weeks of Pharmacotherapeutics III. Scores on this exam and those of the first two Pharmacotherapeutics III exams (PTX 1 and PTX 2) were compared between students who had and had not taken Basic Concepts in Antibacterial Pharmacotherapy, an elective offered during the preceding semester. Comparisons were performed using unpaired t-tests (a priori level of significance, p<0.05).
RESULTS: Fifty-six students had taken the elective, ìBasic Concepts in Antibacterial Pharmacotherapyî; 65 had not taken the elective. The mean score on the ABX (50.7 vs 20.6%, 95% CI for difference of 14.8-25.3) and PTX 1 (80.2 vs 76.3%, 95% CI for difference 0.7-7.0) exams was significantly greater for students who had taken the elective. The difference in the mean score on the PTX 2 exam was not statistically significant (84.4 vs 81.9%, 95% CI for difference 0.0-4.9).
CONCLUSION: Students who take Basic Concepts in Antibacterial Pharmacotherapy appear to have a greater antibacterial knowledge base upon entering Pharmacotherapeutics III than those who have not taken this elective. This advantage may translate into better performance on infectious diseases Pharmacotherapeutics' exams. Findings from this study suggest that it may be beneficial to require that all students partake in a course such as Basic Concepts in Antibacterial Pharmacotherapy to facilitate their understanding of this important area of pharmacotherapy.

37. The prevalence of cultural competency training at schools and colleges of pharmacy. *Kelly M. Rudd, Pharm.D., BCPS*[1], Nicole M. Stack, Pharm.D.[2]; (1)Bassett Healthcare, Cooperstown, NY; (2)Albany College of Pharmacy, Albany, NY.

PURPOSE: Accreditation Council for Pharmacy Education accreditation standards for pharmacy programs require institutions of pharmacy education to create a teaching environment that values diversity and provides instruction about working with diverse colleagues and patients. Diversity is one key factor in developing cultural competency. Importantly, increasing cultural competency has been shown to reduce disparities in healthcare stemming from a breakdown in effective patient-provider communication. This study is designed to quantify the degree of focused cultural competency training in pharmacy school curriculums.
METHODS: The authors conducted a review of the curriculums of the existing United States (U.S.) and U.S. Affiliate Schools of Pharmacy as recognized in the 2004/2005 American Association of Colleges of Pharmacy Roster. Curriculums were accessed via their online listings and class descriptions available at each institution's Web site (accessed between December 1, 2004, and August 12, 2005.)
RESULTS: Ten of the 97 schools of pharmacy (10.3%) studied offer focused classes, either required or elective, on diversity and/or the development of skills necessary to achieve cultural competence.
CONCLUSIONS: A review of pharmacy school curriculums shows that many new and experienced practitioners may not have had adequate exposure to focused and in-depth cultural competency training via their formal pharmacy education.

38. Evidence-based medicine in the classroom: student attitudes and comfort with literature evaluation terms. *Jill S. Burkiewicz, Pharm.D.*; Midwestern University Chicago College of Pharmacy, Downers Grove, IL.

PURPOSE: The purpose of this investigation is to determine 1) the attitudes of pharmacy students in a Landmark Trials elective course toward evidence-based medicine (EBM); 2) the impact of the elective on comfort with technical terms used in drug literature; and 3) student-reported access to PubMed.
METHODS: A questionnaire was administered to students in a third professional year Landmark Trials elective course on the first and last day of class. The pre- and post-questionnaire assessed the student attitudes toward EBM, self-assessed comfort with technical terms used in evidence-based medicine, and access to PubMed. Ordinal scale measures were used to assess attitudes and comfort levels, while nominal measures were used to assess access to PubMed.
RESULTS: Completed responses were received from 27 students over two years (100% response rate). Overall, students had positive attitudes toward EBM both before and after the course (59.3% positive, 37% somewhat positive v. 77.8% positive, 18.5% somewhat positive, p=0.26). Students thought research findings were useful to pharmacy practice (96.3% positive or somewhat positive) and these thoughts were unchanged post-course (Wilcoxon Signed Rank p=0.097). After the course, students were more likely to feel that pharmacists should rely on practice guidelines to make patient-care decisions (p=0.007). Although 96% of students admitted to having internet access at home, only 63% of students identified that they had PubMed access at home. The course increased self-assessed comfort with technical terms used in literature evaluation: relative risk (p=0.005), absolute risk (p=0.008), number needed to treat (p=0.001), odds ratio (p=0.014).
CONCLUSIONS: Pharmacy students in a Landmark Trials elective course have positive attitudes toward evidence-based medicine and the application of research findings to practice. The course increased self-assessed comfort with technical terms used in literature related to evidence-based medicine. Further education on access of PubMed via the Internet may be required.

39. An inquiry into research interests and support needs of clinical pharmacy faculty. *A. Simon Pickard, Ph.D.*, Jerry L. Bauman, Pharm.D.; University of Illinois College of Pharmacy, Chicago, IL.

PURPOSE. To determine the research interests and types of support that would facilitate scholarship in research among clinical (non-tenure) track (CT) pharmacy faculty.
METHODS: A cross-sectional survey of CT faculty at UIC was completed by self-report via the Web in November 2005. Faculty were asked to indicate their level of interest (none, a bit, a lot, extreme) in several pharmacy-related topics (pharmacokinetics, pharmacogenomics, and drug treatment outcomes) and in support from the department regarding: study design, analysis, data management, development of research questions/hypotheses, sample size calculations, IRB preparation, awareness of funding opportunities, grant writing, grant management and writing for journals.
RESULTS: Of 39 respondents, 100% indicated they were interested in being co-investigators, and 77% lead investigators, on research studies. The median number of publications over the past 2 years was 1 (range 0 to 21). Less than 50% (18/39) were satisfied with current scholarly productivity. The majority of respondents expressed "a lot" or "extreme" interest in support for all areas, particularly sample size calculations, selection of appropriate statistical tests, grant writing, and writing for journals. CT faculty expressed "a lot" or "extreme" interest in the following topics: 87% drug treatment outcomes; 56% pharmacogenetics; 33% pharmacokinetics (p<0.001). Comments and issues included: lack of confidence in ability, need for balancing

responsibilities, creation of specific research interest groups, and a need for greater mentorship and statistical support.
CONCLUSIONS: In general, research productivity by CT faculty will likely remain low unless support for such scholarly activity is promoted and provided. Recommendations include rewarding publications/proposal submissions with protected time for research, mentorship pairing with tenure-track faculty, study protocol and grant development workshops, and special interest research groups. Although this study was limited to UIC faculty, these issues and solutions may resonate with CT faculty nationally and internationally.

40. Development of a reliable assessment for continuing professional development portfolios. Sharon L. Haughey, B.Sc.[1], Ronan Warnock, MPharm[1], Carmel M. Hughes, Ph.D.[1], *Colin G. Adair, Ph.D.*[2], Heather M. Bell, Ph.D.[2]; (1)Clinical & Practice Research Group, School of Pharmacy, The Queen's University of Belfast, United Kingdom; (2)NI Centre for Postgraduate Education & Training, School of Pharmacy, The Queen's University of Belfast, Belfast, United Kingdom.

PURPOSE: All practicing pharmacists within the UK and Northern Ireland are required to participate in, and document, their continuing professional development (CPD) using a portfolio system based on the four-stage Kolb model. On an annual basis a random sample of pharmacists will be required to submit their portfolio for assessment in order to remain on the pharmaceutical register. However, portfolio assessment has been questioned in medical education due to a lack of evidence to support the reliability of assessment methods. Thus, the aim of this research was to determine the reliability of a seven-point portfolio assessment system that had been developed as part of a CPD pilot prior to the introduction of mandatory CPD for pharmacists in Northern Ireland.
METHODS: In order to test the reliability of the assessment, 10 trained assessors undertook the evaluation of five CPD portfolios, comprising a total of 30 individual CPD cycles, using the assessment criteria and assessment guidelines. Inter-assessor agreement for each criterion, in each of the 30 CPD cycles, was expressed as the kappa (κ) statistic.
RESULTS: Of the seven assessment criteria, two criteria had an agreement level of κ; >0.8 (excellent inter-assessor agreement), four criteria had an agreement level between κ 0.7-0.75 (substantial inter-assessor agreement) and one criterion had an agreement level of κ; 0.45 (moderate inter-assessor agreement).
CONCLUSION: The levels of inter-assessor agreement found in this study were generally higher than those reported in previous research involving assessment criteria and portfolios. Previous studies have reported inter-assessor agreement levels at a "slight" to "moderate" level. This research shows that higher levels of inter-assessor agreement can be achieved using a clear portfolio structure in conjunction with straightforward assessment criteria and assessment guidelines. Further investigation is ongoing to determine inter-assessor agreement for the summative assessment of CPD portfolios.

Endocrinology

41E. Projected coronary heart disease risk benefit of extended-release niacin/lovastatin versus fenofibrate in patients with type 2 diabetes mellitus. *Scott L. Charland, Pharm.D.*, Mark E McGovern, M.D., Carolin Malott, Ph.D., Eric J. Stanek, Pharm.D.; Kos Pharmaceuticals, Inc, Cranbury, NJ.

BACKGROUND: Fenofibrate, while not currently approved for use in combination with a statin, is often recommended/utilized before niacin monotherapy or combination therapy for treating atherogenic dyslipidemia in patients with Type 2 diabetes mellitus (T2DM). Since comparative clinical data of these alternative approaches are sparse, application of a valid, diabetes-specific risk prediction model may provide a useful means of assessment.
METHODS: Baseline and end-treatment projected 10-year CHD and stroke risks were calculated using the UK Prospective Diabetes Study risk model in patients with complete follow-up from a randomized, double-blind, placebo-controlled, 20-week trial of extended-release niacin/lovastatin (ERN/L) 1000/40 mg (N=48) and 1500/40 mg qhs (N=51) versus fenofibrate 200 mg qd (FENO; N=58). All patients had T2DM treated with a thiazolidinedione and/or metformin, low HDL-C (<40 mg/dL men; <50 mg/dL women) and TG >150 mg/dL. The risk model includes: age, gender, ethnicity, smoking status, presence of atrial fibrillation, duration of T2DM, HbA1c, systolic blood pressure, total cholesterol and HDL-C. The primary endpoint was projected 10-year CHD relative risk reduction for ERN/L compared with FENO using one-way ANOVA with post-hoc significance testing.
RESULTS: Baseline model variables were similar between the treatment groups except for duration of T2DM (FENO 10±9 yrs; ERN/L 1500/40 mg 8±7 yrs; p<0.05). Baseline 10-year CHD, fatal CHD, stroke and fatal stroke risks were similar in the 3 treatment groups, and decreased significantly on therapy. Risk reductions for fatal and non fatal CHD (43% versus 24%), fatal CHD (43% versus 25%) and stroke (27% versus 18%) were significantly greater for ERN/L 1500/40 mg versus FENO (p<0.05).
CONCLUSION: ERN/L provides a significant additional reduction in predicted 10-year CHD risk compared with maximum dose fenofibrate in patients with T2DM.
Published in Circulation 2005;112:II-838.

Gastroenterology

42E. Medication usage evaluation of proton pump inhibitors for gastrointestinal prophylaxis in non-ICU settings. *Joanne Y. Chang, Pharm.D.*[1], Julie Simonson, Pharm.D.[2], Mona Shah, Pharm.D.[3], Alan S. Rosman, M.D.[4]; (1)Long Island University, Arnold & Marie Schwartz College of Pharmacy and Health Sciences, Brooklyn; (2)Pfizer Com, New York, NY; (3)New York Presbyterian Hospital, New York, NY; (4)James J Peters VA Medical Center, Bronx, NY.

PURPOSE: To assess the appropriateness of proton pump inhibitor (PPI) usage in a non-ICU setting and establish whether pharmacy intervention is necessary or not according to published guidelines for PPIs. Our goal is to establish guidelines or criteria for PPI usage in non-ICU settings and reduce PPI usage deemed inappropriate.
METHODS: A total of 368 admitted adult patients to non-ICU units receiving acid suppression agents as part of routine clinical care between March 2003 to October 2005 were evaluated for appropriate usage. These patients were divided into two arms in a prospective pre and post intervention study. Patients receiving a PPI or an H2-blocker for stress ulcer prophylaxis (SUP) as documented in the medical record were evaluated for the following: appropriate use and continuation of PPIs after discharge, and gastrointestinal bleed (GIB) events at 3, 6, and 12 months after pharmacy intervention.
RESULTS: Upon admission, questionable PPI use was 71% in the control group and 69% in the intervention group. Despite the high opportunity in the control group (31%) to modify therapies to be in accordance to PPI guidelines, therapies were discontinued two times more frequently in the intervention group (13%, P=0.007) upon discharge. The accepted interventions recommended by the pharmacy was 81% to either discontinue or dose adjust PPI. Overall, there were no significant differences in GIB events between the two groups at the end of 12 month follow-up.
CONCLUSION: We found a high frequency of inappropriate PPI use for GIB prophylaxis in the non-ICU settings. The majority of these patients do not have ASHP-identified risk factors, except prior history for peptic ulcer disease or upper GIB. It is important to establish criteria for physicians in the non-ICU settings for patients with low risk factors to reduce unnecessary cost and minimize the risk for pneumonia.
Presented at the Midyear Meeting of the American Society of Health-System Pharmacists, Orlando, FL, December 4-8, 2004.

Geriatrics

43. Improving treatment guideline adherence in long-term care facility patients. Kristin K. Horning, Pharm.D., *James D. Hoehns, Pharm.D.*; University of Iowa College of Pharmacy/Northeast Iowa Family Practice Center, Waterloo, IA.

PURPOSE: Numerous studies have shown that adhering to established treatment guidelines has benefits of reducing disease morbidity and mortality. However, no published benchmarks exist that demonstrate the rate of adherence in patients residing in long-term care facilities (LTCFs). Our goal was to evaluate guideline adherence in patients from LTCFs who receive care from pharmacists that emphasize disease state management compared to patients from other LTCFs.
METHODS: A retrospective chart review was conducted on 107 patients in two LTCFs receiving disease state management services and 304 patients in four other LTCFs. Treatment guideline adherence was evaluated for the following conditions: diabetes, coronary artery disease (CAD), stroke, congestive heart failure (CHF), hypertension, hyperlipidemia, and osteoporosis. In addition, the six most recent pharmacist recommendations for each patient were classified according to intervention type and disease state.
RESULTS: Adherence to guidelines was significantly better in patients receiving disease state management. Greater adherence was seen in the following parameters (all p<0.05): diabetes, HbA_{1c} <7% (86.2% vs. 62.0%); CAD, aspirin or clopidogrel use (88.2% vs. 56.1%), ace-inhibitor (ACEI) or angiotensin receptor blocker (ARB) use (82.4% vs. 40.9%); CHF, ACEI or ARB use (73.3% vs. 44.9%); osteoporosis, calcium use (85.0% vs. 56.3%). Disease state performance measures were similar between groups for hypertension, hyperlipidemia, and stroke. The mean number of pharmacist recommendations per patient per month was greater in facilities emphasizing disease state management(0.76 vs. 0.23, P<0.001). Pharmacists with a disease state focus were more likely to make a recommendation to improve disease

management (54.1%) than were pharmacists in control facilities (32.4%) (P<0.001).
CONCLUSION: We observed significantly greater treatment guideline adherence for four of seven disease states evaluated in patients receiving disease management services. Placing greater emphasis on a disease state focused approach to pharmacist consulting at LTCFs may improve patient care.

44E. Effect of 80 mg versus 10 mg of atorvastatin in patients ≥65 and <65 years of age with stable coronary heart disease. *Nanette Wenger, M.D.*[1], Sandra J. Lewis, M.D.[2], David M. Herrington, M.D.[3], Vera Bittner, M.D.[4], Francine K. Welty, M.D.[5]; (1)Emory University School of Medicine, Atlanta, GA; (2)Northwest Cardiovascular Institute, Portland, OR; (3)Wake Forest School of Medicine, Winston-Salem, NC; (4)University of Alabama at Birmingham, Birmingham, AL; (5)Beth Israel Deaconess Medical Center, Boston, MA.

INTRODUCTION: Intensive lipid-lowering treatment with atorvastatin 80 mg in patients with stable coronary heart disease (CHD) in the Treating to New Targets study provided significant clinical benefit beyond treatment with atorvastatin 10 mg. The present analysis provides a post hoc assessment of the efficacy and safety of high-dose atorvastatin therapy in patients ≥ 65 years and in those <65 years of age.
METHODS: A total of 10,001 patients (3809 ≥ 65 years) were randomized to double-blind therapy with atorvastatin 10 or 80 mg/day for a median follow-up of 4.9 years. The primary end point was the first major cardiovascular event (death from CHD, nonfatal non-procedure-related myocardial infarction, resuscitated cardiac arrest, or fatal or nonfatal stroke).
RESULTS: Mean changes in LDL-C, HDL-C and TG were similar in both groups. In patients both older and younger than 65, intensive therapy with atorvastatin 80 mg significantly decreased the rate of major cardiovascular events. Secondary measures of clinical efficacy in each subgroup were consistent with those in the overall study. More patients on 80 mg discontinued treatment due to treatment-related adverse events (<65 years: 5.1% vs 6.7%; ≥ 65 years: 5.6% vs 8.0% in atorvastatin 10 and 80 mg, respectively).
CONCLUSIONS: Intensive lipid-lowering treatment with atorvastatin 80 mg in patients with stable CHD produced significant reductions in relative risk for major cardiovascular events in both older (≥ 65 years of age) and younger patients (<65 years of age).

	≥ 65 years		<65 years	
	Atorva 10 mg n=1872	Atorva 80 mg n=1937	Atorva 10 mg n=3134	Atorva 80 mg n=3058
Mean LDL* (mg/dL)	96.7	71.6	100.2	73.3
Mean HDL* (mg/dL)	49.3	49.0	46.4	45.8
Mean TG* (mg/dL)	142.4	121.4	157.6	132.7
Primary events (n, %)	235 (12.6)	199 (10.3)	313 (10.0)	235 (7.7)
HR (95% CI) Atorva 80 mg vs 10 mg	0.81 (0.67-0.98), P=0.03		0.76 (0.64-0.90), P=0.001	

*On-treatment values
Presented at the American Heart Association Scientific Sessions 2005, Dallas, TX, November 13-16, 2005.

45. Rating the anticholinergic potential of selected medications. *Kelly M. Rudd, Pharm.D., BCPS*[1], Cynthia L. Raehl, Pharm.D., FASHP, FCCP[2]; (1)Bassett Healthcare, Cooperstown, NY; (2)Texas Tech University-HSC-School of Pharmacy, Amarillo, TX.

PURPOSE: This study produced an efficient system of quantifying, comparing and reducing medication-related anticholinergic exposure by 1) creating an anticholinergic rating for various medications common in geriatric practice, and 2) proposing a methodology for clinician utilization of the rating system. Reducing medication-related anticholinergic exposure is a key practice in geriatric pharmacotherapy to 1) improve patient's quality of life 2) decrease adverse drug-events, and 3) decrease morbidity and mortality in the geriatric population.
METHODS: Radioreceptor assay (RRA) determinations of atropine equivalent values, an in vitro standardized marker of anticholinergic activity, was derived from the Medline database (1966-June 2005) and via personal communication with experts in this line of research.
RESULTS: The atropine equivalent values were converted to a standardized rating system to rank relative potency of anticholinergic properties. A consensus panel of clinician experts in the field of geriatric pharmacotherapy reviewed the rankings, resolving discrepancies to create an objective and qualitative rating of anticholinergic potential.
CONCLUSION: The culmination of data led to the creation an objective scoring method that clinicians can use to qualitatively compare the anticholinergic potential of various medications, methodology that is currently a void in the existing literature. Likewise, the study authors propose it may be possible to quantify the anticholinergic potential expressed by individual medications and by the entire medication regimen to decrease anticholinergic exposure in the geriatric population.

46. Evaluation of acetylcholinesterase inhibitor formulary therapeutic substitution in a Veterans Affairs population. *Sheila R. Botts, Pharm.D., BCPP*[1], Courtney Vincent Eatmon, Pharm.D.[2], Melody Ryan, Pharm.D., BCPS, CGP[1]; (1)University of Kentucky College of Pharmacy, Lexington, KY; (2)Lexington VAMC, Lexington, KY.

PURPOSE: Acetylcholinesterase inhibitors (AChE-Is) are first-line agents for moderate cognitive decline in Alzheimer's Dementia. No comparative efficacy trials exist differentiating outcomes between AChE-Is; and commonly health systems may change preferred formulary agents based on cost. Once initiated, AChE-Is are usually changed only if the patient experiences adverse effects or inadequate response. Literature is limited regarding changing AChE-Is in patients stabilized on the first agent. Our institution made galantamine the preferred AChE-I and required therapeutic substitution for all patients receiving donepezil. We evaluated the clinical outcomes associated with this formulary substitution.
METHODS: Eligible patients were evaluated in a pharmacy clinic prior to and eight weeks after the substitution. Cognitive functioning was assessed with the Mini-Mental State Exam (MMSE); daily functioning was assessed by the Alzheimer's Disease Cooperative Study Activities of Daily Living Inventory (ADCS-ADL). Galantamine was initiated at 4 mg bid after a 3-day washout period and increased to 8 mg bid after 4 weeks. If patients did not tolerate galantamine or had a decline in function or cognition, they were changed back to donepezil. Paired t tests were used to determine cognitive or functional change.
RESULTS: Seventy-one patients were converted to galantamine. At the 8-week assessment, 71.8% remained on galantamine, 21% restarted donepezil, and 1.4% were not on any AChE-I. Patients who remained on galantamine had no significant change in MMSE (+5.11, p=0.22) or ADCS-ADL (-0.34, p=0.76) scores from baseline to 8 weeks. Eight (11.3%) patients restarted donepezil due to lack of efficacy (MMSE -3.87, ns; ADCS-ADL -12.92, p=0.04). Seven patients (9.9%) were unable to tolerate galantamine (5/7 had gastrointestinal complaints).
CONCLUSIONS: Most patients stabilized on donepezil were successfully changed to galantamine. A few patients experienced a decline during the conversion. Given the irreversible nature of cognitive decline, patients should be monitored closely during a change in AChE-I.

Health Services Research

47. Physician perceptions of medication therapy management services (MTMS): developing outpatient clinical services. *Rosalyn S. Padiyara, Pharm.D.*, Suzanne M. Rabi, Pharm.D., Ramesh V. Patel, Pharm.D.; Swedish Covenant Hospital, Chicago, IL.

PURPOSE: With the approval of MTMS CPT codes, pharmacists will be able to bill applicable third party payors when providing MTMS services. MTMS services can be provided for patients who are covered under the Medicare Part D prescription drug benefit and include selecting, initiating, modifying or administering medication therapy, monitoring and evaluating patient response to therapy, patient/family medication consulting, and disease and wellness prevention programs. The objective of this study is to describe current physician attitudes toward implementing clinical pharmacy services that have not previously existed in a hospital setting and to determine which MTMS-related outpatient services physicians desire pharmacists to provide.
METHODS: Physicians at a 300-bed community hospital were asked to complete a 5-question survey. Surveys evaluated if physicians worked with a clinical pharmacist in an outpatient setting in the past, the types of services they would consider pharmacists to provide, and which specific services they would recommend for their patients. All surveys were analyzed using descriptive statistics.
RESULTS: Two-hundred fifty physicians were provided a survey regarding MTMS services. The response rate was 18% (N=44). The majority of physicians worked in internal medicine or family practice. Twenty-five percent worked with a clinical pharmacist in the ambulatory care setting in the past; 88% would recommend the use of a pharmacy-related service. Anticoagulation (25%), smoking cessation(20%), and diabetes (18%) were among the top three clinical services physicians would use. Physicians with advanced training (fellowship) were less likely to feel a need for pharmacist services.
CONCLUSIONS: The majority of physicians at this hospital show strong support for pharmacist-provided services. The majority of interest was shown for complicated disease states. Results may be used to develop MTMS-related outpatient clinical services at various institutions that will allow pharmacists to work effectively with other disciplines.

Hematology/Anticoagulation

48. Clinical outcomes using subcutaneous unfractionated heparin and warfarin after elective total hip or total knee arthroplasty. *William Dager, Pharm.D.*, Jeff King, Pharm.D., John Meehan, M.D., Jennifer Branch,

Pharm.D., Richard White, M.D.; University of California, Davis Medical Center, Sacramento, CA.

PURPOSE: In patients having elective total hip arthroplasty (THA) or knee arthroplasty (TKA), prophylaxis with an anticoagulant is required to prevent complications associated with venous thromboembolism (VTE). Anticoagulation regimens that have been studied in clinical trials generally have compared the efficacy of two different drugs over a specified time period. In trials comparing warfarin to other anticoagulants, no heparin was administered during the time required for warfarin to reduce the level of clotting factors. The reported incidence of symptomatic VTE and major bleeding for warfarin alone in clinical trials is in the range of 0.3–1.8% and ~3.3%, respectively. At UC Davis, patients undergoing TKA or THA receive 7500 units unfractionated heparin (UFH) subcutaneous (SC) plus warfarin starting the evening after surgery. Warfarin is continued for approximately 1 month with a target INR of 2.0 (range 1.5–2.5). The outcome of this practice has not been prospectively evaluated.
METHODS: Patients undergoing an elective TKA or THA receiving UFH, 7500 units SC q 12 hours for 2–5 days plus warfarin for 4 weeks. Patients were followed up by review of medical records and by a phone interview one month after hospital discharge. 170 consecutive consenting patients were available for analysis.
RESULTS. The duration of warfarin therapy was 29.3 +/- 8.9 days; the average INR = 1.66 +/- 0.37 (range 1.1-4.2). 12 minor bleeding episodes were reported (average INR =1.75 +/- 0.58), none requiring intervention. No symptomatic thrombotic events or episode of heparin-induced thrombocytopenia were observed.
CONCLUSION: Combining initial postoperative short-term 7500 units UFH SC every 12 hours, plus warfarin for 4 weeks targeting an INR of 2.0 appears to be safe and effective for minimizing the risk for symptomatic VTE or bleeding complications.

49. Adherence to national guidelines for the management of elevated international normalized ratios associated with warfarin therapy. Emily Beth Devine, Pharm.D., M.B.A., BCPS, FASHP[1], *Alan W. Hopefl, Pharm.D.*[2], Ann K. Wittkowsky, Pharm.D., CACP, FASHP[1]; (1)University of Washington, Department of Pharmacy, Seattle, WA; (2)Amerinet, Inc., St. Louis, MO.

PURPOSE: To evaluate current practice patterns in managing patients with excess warfarin anticoagulation, and to evaluate adherence to guidelines for reversal of excess anticoagulation, as recommended by the American College of Chest Physicians 7th Conference on Antithrombotic and Thrombolytic Therapy
METHODS: This is an observational study of cases receiving treatment for excessive warfarin anticoagulation (International Normalized Ratio ≥ 4.5). Cases were drawn from 22 institutions where warfarin was managed in clinic or acute care settings.
RESULTS: 433 cases were reviewed. The mean INR value was 7.7. Indications for warfarin were: atrial fibrillation, 194 (45%); deep venous thrombosis/pulmonary embolus, 94 (22%); prosthetic heart valve, 56 (13%); secondary prevention of stroke, myocardial infarction (MI) or death, 41 (10%); orthopedic procedures 33 (8%); and primary prevention of acute MI, 10 (2%). The number and proportion of total cases, categorized by each INR level specified in the guidelines were: INR <5, 107 (25%); INR ≥ 5.0-8.9, 200 (46%); INR ≥ 9.0-19.9, 44 (10%); INR>20 or serious bleeding, 79 (18%); life-threatening bleeding, 3 (0.7%).
Treatment for 173 (40%) cases did not adhere to current guidelines. Lack of adherence was attributed primarily to the under- or overuse of vitamin K, and to overuse of fresh frozen plasma. Of those that were not adherent, 27 (16%) were under-treated, and 89 (51%) were over-treated. In 116 of 173 (67%) cases, lack of adherence was attributed to administration of less preferred routes of administration of vitamin K—subcutaneous or intramuscular, instead of oral or intravenous.
CONCLUSION: Adherence to national guidelines for the management of excessive anticoagulation is low. Potential exists for education and improvement in adherence to these national guidelines in both clinic and acute care settings.

50E. Capturing the financial impact of heparin-induced thrombocytopenia. *Maureen Smythe, Pharm.D.*[1], John M. Koerber, Pharm.D.[2], Joan C. Mattson, M.D.[3]; (1)Department of Pharmacy, William Beaumont Hospital and Department of Pharmacy Practice, Wayne State University, Detroit, MI; (2)William Beaumont Hospital, Royal Oak, MI; (3)Department of Clinical Pathology, William Beaumont Hospital, Royal Oak, MI.

Data evaluating the financial impact of heparin-induced thrombocytopenia (HIT) is lacking. The goal of this case-control study was to evaluate the financial impact of HIT. Case patients were those with a new diagnosis of HIT from April 2003 to March 2004 for whom matched controls were available. Controls for each case patient were matched for the DRG under which the hospital was reimbursed, the patients' primary diagnosis code and their primary procedure code. Case patients required identification of >1 control for inclusion. The hospital s financial database was queried for length of stay (LOS), total cost, and reimbursement. For each case patient, the cost and reimbursement were compared to the cost and reimbursement for each group of matched controls. In an effort to eliminate the impact of variable reimbursement, a subset of only Medicare case and control patients was also evaluated. Of 72 new HIT patients, matched controls were identified for 31. The mean LOS for the case and control patients was 22.8 and 11.6 days respectively (p=0.006). The mean hospital cost of case and control patients was $55,440 and $26,505 respectively. From reimbursement minus cost calculations, our institution lost an average of $13,429 per HIT patient compared to $393 per control patient (p=0.005). The mean LOS for Medicare cases (n=21) and matched Medicare controls was 26 and 14.6 days respectively (p=0.041). The mean hospital cost of Medicare case and control patients was $58,842 and $30,210 respectively. From reimbursement minus cost calculations for the Medicare subset, our institution lost an average of $20,229 per HIT case compared with $1844 per control patient (p<0.0001). Assuming 72 cases of HIT per year, our institution incurs a projected annual loss of $980,000 from HIT. The use of alternate anticoagulants, although having a higher acquisition cost, may offset this loss through HIT avoidance.
Presented at the Annual Meeting of the American Society of Hematology, Atlanta, GA, December 12, 2005.

51E. Identifying the incidence of heparin-induced thrombocytopenia. *Maureen Smythe, Pharm.D.*[1], John M. Koerber, Pharm.D.[2], Joan C. Mattson, M.D.[3]; (1)Department of Pharmacy, William Beaumont Hospital and Department of Pharmacy Practice, Wayne State University, Detroit, MI; (2)William Beaumont Hospital, Royal Oak, MI; (3)Department of Clinical Pathology, William Beaumont Hospital, Royal Oak, MI.

Heparin-induced thrombocytopenia (HIT), an immune-mediated syndrome which may result in life-threatening thrombosis, is estimated to occur in up to 5% of patients receiving unfractionated heparin (UFH). The risk of HIT depends on patient type (surgical or medical) and the amount/route of UFH. The goal of this project was to determine the incidence of HIT within our 1064-bed tertiary-care institution over a one-year period. The hospital admissions database was queried to identify the number of patient admissions. The pharmacy system database was queried to identify the number of patients receiving intravenous (IV) and/or subcutaneous (SQ) UFH as well as the number of patients (excluding cardiac catheterization) who received a direct thrombin inhibitor (DTI). Medical records of patients receiving a DTI were reviewed to categorize the indication for DTI therapy (clinical diagnosis of HIT, suspected HIT, history of HIT and other). Criteria for all categories were developed a priori. New HIT patients included those with a clinical diagnosis of HIT or suspected HIT (unable to rule out). The laboratory system database was queried to retrieve heparin platelet factor 4 (HPF4) immunoassay results in new HIT patients. During the study period, 58 814 patient admissions occurred with an estimated 24 068 patients being exposed to UFH. DTI therapy was administered in 133 patients. Of these, 72 new HIT patients (46% medical and 54% surgical) were identified. Eighty percent of the surgical patients underwent cardiovascular surgery. A positive HPF4 result occurred in 69.4% of new HIT patients. The overall incidence of HIT was 0.3%. Cardiovascular surgery patients were the most likely to develop HIT. The incidence of HIT in patients receiving therapeutic-dose IV heparin was 1.0% whereas the incidence in patients receiving only antithrombotic prophylaxis was <0.1%. These estimates are conservative since DTI therapy was required in order for a new HIT case to be captured.
Published in J Thromb Haemost 2005;Vol 3(Suppl 1):P1143.

52. Symptomatic venous thromboembolism rates after orthopedic surgeries in patients treated with unfractionated heparin, enoxaparin, dalteparin or fondaparinux. *Matthew W. Sarnes, Pharm.D.*[1], Andrew Shorr, M.D., M.P.H.[2], Mitchell Higashi, Ph.D.[3], Laura Happe, Pharm.D., M.P.H.[4], Eileen Farrelly, M.P.H.[4]; (1)Applied Health Outcomes, Havertown, PA; (2)Washington Hosptial, Washington, DC; (3)GlaxoSmithKline, Philadelphia, PA; (4)Applied Health Outcomes, Tampa, FL.

PURPOSE: To assess differences in symptomatic VTE rates among anticoagulants used for prophylaxis in orthopedic surgery patients.
METHODS: This was a retrospective analysis of inpatient data from over 500 hospitals in the United States. Patients hospitalized for hip or knee replacement or hip fracture surgery between January 2003 and March 2005 were eligible for study inclusion. Patients receiving unfractionated heparin (UFH), enoxaparin, dalteparin or fondaparinux within 2 days of surgery were included in the analysis. Patients were excluded if they were <18 yrs of age or if they received more than one anticoagulant of interest during their hospitalization. The occurrence of VTE was determined by the presence of an ICD-9 code for DVT or PE during the hospitalization. Logistic regression models were then used to assess differences in VTE rates between the anticoagulants, controlling for age, gender, severity of illness (Charlson), length of stay, presence of other hypercoaguable states, number of

hospitalizations prior to index visit, and coumadin use.
RESULTS: A total of 138,026 patients were included in the analysis: fondaparinux=11,633; dalteparin=14,713; enoxaparin=92,776; UFH=18,904. The unadjusted VTE rates in each cohort were: fondaparinux=0.3%, dalteparin=0.5%, enoxaparin=0.9%, UFH=2.2%. After controlling for baseline covariates, patients on fondaparinux were least likely to experience a symptomatic VTE. The odds of VTE for each anticoagulant when compared to fondaparinux were: dalteparin OR=1.4, p=0.081; enoxaparin OR=2.4, p<0.0001; UFH OR=4.5, p<0.0001.
CONCLUSIONS: Differences in symptomatic VTE rates exist in hospitalized orthopedic surgery patients depending on the anticoagulant used for prophylaxis. Fondaparinux patients had the lowest risk of symptomatic VTE while patients receiving UFH experienced the highest risk.

53E. Clinical benefit and survival endpoints from a phase III trial comparing decitabine vs supportive care in patients with advanced myelodysplastic syndromes. *Gene Wetzstein, Pharm.D., BCOP*[1], Shane Fishco, Pharm.D.[2], Carlos M. De Castro, M.D.[3], Hussein I. Saba, M.D., Ph.D.[1]; (1)H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL; (2)James A. Haley Veterans' Hospital, Tampa, FL; (3)Duke University Medical Center, Durham, NC.

PURPOSE: Myelodysplastic syndrome (M.D.S) is a blood disorder characterized by dysplasias of hematopoetic cells resulting in cytopenias and progression to acute myelogenous leukemia (AML). There is only one approved therapy for M.D.S. Decitabine (Dacogen) is a cytosine analog that reverses aberrant DNA methylation leading to re-expression of silenced tumor suppressor genes. Results of adjudicated data will be presented.
METHODS: We report a phase III, randomized, open-label trial of decitabine (DAC) vs supportive care (SC) in M.D.S patients with International Prognostic Scoring System (IPSS) Intermediate (Int)-1 (31%), Int-2 (44%), and high-risk disease (26%). Secondary M.D.S (14%)/previously treated (21%) patients were included. Co-primary endpoints were response rate (CR + PR) and Time to AML or Death (TTAML/D).
RESULTS: 170 patients received either DAC (n = 89) (3-hr infusion; 15 mg/m^2/hr q 8 hrs for 3 days q 6 wks) plus SC or SC alone (n = 81). Response rate according to International Working Group (IWG) M.D.S criteria was 17% for DAC (9%, CR; 8%, PR) vs 0% for SC (p <0.001). Responses occurred in all IPSS groups and were durable. DAC responders vs all nonresponders had a median of 491 vs 274 AML-free days until death, a median of 657 vs 384 days of survival, and remained or became RBC/platelet transfusion independent during response. Median TTAML/D in all pts was 340 days for DAC vs 219 days for SC (p=0.043 Wilcoxon, 0.160 Log-rank). Using a Cox proportional hazards model, the probability of progression to AML or death was 1.72-fold greater for SC than DAC (p=0.017). Quality-of-life evaluations showed DAC to be superior for global health status, physical functioning, fatigue, and dyspnea. As expected, the primary toxicity was myelo-suppression, with the major Grade 3-4 toxicity being febrile neutropenia.
CONCLUSION: DAC is a promising therapy for M.D.S, with predictable toxicity.
Presented at the 2005 Annual Meeting of the American Society of Clinical Oncology, Orlando, FL, May 13-17, 2005.

HIV/AIDS

54. Results of the PALS study: Pacific Oaks atazanavir/lopinavir switch. *James D. Scott, Pharm.D., M.Ed., B.S.*[1], Peter R. Wolfe, M.D.[2], Anthony Scarsella, M.D.[3]; (1)Western University of Health Sciences, Pomona, CA; (2)Private Practice, Los Angeles, CA; (3)Pacific Oaks Medical Group, Beverly Hills, CA.

INTRODUCTION: Although the efficacy of lopinavir/ritonavir (LPV/r) based therapy for HIV has been demonstrated, a high incidence of triglyceride (TG) elevations is often seen. The current study assessed the clinical and lipid outcomes associated with switching virologically suppressed pts with elevated TG on LPV/r therapy to ATV/r therapy.
METHODS: 12 pts with viral load (VL) <50 c/mL for ≥ 6 months and fasting TG >200 mg/dL on a stable regimen containing LPV/r were changed to ATV/r plus their original NRTIs in this 24wk pilot study. Assessments at Baseline (BL) and Weeks 4, 8, 16, and 24 included VL, CD4, lipids, chemistries; adherence and quality of life (QOL) were assessed at BL and 24 wks. Statistical analysis was performed using paired samples t-test and repeated measures ANOVA.
RESULTS: BL demographics: age=42 (± 7.0), CD4=560 (± 313) cells/mm^3, total cholesterol (TC) = 213 (± 44) mg/dL, fasting TG = 454 (± 265) mg/dL, total bilirubin (TB) = 0.8 (± 0.2) mg/dL. 1 pt withdrew at 4 wks due to diarrhea. There were no statistically significant changes in CD4 or TC at any time point. All pts maintained VL <50 c/ml. Compared to BL, TG trended to improve (p=0.06) at 4 wks (277 ± 131) and 8 wks (270 ± 158), and significantly improved (p<0.05) at 16 wks (256 ± 90) and 24 weeks (233 ± 102). TB also increased significantly (p<0.001) at all time points. No changes were seen in QOL or adherence.
CONCLUSION: Switching LPV/r to ATV/r did not affect immunologic or virologic outcomes, but did lead to significant decreases in TG by 16 weeks. There were no changes at 24 wks in CD4, VL, TC, adherence and QOL. ATV/r was associated with increases in TB that were not considered clinically relevant.

55. Clinical outcomes with concurrent atazanavir and proton-pump inhibitor use. *Eric G. Sahloff, Pharm.D.*[1], Joan M. Duggan, M.D.[2]; (1)University of Toledo College of Pharmacy, 2801 West Bancroft, Toledo, OH; (2)Medical University of Ohio, 2801 West Bancroft, Toledo, OH.

PURPOSE: The purpose of this study was to describe clinical outcomes [viral load (VL)/CD4 counts] in patients receiving concomitant atazanavir(ATV) and proton pump inhibitors(PPIs). PPIs have the potential to decrease ATV solubility and/or absorption leading to subtherapeutic plasma ATV concentrations. Pharmacokinetic data have shown statistically significant decreases in ATV exposure when administered with PPIs. Evidence of the clinical significance of the ATV-PPI interaction is limited. In our clinic, we currently have patients requiring the administration of ATV±ritonavir(RTV) with a concurrent PPI.
METHODS: A retrospective chart review of all HIV positive patients ≥18 years prescribed ATV±RTV and a PPI for ≥ 2 months was performed. The primary outcome was achievement/maintenance of VL<400 cp/ml for ≥ 2 months while on concomitant ATV-PPIs. Data collected included: VL/CD4 count at ATV initiation, genotype/phenotype, prior PI experience, durability (time on ATV-PPI), and adherence.
RESULTS: Six males and six females met inclusion criteria. Temporal separation of PPI and ATV daily dosing was unavailable. Five of 12 subjects had VL<400 cp/mL at initiation of ATV±RTV which was maintained while receiving concurrent ATV-PPIs. Four additional subjects with VL>400 cp/mL achieved undetectable VL while on concurrent ATV-PPI. Durations of concurrent therapy ranged from 2-23 months. Of the 3 subjects not maintaining VL<400 cp/mL, 1 subject had one VL<400 cp/mL value at 4 months. All subjects not achieving undetectable VL had ATV susceptibility per genotype resistance testing. One of 3 had decreased ATV susceptibility after 19 months on therapy. All 3 not achieving undetectable VL had known adherence issues.
CONCLUSIONS: Nine of 12(75%) subjects achieved successful clinical outcomes associated with concurrent use of ATV-PPIs. Subjects maintaining adherence to prescribed regimens were able to achieve and maintain VL<400 cp/mL. In our experience, the drug interaction between ATV and PPIs is not clinically significant for patients under good virologic control.

Infectious Diseases

56E. Meta-analyses of the impact of inappropriate antibiotic therapy on mortality in patients with ventilator-associated pneumonia and blood stream infections. *Effie L. Gillespie, Pharm.D.*, Aarti A. Patel, M.B.A., Pharm.D., Craig I. Coleman, Pharm.D.; University of Connecticut School of Pharmacy, Storrs, CT and Hartford Hospital, Hartford CT, Hartford, CT.

OBJECTIVES: Several studies have found that initial treatment of ventilator-associated pneumonia (VAP) and blood stream infections (BSI) with inappropriate antimicrobial therapy (IAT) is associated with higher rates of mortality, but additional studies have failed to confirm these findings. To provide a stronger quantitative basis, we conducted a series of meta-analyses of existing relevant studies.
METHODS: Three investigators systematically searched databases from 1966-September 2005 and reviewed citations in relevant articles to identify studies that met the following inclusion criteria: (1) randomized or observational trials, (2) compare VAP or BSI patients receiving appropriate antimicrobial therapy (defined as an antibiotic regimen with demonstrated in-vitro activity against identified bacterial species associated with infection) and IAT (3) report data on incidence of mortality. We conducted mortality analyses, both with and without adjustment for confounding factors. A random-effects model was utilized.
RESULTS: All studies included were observational. A meta-analysis of VAP studies utilizing unadjusted mortality data (n=8 studies) demonstrated IAT significantly increased patients' odds of mortality [odds ratio (OR); 2.03 (95%CI 1.35-3.06); Q statistic p-value = 0.23]. Similar results were seen upon meta-analysis of adjusted mortality data (n=9 studies) [OR; 2.00 (95%CI 1.32-3.05); Q statistic p-value = 0.06]. A meta-analysis of BSI studies utilizing unadjusted mortality data (n=16 studies) demonstrated IAT significantly increased patients' odds of mortality [OR; 2.29 (95%CI 1.88-2.78); Q statistic p-value = 0.0003]. Similar results were seen upon meta-analysis including adjusted mortality data (n=16 studies) [OR; 2.11 (95%CI 1.53-2.92); Q statistic p-value < 0.0001]. Assessment of the funnel plots and Egger's weighted regression statistics (p-value > 0.34 for all) demonstrated a low probability of significant publication bias in the VAP and BSI analyses.

CONCLUSIONS: There appears to be an association between IAT and higher mortality in patients with VAP and BSI, thus emphasizing the critical importance of early appropriate antimicrobial therapy.
Presented at the 16th European Congress of Clinical Microbiology and Infectious Diseases, Nice, France, April 1-4, 2006.

57. Increasing linezolid minimum inhibitory concentrations (MIC) in methicillin-resistant *Staphylococcus aureus* at a large academic teaching institution. *Nathan P. Wirick, Pharm.D.*[1], Debra A. Goff, Pharm.D.[2], Julie Mangino, M.D.[2]; (1)Hillcrest Hospital- Cleveland Clinic Health System Eastern Region, Mayfield Heights, OH; (2)*The Ohio State University Medical Center, Columbus, OH.

BACKGROUND: Linezolid (L) was added to the formulary in 2000 for treating MRSA and vancomycin resistant enterococcal infections. (L) is not restricted, yet use is monitored. Our purpose is to assess (L) MICs for MRSA over time.
METHODS: A retrospective analysis of 2,827 MRSA isolates (2001-2004) was performed for (L) MIC data. (L) susceptibility was determined by: E-test (01/01-08/02) and by microdilution MIC using Microscan® panels (09/02-12/04). Clinical and Laboratory Standards Institute (CLSI) breakpoints were used identifying MICs>4 as non-susceptible. Isolates with a MIC ≥ 4 had patient data reviewed for antibiotic exposure, risk factors for MRSA, and demographics. The percent of MRSA with MIC ≥ 4 from each year were compared statistically by Fischer's Exact Test. Defined Daily Dose/1000 patient days (DDD) was collected for (L) and vancomycin to determine use.
RESULTS: A significant increase of MRSA isolates with an MIC = 4 was observed from 2002-2003. Patients had a history of prior antibiotic use and hospitalization. DDD of linezolid also increased.

	2001	2002	2003	2004
Vancomycin DDD	62	63	65	79
Linezolid DDD	11	9	16	15
MRSA isolates (#)	-	770	918	1139
-linezolid MIC > 4 (#)	0	1	4	0
-linezolid MIC = 4 (#)	0	49	94	39
Rate of linezolid with MIC = 4 (%)	0	6.3	10.2*	3.5

*$p<.05$

CONCLUSIONS: Although few MRSA isolates were non-susceptible, there was a significant increase in number of isolates with linezolid MIC=4 in 2002-2003. This correlated with increased linezolid use, but this increase was not sustained through 2004. Due to recent national guidelines for hospital-acquired pneumonia, linezolid use may increase. Further observation of linezolid MICs to MRSA is warranted.

58E. In vitro pharmacodynamics of anidulafungin and caspofungin against clinical isolates of Candida glabrata including strains with elevated MICs to caspofungin. *Jason M. Cota, Pharm.D.*[1], Nathan P. Wiederhold, Pharm.D.[1], David S. Burgess, Pharm.D.[1], Laura K. Najvar, B.S.[2], John R. Graybill, M.D.[2]; (1)University of Texas at Austin, San Antonio, TX; (2)University of Texas Health Science Center at San Antonio, San Antonio, TX.

BACKGROUND: The echinocandins anidulafungin and caspofungin have activity against most isolates of *Candida glabrata*, a species of increasing clinical significance. We performed an in vitro evaluation of the pharmacodynamics of anidulafungin and caspofungin against clinical isolates of *C. glabrata* including those with increased MICs to caspofungin.
METHODS: MICs and MFCs were determined for 19 *C. glabrata* isolates using CLSI M27-A2 methods. Pharmacodynamic analysis was performed in triplicate using the XTT viability assay at anidulafungin and caspofungin concentrations ranging from 0–128 µg/mL. IC50 and IC90 values (µg/mL) were calculated by fitting XTT data to a four-parameter logistic model (Hill equation). Goodness of fit for each isolate-drug combination was assessed by R^2 and standard error of the IC50 value. Pharmacodynamic results for isolates with elevated MICs to caspofungin were verified by time-kill assay.
RESULTS: MIC values were at least 2 dilutions lower for anidulafungin than caspofungin for 17 of 19 strains. IC50 and IC90 values for anidulafungin were significantly lower than those of caspofungin for all 19 isolates, including those with elevated MICs to caspofungin. Time-kill results supported data from XTT viability studies.

	Anidulafungin		Caspofungin	
Isolates with elevated caspofungin MICs	MIC/MFC	IC50/90	MIC/MFC	IC50/90
C. glabrata 7755	2/4	0.17/7.8	8/64	17/>128
C. glabrata 04-1748	4/8	0.83/5.3	64/>128	22/>128
C. glabrata 04-2596	4/8	2.4/3.6	64/64	27/>128
C. glabrata 05-62	1/2	0.08/1.8	32/>128	7.4/>128

CONCLUSION: Anidulafungin has potent *in vitro* activity by MIC and pharmacodynamic analysis against *C. glabrata* strains. The activity of anidulafungin was maintained even against *C. glabrata* isolates for which caspofungin was not fungicidal and had elevated MICs.
Presented at the 45th Interscience Conference on Antimicrobial Agents and Chemotherapy, Washington, D.C., December 16-19, 2005.

59E. Multicenter cohort analysis of epidemiology, inadequate antibiotic therapy (IAT), and outcomes of patients with Gram-negative bacteremia (GNB) in the ICU. Susan L. Davis, Pharm.D.[1], John Mohr, Pharm.D.[2], Thomas Lodise, Pharm.D.[3], *Peggy S. McKinnon, Pharm.D.*[4]; (1)Henry Ford Hospital and Wayne State University, Detroit, MI; (2)The University of Texas Health Science Center at Houston, Houston, TX; (3)Albany College of Pharmacy, Albany, NY; (4)Barnes-Jewish Hospital, St. Louis, MO.

PURPOSE: While IAT has been identified to predict poor patient outcomes, most institutions do not have a means to assess rates of IAT or outcomes.
METHODS: A standardized tool was developed to collect epidemiology, microbiology, therapy and outcomes data. A cohort analysis was performed at 3 US hospitals in consecutive adult ICU patients with GNB. Rates and outcomes of IAT (no therapy with in-vitro activity within 48 hrs) were evaluated.
RESULTS: 200 patients were identified. ICU types were: medical 70%, surgical 15%, other 15%. Organisms identified included: E. coli 31% (range 25-34% between hospitals), *K. pneumoniae* 15% (3–19%), *P. aeruginosa* 15% (11–20%). 23% of infections were polymicrobial and 70% were healthcare-acquired. Source of bacteremia: urine 22%, IV catheter 17%, and respiratory 17%. Antimicrobial susceptibility varied between institutions, and IAT averaged 17% (2–27%). Clinical success was 77% (68–88%), and crude mortality was 29% (22–37%). Clinical failure and in-hospital and attributable mortality were higher in patients with IAT vs appropriate therapy (63% vs 16%, 62 vs 23%, 42 vs 10%, P <.001). Multiple logistic regression analysis identified independent risk factors for clinical failure as: inappropriate empirical therapy (OR 14.0, 95%CI 4.6–42.9), high risk source (3.5, 1.3–9.6), and ICU type (2.9, 1.3–6.5). The same factors were associated with mortality: inappropriate empirical therapy (OR 9.7, 95%CI 3.2–28.9), high risk source (5.2, 2.0-13.6), and ICU type (2.5, 1.2–5.2)
CONCLUSIONS: IAT is associated with clinical failure and mortality in ICU GNB. The rate of IAT varied among institutions. The standardized tool was useful to track and compare appropriate empiric tx selections, IAT, and outcomes in various hospital settings.
Presented at the 45th Interscience Conference on Antimicrobial Agents and Chemotherapy, Washington, D.C., December 16–19, 2005.

60. Investigation of the mutant prevention concentration (MPC) of linezolid for Enterococci and Staphylococci. *George P. Allen, Pharm.D.*, Betsy C. Bierman, Pharm.D.; Oregon State University College of Pharmacy, Portland, OR.

BACKGROUND: The development of linezolid (LZ) has expanded the antimicrobial arsenal against resistant bacteria, but resistance by chromosomal mutation has been selected in vitro and observed clinically in *Enterococcus faecalis*, *E. faecium*, and *Staphylococcus aureus*. LZ-resistant isolates may continue to emerge as bacterial exposure to LZ increases. Thus, mechanisms by which to combat LZ resistance are required. The mutant prevention concentration (MPC) has been proposed as an alternative to the minimum inhibitory concentration (MIC) as an antimicrobial susceptibility index. The MPC is the MIC of the most resistant first-step mutant of a heterogeneous bacterial population. In theory, antimicrobial concentrations above the MPC will prevent selection of resistant bacteria. Antimicrobial concentrations that fall in the range of concentrations between the MIC and MPC (mutant selection window [MSW]) promote resistance selection. Little research has evaluated the MPC concept for LZ.
METHODS: MPCs of vancomycin-susceptible and -resistant *E. faecalis* (VREFc, VSEFc), *E. faecium* (VREFm, VSEFm) and methicillin-susceptible and -resistant *S. aureus* (MSSA, MRSA) were determined by plating 10^{10} colony-forming units on LZ-containing agar. The MPC was recorded as the lowest concentration completely inhibiting growth.
RESULTS: MIC/MPC (mg/L) of LZ were 2/4, 2/8, 2/4, 2/8, 2/4, and 1/8 for VSEFc, VREFc, VSEFm, VREFm, MSSA, and MRSA, respectively. Based on population pharmacokinetics (peak 21.2 mg/L, trough 6.15 mg/L, half-life 5.4 hours), it is predicted that LZ concentrations are maintained above the MPC for 7.6 hours (63% of the dosing interval) for VREFc, VREFm, and MRSA, and 12 hours (100% of the dosing interval) for VSEFc, VSEFm, and MSSA.
CONCLUSIONS: Oral LZ 600 mg twice daily yields concentrations that fall in the MSW for 3 of the 6 bacteria tested. LZ-resistant mutants may be selected during therapy. Further study is needed to determine the utility of the MPC in evaluating bacterial resistance to LZ.

Managed Care

61E. Concurrent statin/warfarin prescriptions in a managed care population. *Garrett M. Fitzmaurice, Ph.D.*[1], John Kochevar, Ph.D.[2], Tracy J.

Mayne, Ph.D.[3]; (1)Harvard School of Public Health & Division of General Medicine, 1620 Tremont Street, Boston, MA; (2)Kochevar Research Associates, Charlestown, MA; (3)Pfizer Inc, New York, NY.

BACKGROUND: Warfarin interacts with certain statins to produce clinically significant rises in INR and increased risk of bleeding.
OBJECTIVE: Determine the probability of overlapping statin/warfarin prescriptions in a large managed care database and project over time to the U.S. population.
METHOD: Retrospective claims analysis in a large managed care database (annual enrollment ~ 1.2 million). Patients were ≥ 18 years of age with ≥ 1 year of continuous enrollment from 1996 to 2002, and ≥ 1 statin prescription claim in a given year during the study period (N= 243,511).
RESULTS: There were 131,794 statin users in the sample; 94.5% were ≥ 45 years of age. The prevalence of statin/warfarin prescription overlap by ≥ 1 day was 5.8% for the total period of time. The decade and lifetime probability of statin/warfarin concurrent use are shown in table 1. Projecting these results to the U.S. population yielded estimates of 1.22 million overlapping statin/warfarin prescriptions in 2002 growing to 2.52 million in 2020.

					Probability of overlap (%)		
					Cumulative* lifetime risk		
Age	Gender	Total patients	Patients with events	Years on statin	5	6	7
35-44	Male	6,769	87	2.1	-	-	56.1
	Female	4,141	44	1.9	-	-	42.0
45-54	Male	14,613	389	3.2	-	-	55.1
	Female	12,405	209	2.2	-	-	40.9
55-64	Male	14,157	725	6.3	10.9	-	53.7
	Female	13,642	429	4.1	7.6	-	39.6
65-74	Male	17,028	1,359	9.7	16.3	-	48.0
	Female	21,138	978	5.8	9.9	11.8	34.6
75-84	Male	8,714	948	13.9	22.0	27.6	37.9
	Female	12,886	888	8.7	13.8	18.7	25.9
85+	Male	1,105	128	14.2	-	-	14.2
	Female	2,304	153	8.8	-	-	8.8

*Lifetime risk to age 90

CONCLUSION: The lifetime risk of warfarin overlap for patients taking statins in appreciable (55% in men ages 35-64, 41% in women). Physicians should consider current and future drug-drug interactions when deciding which statin to prescribe.
Presented at the 55th Annual Scientific Session of the American College of Cardiology, Atlanta, GA, March 11-14, 2006.

Medication Safety

62E. Safety of coadministration of atorvastatin and warfarin in a Medicare eligible population. *Judith Hey-Hadavi, M.D.*, Erik Kuntze, M.D., Don Luo, M.D., Paul Silverman, M.D., Donald Pittman, M.D., Barbara LePetri, M.D.; Pfizer Global Pharmaceuticals, New York, NY.

PURPOSE: Elderly people are at high CVD risk including stroke. Warfarin (WA) is a widely used medication in the elderly, but has a narrow therapeutic index. Atorvastatin (ATV) has no consistent effect on the anticoagulant activity of WA and dose adjustments should not be necessary. We evaluated safety data in patients ≥ 65 years, in particular in those taking WA and ATV.
METHODS: This was a pooled analysis of data in pts ≥ 65 years from 50 randomized ATV trials completed by Sept 15, 2004. Treatment-associated AEs, serious AEs and musculoskeletal and hepatic AEs were assessed across the ATV 10–80 mg dose range and for placebo (Pbo). Specific AE data in patients receiving WA and ATV concomitantly were analyzed.
RESULTS: The analysis included 5924 patients ≥ 65 years: Pbo (n=995), ATV 10 mg (n=2042), 20 mg (n=667), 40 mg (n=522), and 80 mg (n=1698). WA was used by 397 (6.7%) patients as concomitant medication (339 ATV and 58 Pbo). The AE profiles for Pbo and ATV subjects on WA were similar. There were no persistent CPK elevations (>10xULN) in any group and 2 (0.6%) ATV patients reported abnormal LFTs. Incidence of treatment-associated myalgia was 2.1% across ATV doses. The incidence of specific AEs related to warfarin use were low in both groups (table).
CONCLUSIONS: Elderly patients receiving concomitant ATV and WA did not experience an increased risk of AEs versus patients who received WA and Pbo. These results support the concomitant use of ATV and WA in the elderly population.

Specific adverse events	Pbo + WA (n=58)	ATV + WA (n=339)
Decreased prothrombin time	0	3 (0.9%)
GI bleeding	1 (1.7%)	6 (1.8%)
Embolus	1 (1.7 %)	0
Injection site hemorrhage	1 (1.7 %)	0
Thrombosis	1 (1.7 %)	1 (0.3 %)
Bloody diarrhea	0	1 (0.3%)
Abnormal LFT	0	2 (0.6%)

Presented at the 55th Annual Scientific Session of the American College of Cardiology, Atlanta, GA, March 11-14, 2006.

63. An evaluation of adverse events related to peripheral intravenous catheter use in hospitalized patients: implications for clinical practice. *Brian A. Hemstreet, Pharm.D., BCPS*, Douglas N. Fish, Pharm.D., Patrick W. Sullivan, Ph.D., Marianne McCollum, R.Ph., Ph.D., BCPS; University of Colorado at Denver and Health Sciences Center School of Pharmacy, Denver, CO.

PURPOSE: This prospective observational study evaluated peripheral intravenous catheter (PIVC) use in hospitalized adults. Catheter related adverse events (CRAEs) and patient eligibility for oral drug therapy were evaluated.
METHODS: Adult patients consecutively admitted to a general medicine floor of a tertiary care academic medical center were assessed daily for PIVC use during their hospital stay. Information collected related to PIVC use included total hospital days with an indwelling catheter, CRAEs, and patient eligibility for oral drug therapy. Demographics and medical history were obtained from the patient's medical record. Evidence of CRAEs was assessed daily using computerized nursing records. CRAEs were defined as catheter occlusion, infiltration, extravasation, phlebitis, hematoma, infection, or thrombosis. Eligibility for oral therapy was assessed daily and was defined as documentation of at least one scheduled oral medication on the patient's drug profile. Descriptive statistics were used for patient demographics and CRAE rates. Length of stay (LOS) was evaluated using Kaplan-Meier survival analysis. All patients signed an informed consent.
RESULTS: Eight hundred eighty nine total PIVC days in 227 patients (129 male, 98 female, mean age 55.8 years) were evaluated. Mean LOS was 3.92 days. A total of 60 CRAEs were documented, equating to 26/100 admissions and 67/1000 catheter days. Forty-five (19.8%) patients experienced at least one CRAE. Ninety-eight percent of patients with CRAEs were deemed eligible for oral drug therapy on the day the CRAE occurred. Mean LOS was greater in patients experiencing a CRAE (4.76 days) compared to those without a documented CRAE (3.71 days, $p<0.001$).
CONCLUSIONS: PIVC-related CRAEs are common in hospitalized patients. Most patients with documented CRAEs are eligible for oral drug therapy. Identification of patients eligible for oral drug therapy may lead to reductions in the need for medication administration via PIVCs and potential avoidance of subsequent CRAEs.

Nephrology

64E. Vancomycin dosing guidelines in obese, hemodialysis patients lead to inadequate serum concentrations. *Michael H. Schwenk, Pharm, D*[1], Daniel A. Blaustein, M.D.[2], Morrell M. Avram, M.D.[2], Rakhi Khanna, M.D.[2], Sudha Rani, M.D.[2]; (1)The New York Hospital Medical Center of Queens, Flushing, NY; (2)The Long Island College Hospital, Brookyln, NY.

PURPOSE: Common references (The Sanford Guide To Antimicrobial Therapy 2005, Drug Prescribing In Renal Failure 4th ed.(American College of Physicians)), recommend a 1000 mg vancomycin dose, repeated every 4-7 days, when the GFR is less than 10 mL/min, regardless of patient weight. We studied 6 obese (BMI>30) chronic hemodialysis patients treated with this regimen to determine its adequacy in achieving therapeutic vancomycin concentrations.
METHODS: Patients were treated for presumed/documented infections and studied during an interdialytic period (no recent vancomycin therapy). The recommended vancomycin dose of 1000 mg was infused over 60 minutes and a vancomycin level obtained 6h after completion of the dose (post-distribution). In 4 patients an additional vancomycin dose of 20 mg/kg of total body weight, minus 1000mg, was then given at a rate of 1g/h and another level 6h post-dose was obtained.
RESULTS: There were 4F/2M, 142.5 ± 28.8 kg, BMI = 48.1 ± 9.4 who received an initial dose of 1000 mg (7.3 mg/kg) of vancomycin. The 6h postdose vancomycin level was 9.9 ± 2.4 mg/L, with Vd of 0.79 ± 0.35 L/kg, in close agreement with reported values in non-obese patients. In 4 patients given the 2nd dose of vancomycin (average = 1500 mg) 6h postdose vancomycin levels were 27.5 ± 10.2 mg/L. Thus, after the initial 1000 mg dose, all patients were ready for redosing, and would have remained at subtherapeutic vancomycin levels (<12-15 mg/L) until such time. There were no adverse events associated with this dosing regimen.
CONCLUSIONS:We conclude that obese chronic hemodialysis patients will be underdosed and have subtherapeutic vancomycin levels if current dosing guidelines are utilized. A vancomycin loading dose of 20 mg/kg of total body weight infused at a rate of 1g/h will produce vancomycin levels that should remain therapeutic (> 12-15 mg/L) until at least after their next hemodialysis treatment.
Published in J Am Soc Nephrol 2005;16:A844.

65. Urinary cotinine excretion as a measure of smoking exposure in patients with chronic kidney disease. *Ghazal Vessal, Pharm.D.*[1], Charlotte Jones-Burton, M.D.[2], Jeanine Brown, M.S., RN, CIC[2], Thomas C. Dowling, Pharm.D., PHD[1], Jeffrey C. Fink, M.D.[2]; (1)University of Maryland, Dpt. of Pharmacy Practice and Science, School of Pharmacy, Baltimore, M.D.; (2)University of Maryland, Department of Medicine, Nephrology, Baltimore, M.D.

BACKGROUND: Smoking has been identified as a modifiable risk factor for chronic kidney disease (CKD); however it is not known whether the effect of smoking on the kidney is dose-dependent. Urinary cotinine (a nicotine metabolite) is useful for evaluating nicotine exposure, but has not been validated in the CKD population. In this study we evaluated the validity of 24-hour urinary excretion of cotinine (Ucot) as a quantitative measure of smoking exposure in CKD patients.
METHODS: This was a cross-sectional study targeting smokers and non-smokers with CKD. Quantitative measurements of smoking exposure included a self-reported smoking history questionnaire, expired carbon monoxide (eCO) and Ucot. Kidney function was estimated using the M.D.RD equation for glumerular filtration rate (eGFR). Ucot concentrations were quantified using HPLC with UV detection.
RESULTS: 47 patients were enrolled, 70% were current smokers (mean self-reported cigarettes were 11± 7 per day). The mean eGFR was 49 ± 24.5 mL/min/1.73 m2 and 33.8±17 mL/min/1.73 m2 in smokers and non-smokers respectively (p=0.27). The eCO and Ucot were significantly higher in smokers compared to non-smokers (mean 13.6±7% and 1.3±1%, and 1343.9±672.9 µg/L and 134.6±401 µg/L, respectively, p<.001). Both eCO and Ucot were significantly correlated with self-reported quantity of smoking (R=0.70, p<0.001 and R=0.64, p<0.001, respectively) and correlated with each other (R=0.81, p<0.001). There was no significant relationship between eGFR or proteinuria and Ucot (R=0.24, p=0.09, and R= -0.033, p=0.8 respectively).
CONCLUSION: 24 hour urinary cotinine excretion is not correlated with renal function, suggesting that this method can be used as an objective tool to measure smoking exposure in CKD patients, in smoking reduction/cessation programs.

66E. Effect of IV iron administration on iron indices of hemodialysis patients with elevated serum ferritin: preliminary data from the DRIVE study. Daniel W. Coyne, M.D.[1], Toros Kapoian, M.D.[2], John Moran, M.D.[3], *Adel R. Rizkala, Pharm.D., M.S.*[4], the DRIVE Study Group, .[4]; (1)Washington University School of Medicine, St. Louis, MO; (2)UM.D.NJ-Robert Wood Johnson Medical School, New Brunswick, NJ; (3)Satellite Healthcare, Inc., Mountain View, CA; (4)Watson Laboratories, Inc., Morristown, NJ.

PURPOSE: Dialysis Patients' Response to IV Iron with Elevated Ferritin (DRIVE) trial aims to investigate the effect of administration of IV iron on hemoglobin levels of hemodialysis patients with elevated ferritin and low TSAT, who remained anemic despite receiving large doses of rHuEPO (Hgb <11.1g/dL, ferritin of 500–1,200 ng/mL, TSAT <26%, rHuEPO at least 225IU/Kg/week or 22,500 IU/week). Patients are randomized to receive 25% increase in rHuEPO alone (Control Group) or 25% increase in rHuEPO plus 1g of IV ferric gluconate (IV Fe Group). The purpose of this analysis is to investigate if administration of IV iron to this patient population results in dramatically higher ferritin and TSAT levels.
METHODS: Starting week 1 all patients received a 25% increase in their baseline rHuEPO doses. Patients in IV Fe Group also received 125 mg of ferric gluconate with 8 consecutive hemodialysis sessions. rHuEPO doses remained constant throughout the trial. No maintenance IV or oral iron dosing was allowed. Among other biochemical parameters, iron studies were collected at baseline (Week 0) and at the endpoint (Week 6).
RESULTS: Results of the first 56 patients who completed the trial were analyzed. Control Group median ferritin decreased from 708 ng/mL to 556 ng/mL (p=0.005) and median TSAT increased from 19% to 21% (p=0.04). IV Fe Group median ferritin increased from 713 ng/mL to 757 ng/mL (p=0.023) and median TSAT increased from 19% to 25% (p<0.0001).
CONCLUSIONS: Administration of 1g ferric gluconate to rHuEPO-treated hemodialysis patients with elevated ferritin and low TSAT results in significant improvement in TSAT without leading to a clinically significant increase in ferritin. The administered IV iron is bioavailable as indicated by clinically and statistically significant increases in TSAT. There need be no concern for iron overload resulting from administering 1g of ferric gluconate with increased rHuEPO doses in hemodialysis patients with high ferritin and low TSAT.
Published in J Am Soc Nephrol 2005;16:489A.

Neurology

67. Quetiapine for the management of chorea in Huntington's disease: a case series. *Jack J. Chen, Pharm.D.*[1], David M. Swope, M.D.[2]; (1)Loma Linda University Movement Disorders Center and School of Pharmacy, Loma Linda, CA; (2)Loma Linda University, Loma Linda, CA.

PURPOSE: Huntington's disease (HD) is a progressive neurodegenerative disorder characterized by movement disorders and cognitive changes. Chorea is a common movement disorder associated with HD and can interfere with daily activities, such as eating or walking. Current symptomatic treatment of chorea with clonazepam, conventional neuroleptics, and dopamine-depleting agents are associated with prominent side effects and variable effectiveness. In recent years, several atypical antipsychotics have been reported to provide symptomatic effects in the treatment of chorea associated with Huntington's disease. This pilot study evaluated the effectiveness and tolerability of quetiapine in the treatment of Huntington's chorea.
METHODS: This study was approved by the participating institutional review boards. A retrospective chart review from January 2002 to April 2005 was conducted to identify patients with HD (via use of ICD-9 codes). Data were collected on patient demographics, severity and characteristics of chorea, use of quetiapine (including dosage, side effects, effectiveness), use of adjunctive medications, and relevant medical history.
RESULTS: A total of five patients with HD and treated with quetiapine were included in the analysis. One patient experienced intolerable diarrhea at a daily dose of quetiapine 25 mg and required discontinuation of the drug. In the remaining four patients, mild to moderate improvements in chorea were associated with quetiapine (daily dose up to 200mg). Favorable responses were also documented in gait, fine motor tasks, and speech. Quetiapine was not noted to improve performance of activities of daily living, severity of facial grimacing or ocular movements. All patients, except one, were also on stable doses of one or more concomitant agents for chorea (including amantadine, clonazepam, or levetiracetam). Quetiapine throughout the dose range was well tolerated with transient sedation and dry mouth noted.
CONCLUSION: Quetiapine demonstrates modest effectiveness in the management of HD chorea. Further investigations are warranted.

68. Optimizing use of hypertonic saline in the neuroscience intensive care unit. *Kiranpal S. Sangha, Pharm.D.*[1], Lori A. Shutter, M.D.[2]; (1)The University Hospital, University of Cincinnati Medical Center, Mail Location 0740, Cincinnati, OH; (2)The University of Cincinnati Medical Center, Cincinnati, OH.

INTRODUCTION: Pharmacotherapy for reducing cerebral edema now includes hypertonic saline (HT). We developed a clinical protocol to assist the healthcare provider with managing this complex therapy. We report the initial results using our protocol.
METHODS: We assessed 30 consecutive patients in the neuroscience intensive care unit (NSICU) treated with 3% sodium chloride (HT) using the new protocol. Data collected included patient diagnosis, demographics, serum chemistries, HT dosing rates, intracranial pressure (ICP) measurements and adverse effects. Patients were excluded if they were on HT for less than 24 hours or if they had no ICP monitor.
RESULTS: Four patients were excluded; two were on HT less than 24 hours and two had no ICP monitor, leaving 26 patients. Twenty-three patients (88%) had a diagnosis of traumatic brain injury (TBI). The median age was 37 years (range: 15–68) with a median initial GCS score of 7 (range: 3–15). Goal sodium range was achieved in 19 patients (63%) within 24 hours, and the median time to achieve goal was 14.55 hrs (range: 2 to 50). During target hypernatremia, median HT infusion rate and duration were 0.48 mL/kg/hr (range: 0.12–0.83) for 47 hours (range: 0–170). The median baseline and highest creatinine values during treatment were 0.8 (range: 0.5–1.4) and 0.95 (range: 0.5–1.6). Critical sodium and osmolality values were observed in 5.27% (sd: 9.2) and 5.85% (sd: 11.44) of all measurements. The median numbers of rescue interventions required for elevated ICP were 2.5 (range: 0–13).
CONCLUSIONS: HT for cerebral edema after severe neurological injury is safe if managed with a dosing protocol. Additional studies are required to define the optimum dosing of this potentially high-risk therapy to minimize complications.

Oncology

69E. Safety of bevacizumab plus chemotherapy as first-line treatment of patients with metastatic colorectal cancer: preliminary results from a large observational study in the U.S. (BRiTE). Mark Kozloff, M.D.[1], Allen Cohn, M.D.[2], Neal Christiansen, M.D.[3], Patrick Flynn, M.D.[4], Fairooz Kabbinavar, M.D.[5], Robert Robles, M.D.[6], Marianne Ulcickas Yood, M.D.[7], Charles Blanke, M.D.[8], Somnath Sarkar, Ph.D.[9], Mary Sugrue, M.D., Ph.D.[9], *Kevin Kuzma, Pharm.D., BCOP.*[9], Axel Grothey, M.D.[10]; (1)Ingalls Hospital, Harvey and the University of Chicago, Chicago, IL; (2)Rocky Mountain Cancer Center, Denver, CO; (3)South Carolina Oncology Associates, Columbia, SC; (4)Abbott Northwestern Hospital, Minneapolis, MN; (5)University of California at Los Angeles, Los Angeles, CA; (6)John Muir Hospital, Walnut Creek, CA; (7)Josephine Ford Cancer Center, Detroit, MI; (8)Oregon Health Sciences University, Portland, OR; (9)Genentech, Inc., San Francisco, CA; (10)Mayo Clinic, Rochester, MN.

PURPOSE: To evaluate targeted safety events in unselected patients with metastatic colorectal cancer (mCRC), 1987 patients receiving bevacizumab (BV, Avastin) in combination with first-line chemotherapy (regimen choice at physician's discretion) were enrolled at 248 sites in 49 states.
METHODS: To facilitate and evaluate enrollment of a typical community-based mCRC population, eligibility criteria were minimized and the demographics of the resulting cohort were consistent with the NCI Surveillance, Epidemiology, and End Results (SEERs) database for patients with mCRC. Baseline data included history of hypertension, stroke or myocardial infarction, diabetes, hypercholesterolemia, atrial fibrillation, chronic anticoagulant or aspirin use, peptic ulcer disease, diverticulosis, and recent surgery or endoscopy. Patients are followed for up to 3 years, and clinical data (including survival, disease progression, changes in chemotherapy or BV, interim surgery or endoscopy, and serious adverse events [SAEs]) are updated every 3 months.
RESULTS: Patients were enrolled from 2/04 through 6/05; the abstract data cutoff date was 7/17/05. The median age was 64 (range 22–95); age ≥ 65, 46%; male, 56%; white/black/other, 82/11/7%; ECOG status 0-1, 85%. As of 7/17/05, 87% of patients are alive; 68% are progression-free. Chemotherapy choice was FOLFOX (54%), FOLFIRI (14%), IFL (10%), other (22%). BV-associated SAEs reported in 9.6% of patients; gastrointestinal perforation (1.7%), postoperative bleeding/wound healing complications (0.8%), arterial thromboembolic events (1.7%), and grade 3-4 bleeding (1.4%). Based on 628 progression events, the overall median progression-free survival (PFS) is 12.2 months.
CONCLUSIONS: The safety profile of BV in a community-based population of mCRC patients receiving a variety of chemotherapy regimens appears consistent with that observed in the pivotal trial. PFS in this preliminary dataset is longer than that reported in the pivotal trial. Updated efficacy and safety data will be presented.
Published in Proc Am Soc Clin Oncol 2005;23(16S):262s.

70E. First and subsequent cycle pegfilgrastim results in low rates of neutropenic events in patients receiving myelosuppressive chemotherapy. M. E. Rader, M.D.[1], Wendy Breyer, M.D.[2], Susan Luedke, M.D.[3], Donna Truscinski, BS[4], Beiying Ding, Ph.D.[4], *Roger Dansey, M.D.*[4], Howard Ozer, M.D.[5]; (1)Union State Bank Cancer Center, Nyack, NY; (2)Central Utah, Cancer Center, Provo, UT; (3)St Louis, Cancer & Breast Institute, St Louis, MO,, MO; (4)Amgen, Inc, M.S. 27-2-A, Thousand Oaks, CA; (5)University of Oklahoma Cancer Center, Oklahoma City, OK.

PURPOSE: First and subsequent cycle pegfilgrastim dramatically reduces febrile neutropenia in cycle 1 (11% vs <1%) and overall (17% vs <1%; p<0.001) among moderate risk chemotherapy (CT) patients (pts). This community-based study measures neutropenic events among pts receiving common myelosuppressive CT regimens supported with pegfilgrastim.
METHODS: This open-label, single-arm study enrolled 2252 pts (1008 breast cancer) with non-myeloid cancers at 319 sites. Pts received pegfilgrastim after CT in each cycle for up to 8 cycles. End points included neutropenic complications and CT dose reductions and delays.
RESULTS: Cycle 1 and 2 data are available from 444 pts with breast cancer at 162 sites. The mean (SD) age was 53.9 years (11.3). 92% of pts had earlier-stage (I, II, or III) disease, 12% received prior CT, 7% received prior RT, and 16% had significant comorbidities. 56% of pts received one of 4 standard regimens containing doxorubicin and cyclophosphamide (AC): AC every 21 days (n=70); AC every 14 days (n=78); AC followed by paclitaxel every 14 days (n=76); and docetaxel with AC (TAC; n=25). Most of the remaining pts received either an anthracycline- or taxane-based regimen. 10% of pts experienced serious adverse events, which were consistent with those generally observed in pts receiving myelosuppressive CT.

	N = 444 % (95%CL)
Hospitalization related to neutropenia (including febrile neutropenia) in cycle 1	1 (<1, 3)
Febrile neutropenia (ANC<0.5x10^9/L and temperature [image missing here - Recordid=6896]38.2°C) in cycle 1	3 (1, 5)
Neutropenia-related IV antibiotic use in cycle 1	1 (<1, 3)
Neutropenia-related CT dose reductions in cycle 2[a]	2 (1, 3)
Neutropenia-related CT dose delays in cycle 2[a]	0 (0, 1)

[a]physician reported

CONCLUSION: Compared to Vogel et al, there is a similarly low rate of cycle 1 neutropenic events among breast cancer patients supported by pegfilgrastim in a community setting. Final data (n=1008 pts) will be presented.
Presented at the 28th Annual San Antonio Breast Cancer Symposium, San Antonio, TX, December 8-11, 2005.

Pediatrics

71. Evaluation of procainamide therapy in neonates. *Brady S. Moffett, Pharm.D.*[1], Naomi Kertesz, M.D.[2]; (1)Texas Children's Hospital, Department of Pharmacy, Houston, TX; (2)Baylor College of Medicine, Houston, TX.

PURPOSE: Procainamide is often used to treat supraventricular arrhythmias in neonates, but there is a paucity of published data.
METHODS: A 3 year retrospective review included patients that were < 30 days of age, were on intravenous procainamide therapy longer than 6 hours, and had at least 2 therapeutic procainamide levels. Patient demographic information, dosing information, drug levels, and adverse effects were noted. Clearance of procainamide and NAPA was calculated and evaluated in regards to renal function.
RESULTS: Eighteen patients met inclusion criteria, 11 were term infants, seven were <37 weeks gestation, and therapy was started on day of life 9.7 ± 5.7. Supraventricular tachycardia and atrial ectopic tachycardia were the primary indications for therapy. No patients experienced hemodynamic instability or other adverse effects due to procainamide. Procainamide was given as a bolus (9.45 ± 1.79 mg/kg) in 17/18 patients prior to starting a continuous infusion. The mean dose at which two therapeutic levels was achieved was 37.56 ± 13.52 µg/kg/min. Procainamide and NAPA clearance were 6.36 ± 8.85 and 15.22 ± 13.79 ml/kg/min. NAPA to procainamide ratio on the first and second therapeutic levels was 0.36:1 and 0.52:1. Creatinine clearance correlated with procainamide (r = 0.76, p<0.0001) and NAPA clearance (r = 0.74, p<0.001). Five patients experienced 7 supratherapeutic levels while on therapy. All patients with supratherapeutic levels were pre-term, with creatinine clearances ≤ 30 ml/min/1.73m^2. Four patients had 5 pairs of levels drawn after discontinuation of procainamide therapy, and k_e was evaluated (median 0.124 hr^{-1}, range 0.024–0.237 hr^{-1}).
CONCLUSION: Neonates require similar procainamide dosing to infants and children. Doses may need to be reduced in premature infants and in those with renal dysfunction.

72E. Retrospective evaluation of asthma medication utilization in pediatric patients with asthma-related emergency department visits. *Barry A. Browne, Pharm.D.*, Darren Clary, Pharm.D., Aleta Bonner, M.D., Howard Westmoreland, Pharm.D.; Scott & White Hospital, Temple, TX.

PURPOSE: This retrospective analysis reviewed asthma pharmacotherapy in a managed care pediatric patient population before, during, and after an Emergency Department (ED) visit, with emphasis on evaluation of controller medication use.
METHODS: Patients 2–18 years of age with a prescription benefit and continuous enrollment in the managed care organization (MCO) were eligible for inclusion. Patient ICD-9 code data were used to identify individuals with at least one ED visit for an asthma exacerbation over a 3-year period. Pharmacologic interventions in the ED, as well as ED referrals and subsequent pharmacotherapy provided by primary care physicians (PCPs) after the ED visit, were evaluated through electronic medical record review. Pharmacy claims data were used to calculate adherence and medication possession ratio (MPR) 6 months before and 6 months after the index ED visit for each patient. Adherence was calculated for all controller medications with at least 2 refills before or after the ED visit.
RESULTS: A total of 96 pediatric patients met the entry criteria. Twenty-four patients were using a controller medication before the ED visit. Eleven patients were initiated on a controller medication at the ED or by a PCP within 10 days. A total of 34 patients followed up with their PCP. Adherence before the ED visit for inhaled fluticasone, salmeterol, fluticasone/salmeterol and for montelukast was 42.9%, 45.5%, 45.8%, and 57.7%, respectively. Adherence after the ED visit for these medications was 39.8%, 72.5%, 65.7%, and 55.4%, respectively. The MPR for inhaled fluticasone, salmeterol, fluticasone/salmeterol, and montelukast was 25.6%, 41.9%, 42.9%, and 38.6%, respectively.
CONCLUSION: These data indicate that patient adherence to controller medications and PCP follow-up in this MCO population is limited, suggesting health care resources should be allocated to increase patient education regarding the importance of appropriate pharmacotherapy and PCP follow-up.
Presented at the ALCALDE Pharmacy Residency Leadership Conference, Austin, TX, April 7-9, 2005.

73. Pharmacokinetics of methadone in pediatric ICU patients. *Ralph A. Lugo, Pharm.D.*, Kristin Satterfield, B.S., Diana Wilkins, Ph.D., Steven Kern, Ph.D., Robert M. Ward, M.D.; University of Utah, Salt Lake City, UT.

PURPOSE: Methadone is often used in the PICU to treat opioid abstinence syndrome. It is inexpensive and has a long half-life, which allows for infrequent dosing. In adults, the terminal elimination half-life of racemic methadone ranges from 5 to 130 hours, and acute administration results in a longer half-life (54.8 hours) than chronic administration (22.5 hours). The reported clearance of methadone in adults is 84±30 mL/kg/hr. The pharmacokinetics and optimal dosing of methadone in children have not been evaluated. The purpose of this preliminary study is to evaluate the

pharmacokinetics of intravenous methadone in children in the PICU.
METHODS: PICU patients <18 years of age who were receiving fentanyl and/or morphine for sedation/analgesia during mechanical ventilation were eligible for enrollment. Study patients received a single intravenous dose (0.1 mg/kg—maximum 5 mg) of methadone administered over 15 minutes. Up to 12 blood samples (0–96 hours) were collected from an indwelling vascular catheter after the end of infusion. Methadone plasma concentrations were analyzed using LC/MS/MS. Noncompartmental pharmacokinetics were analyzed using WinNonlin. Data are reported as median (range).
RESULTS: Eight patients (5 males, 3 females) with a median age of 5.0 years (0.03–15.0 years) and median weight of 17.0 kg (3.3–48 kg) were enrolled. Pharmacokinetic parameters were as follows: half-life=9.9 hours (5.1–120 hours), Cmax=36.4 ng/mL (16.9-61.9 ng/mL), Vz=5.3 L/kg (3.4–18.9 L/kg), CL=427 mL/kg/hr (98–693 mL/kg/hr), Vss=4.5 L/kg (2.7–16.3 L/kg).
CONCLUSIONS: This preliminary study reveals significant variability in the pharmacokinetics of methadone in PICU patients. Moreover, administration of intravenous methadone to methadone-naive children results in a significantly shorter half-life and a higher clearance as compared with adult data. More frequent dosing and higher daily doses may be required in children compared with adults in order to maintain sufficient plasma concentrations to prevent or treat opioid abstinence syndrome.

Pharmacoeconomics/Outcomes

74E. The relationship between body mass index and VA health care costs. *Ryan McClellan, Pharm.D.*[1], Nancee Waterbury, Pharm.D.[2], Bruce Alexander, Pharm.D.[2]; (1)Drake University, Des Moines, IA; (2)Veterans Health Administration, Iowa City, IA.

BACKGROUND: Obesity is a serious public health problem affecting our healthcare system. Few studies have compared the cost of healthcare among normal weight, overweight, and obese individuals.
METHODS: This retrospective evaluation of patients treated exclusively at the Iowa City Department of Veterans Affairs (VA) Medical Center between October 1, 2003, and September 30, 2004, compared the total direct costs of five body mass index (BMI in kg/m^2) categories. These included normal weight (18.5–24.9), overweight (25.0–29.9), obesity I (30.0–34.9), obesity II (35.0–39.9), and obesity III (>40.0). We obtained demographic and cost data from the patient's electronic database and the VA's decision support software program, respectively. Total inpatient and outpatient direct costs included: medications, laboratory, primary/specialty care visits, procedures, and hospital stays. Total costs were compared with a significance level set at p<0.05.
RESULTS: The study population included 2000 patients (400 in each category) of which 96.1% were male, and the average age was 63 years (SD±13 years). Individual group costs were normal weight $2635; overweight $3131; obesity I $2969; obesity II $4002; obesity III $4248. The cost of healthcare for veterans in obesity categories II and III was significantly greater than the cost of care for veterans in the lower three categories (p<0.001). There was no significant difference in costs among the lower three categories or between the upper two categories.
CONCLUSION: Healthcare administrators should consider allocating resources for treating obese patients to improve their health and to lower overall healthcare system expenditures. A focus on those patients in obesity categories II and III would potentially yield the greatest benefit.
Presented at the Midwest Pharmacy Residents Conference, Omaha, NE, May 5-7, 2005.

75E. United States cost-effectiveness of atorvastatin in individuals with treated hypertension, normal/mildly elevated cholesterol and 3+ additional risk factors (ASCOT-LLA). *Sanford Schwartz, M.D.*[1], Peter Lindgren, Ph.D.[2], Bengt J¨nsson, Phd[3], Joan Mackell, Ph.D.[4]; (1)University of Pennsylvania, Philadelphia, PR; (2) Karolinska Institutet, Stockholm, Sweden; (3)Stockholm School of Economics, Stockholm, Sweden; (4)Pfizer Pharmaceuticals, New York, NY.

PURPOSE: To assess the cost-effectiveness of atorvastatin Rx in ASCOT-LLA. The Anglo-Scandinavian Outcomes Trial lipid-lowering arm (ASCOT-LLA) randomized patients with total cholesterol <251 mg/dL (<6.5 mmol/L), treated hypertension, and >3 additional CVD risk factors to atorvastatin 10 mg (n=5168) or placebo (n=5137). Over 3.3 year median follow-up, atorvastatin Rx was associated with reduced fatal coronary events and non-fatal AMI (36%), fatal and non-fatal CVA (27%), and CV events and procedures (21%).
METHODS: Intent to treat CEA. Data on CV events and resource use were aggregated across all patients for the trial period. CV events and revascularizations, non-fatal AMI, CV deaths and resource use (study drug, concomitant medications, hospitalizations, ambulatory visits) were obtained from the ASCOT-LLA. US costs for CV hospitalizations were assigned using estimates from Radensky 2001, updated to 2005 using the CPI medical component inflator; non-CV hospitalization costs using 2005 mean per diem payments; M.D. inpatient and outpatient costs using representative Medicare allowable costs; and drug costs using WAC. The primary outcome was incremental cost per CV event avoided. ICER confidence intervals using angular transformation (1,000 bootstrap samples) and CE acceptability curves were used. Early stopping of the trial (atorvastatin benefit) by the DSMB precluded direct assessment of survival. Thus, incremental $/YOLS was estimated by extrapolating expected survival benefit from published Framingham and Saskatchewan data and comparison with event reduction in other statin RCTs.
RESULTS: Net cost per patient was $1,755 atorvastatin arm vs. $1,157 placebo arm. Atorvastatin 10 mg cost ($2,209) was largely offset by reduced all-cause hospitalizations, concomitant drugs and outpatient visits, resulting in ICER of $13,771 per CV event avoided and extrapolated survival resulting from observed AMI reduction of $5,356/YOLS.
CONCLUSIONS: Atorvastatin 10 mg Rx in the ASCOT-LLA was highly cost-effective. Thus, statin therapy is clinically effective and cost-effective in this primary prevention population.
Presented at the American Heart Association Scientific Sessions 2005, Dallas, TX, November 13-16, 2005.

76E. The cost of treating stroke: changes from 1991 to 2001. *Gregory P. Samsa, Ph.D.*[1], David B. Matchar, M.D., FACP[1], Asli Memisoglu, ScD[2], Simon Tang, M.P.H.[3], Tracy Mayne, Ph.D.[4]; (1)Duke Center for Clinical Health Policy Research, Wachovia Building, Durham, NC; (2)Abt Associates - HERQuLES, Lexington, MA; (3)Pfizer Inc US Outcomes Research, New York, NY; (4)Pfizer Pharmaceuticals, New York, NY.

PURPOSE: Hospital costs for leading health conditions have increased significantly over the previous decade, and stroke is among the more costly medical conditions. Accordingly, we examined the cost of treating ischemic stroke (IS) during the first year after event, comparing 1991-1993 and 2000-2001.
METHODS: We sampled from Medicare claims files in 1991 and 2000 containing patients hospitalized with a primary ICD-9 code of 434.xx or 436.xx, and followed patients for 12+ months. Using standard techniques of health cost accounting, Medicare-related utilization was classified into categories (hospital, physician, outpatient, home health, skilled nursing, durable medical equipment, rehabilitation), translated into estimated economic opportunity cost (eg, for institutional categories, using cost-to-charge ratios in 1991-1993 and payments in 2000-2001), and aggregated by quarter as per-patient means. Validation efforts included bootstrapping and replication of the analyses by two separate vendors.
RESULTS: Using 2000 dollars, mean costs for treating IS the year after event were approximately $26,000 in 1991-1993 and $25,000 in 2000-2001. Approximately half were attributable to the initial hospitalization. The highest cost categories were hospital facility, physician, rehabilitation, and skilled nursing, the former three decreasing over time and the latter category increasing. The width of the bootstrapped confidence intervals was less than $1,000 and the estimates of the two vendors substantially agreed.
CONCLUSIONS: Despite efforts at cost containment reflected in shorter hospital stays and decreased utilization of rehabilitation, the first-year cost of stroke has approximately kept pace with inflation. Increases in the costs associated with home health and skilled nursing raise the question whether patients are being discharged with lower functional status than before, shifting costs from inpatient to outpatient.
Presented at the American Heart Association Scientific Sessions 2005, Dallas, TX, November 13-16, 2005.

77E. The effects of prescription drug copayments on statin adherence and persistence. *Teresa B. Gibson, Ph.D.*[1], Tami L. Mark, Ph.D.[2], Kimberly McGuigan, Ph.D.[3], Kirsten A. Axelsen, M.S.[3], Sara Wang, Ph.D.[4], Joan Mackell, Ph.D.[5]; (1)Medstat, Ann Arbor, MI; (2)Medstat Group, Inc, Washington, DC; (3)Pfizer Inc, New York, NY; (4)Thomson Medstat, Ann Arbor, MI; (5)Pfizer Pharmaceuticals, New York, NY.

BACKGROUND: We examined the effects of statin prescription drug copayments and statin adherence on cardiovascular utilization patterns and other outcomes of statin therapy.
METHODS: The 2001-2003 MarketScan database was used to study the health care utilization and expenditure patterns of 93,296 continuously enrolled statin users in employer sponsored health plans. A two-stage estimation approach consisted of a multivariate logit model, which estimated the relationship between copayments and adherence in June 2001 through December 2002. Then, Generalized Linear Models were estimated to examine the effects of adherence on utilization patterns and expenditures in 2003.
RESULTS: Higher copayments led to lower levels of statin adherence (Odds Ratio 0.75 p<.01). Higher levels of statin adherence were associated with fewer adverse events: hospitalizations, cardiovascular hospitalizations and emergency room visits (see table). Adherence was associated with a larger number of physician office visits. Predictably, adherence resulted in higher prescription drug expenditures, but adherence had no effect on medical expenditures and total expenditures.

Measure	Effect of Statin Adherence on Measure	p-value
Expenditures	*Partial Elasticity*	
Total Expenditures (Prescription Drug and Medical)	0.158	0.105
Medical Expenditures	0.146	0.389
Prescription Drug Expenditures	0.204	0.001
Utilization	*Odds Ratio*	
Physician Office Visits	14.84	<0.001
Emergency Room Visits	0.219	<0.001
Hospitalizations	0.419	0.012
Cardiovascular-related Hospitalizations	0.425	0.046

CONCLUSIONS: Statin copayments serve as a financial barrier to statin adherence. In turn, lower levels of adherence are associated with adverse cardiovascular and medical outcomes. Policymakers and plan managers should consider the effects of higher copayments on adherence, utilization patterns, and clinical events for patients with hyperlipidemia.
Presented at the 55th Annual Scientific Session of the American College of Cardiology, Atlanta, GA, March 11-14, 2006.

78. Pharmacoeconomic analysis evaluating voriconazole versus liposomal amphotericin B for empiric treatment of febrile neutropenia. *Curtis D. Collins, Pharm.D., M.S.*, Emily R. Stuntebeck, Pharm.D., Daryl D. DePestel, Pharm.D., Bradley J. McCloskey, Pharm.D. candidate, James G. Stevenson, Pharm.D.; The University of Michigan Health System and College of Pharmacy, Ann Arbor, MI.

PURPOSE: Conventional amphotericin B (CAB) is considered the standard empiric antifungal therapy for patients with febrile neutropenia (FN) patients; however, infusion-related reactions and nephrotoxicity limit its use. Although liposomal amphotericin B (LAmB) has demonstrated similar efficacy to CAB, it is not without toxicities and is associated with a high acquisition cost. Despite this high cost, LAmB has been shown to have a pharmacoeconomic advantage over less expensive agents. Voriconazole is a potential alternative for empiric antifungal treatment of FN. An algorithm that recommends voriconazole as the preferred antifungal in adult Hematology patients with FN was implemented at the University of Michigan Hospitals (UMH).
METHODS: A decision analytic model was developed from a hospital perspective based on the FN treatment guidelines implemented at UMH. Data collected in a two-year (2002-2003) retrospective chart review, literature reports, and expert opinion were used to accurately populate the model. Sensitivity analysis and Monte Carlo simulation enhanced the robustness of the model through variation of all probabilities and costs that populated the model.
RESULTS: Sixty-five cases were evaluated in the retrospective chart review. Thirty-three were initiated on voriconazole and 32 on LAmB respectively. Patient demographic data was similar in each group. In the base case, patients initiated on voriconazole displayed a 17% reduction in overall treatment cost over patients initiated on LAmB ($17,380 vs. $20,841). Sensitivity analysis determined the cost advantage in the voriconazole arm was maintained over a wide range of costs and probabilities. Variance in the cost of nephrotoxicity and medication cost did not significantly alter results. Monte Carlo simulation determined the voriconazole arm to be the optimal path in 68% of cases.
CONCLUSION: The decision model indicates that use of voriconazole as the preferred antifungal agent in patients with FN should result in lower overall treatment costs relative to LAmB.

79E. Nursing home costs for individuals with stroke are driven by functional status. *David B. Matchar, M.D., FACP*[1], Siva Narayanan, M.S., MHS[2], Gregory P. Samsa, Ph.D.[1], Tracy J. Mayne, Ph.D.[3]; (1)Duke Center for Clinical Health Policy Research, Wachovia Building, Durham, NC; (2)Abt Associates, Lexington, KY; (3)Pfizer Inc, New York, NY.

PURPOSE: A substantial component of the economic burden of stroke derives from nursing home (NH) care. However, data on NH costs are derived primarily from Medicare, coverage by which is limited to 100 days. To describe costs incurred by NH patients with a diagnosis of stroke.
METHODS: Included patients were admitted to one of the 367 NHs 1/1/02-12/31/03 who stayed >14 days and had ≥ 1 complete Minimum Data Set Assessment (M.D.S) available for study evaluation (N=54,206). Two cohorts were selected from individuals with stays ≥ 100 days: (1) all with an M.D.S diagnosis of stroke (stroke), and (2) a random sample without an M.D.S diagnosis of stroke (no stroke). Reimbursement and/or charges for rendered services were used as a surrogate for cost, and per diem costs were calculated for patients in residence. Data were analyzed using descriptive statistics, and the determinants of total cost were estimated using a general linear model (GLM), including stroke status, activities of daily living (ADL) score midpoint corresponding to assigned Resource Utilization Group, and month from admission.
RESULTS: Of all study patients, 9,320 (17.2%) had stroke; of these 3,904 (41.9%) had stays >100 days. Per diem costs decreased linearly from $320 to $147 from months 1 to 6, and remained constant through 24 months. In month 1, room and board accounted for 57% of costs, followed by therapy (34%), and drugs (8%). At month 6, these proportions were 88%, 9%, and 1%, respectively. The GLM analysis indicated that ADL was significantly associated with per diem costs, but after accounting for ADL, stroke diagnosis per se did not.
CONCLUSION: Nearly 1 in 5 patients had a diagnosis of stroke and more than 2 in 5 stroke patients stayed longer than 100 days. Functional status was more predictive of NH costs than the diagnosis of stroke itself.
Presented at the 55th Annual Scientific Session of the American College of Cardiology, Atlanta, GA, March 11-14, 2006.

80. Inconsistent societal and individual quality of life ratings for women and men with diabetes. *Marianne McCollum, Ph.D., R.Ph.*, Laura B. Hansen, Pharm.D., Patrick W. Sullivan, Ph.D.; University of Colorado School of Pharmacy, Denver, CO.

PURPOSE: The EQ-5D, a generic health-related quality-of-life (QoL) instrument, contains two components. First, respondents indicate their health status in five domains at three levels: no, some, or extreme problems. Scores (0.0–1.0) are assigned using population preferences for each composite health state. Second, a visual analogue scale (VAS) allows respondents to self-rate their health status from 0.0 to 1.0. The objective of this study was to compare EQ-5D index scores (based on societal preferences) and self-rated scores for men and women with diabetes.
METHODS: Data were obtained from the 2001 Medical Expenditure Panel Survey (MEPS). Diabetes was identified by ICD-9-CM code; demographic, clinical, and health status data (e.g., age, body mass index (BMI), comorbidities, depression, and physical limitations, and EQ-5D index and VAS scores) were analyzed using t-tests, X^2, or Fischer's exact tests as appropriate.
RESULTS: A total of 1,653 respondents with diabetes were included (883 women, 770 men). Women with diabetes were older than their male counterparts (61.2 versus 59.1 years, p<0.01) and reported higher BMI (31.4 versus 30.3), more comorbidities (7.8 versus 6.4), more depression, and more physical limitations, (all p< 0.01). EQ-5D index scores were significantly lower for women than men (0.63 versus 0.72, p<0.001), indicating lower population-rated QoL for women than for men with diabetes. However, there was no significant difference between women and men with diabetes when respondents were asked to rate their own QoL using the VAS (p=0.23).
CONCLUSIONS: Women with diabetes have more comorbidities and physical limitations than men with diabetes, differences are reflected in significantly lower EQ-5D scores derived from the general population. In contrast, women self-rate their own health at the same level as men, possibly indicating different health-related expectations and providing explanations regarding care-seeking behavior on the part of women versus men.

81. Use of low molecular weight heparin (LMWH) during dental extractions in a Medicaid population. *Tracy K. Pettinger, Pharm.D.*, Christopher T. Owens, Pharm.D.; Idaho State University College of Pharmacy, Pocatello, ID.

PURPOSE: Evidence-based guidelines recommend against discontinuation of oral anticoagulation therapy during dental procedures due to a lack of severe bleeding complications and an increased risk for thromboembolic events in patients for whom warfarin therapy is interrupted. Although interruption of oral anticoagulation and bridge therapy with LMWH may be indicated for high-risk individuals undergoing certain medical procedures, its use in tooth extractions is expensive, often unnecessary, and not generally recommended. The purpose of this review was to identify and characterize procedural use of LMWH for dental extractions.
METHODS: The Idaho Medicaid claims database was queried to identify patients with a tooth extraction procedure from 2/1/1998-2/28/2005. Patients on warfarin therapy for 2 months prior to tooth extraction were identified as well as claims for LMWH within 30 days of the procedure. Patient profiles were reviewed to determine number of extractions, overall rate of LMWH utilization, indication for anticoagulation, and associated drug costs.
RESULTS: Four hundred fifty-seven warfarin patients with a tooth extraction were identified. Of these, 34 patients (7.5%) received LMWH therapy for 39 total extraction procedures. Seventy-four percent of LMWH claims were for procedures involving less than or equal to three tooth extractions. An analysis of anticoagulation indication revealed that 20% of procedures were in patients with a thromboembolic event greater than three months prior to the procedure and 15% of patients had lone atrial fibrillation. The use of LMWH for these 39 extractions cost $26,321 with an average of $674.91 per procedure in drug costs alone. Statistical analysis and further results will be available at the time of poster presentation.
CONCLUSION: Despite the overall low number of dental procedures in

anticoagulated patients using LMWH bridge therapy, many are still unnecessary. This inappropriate use resulted in excessive costs in this Medicaid population.

82. Decision analysis model evaluating cost effectiveness of risperidone, olanzapine, and haloperidol in the treatment of schizophrenia. *Mark Bounthavong, Pharm.D.*; Western University of Health Sciences, Pomona, CA.

PURPOSE: To evaluate the cost-effectiveness of three antipsychotic medications (olanzapine, ripseridone and haloperidol) in the treatment of schizophrenia.
METHODS: A decision model evaluated the cost-effectiveness of two atypical antipsychotics (risperidone, and olanzapine) and haloperidol. Outcome probabilities were determined from published clinical trials. The main dependent variable of interest was to compare the incremental costs-effectiveness ratios (ICER) of the atypicals with haloperidol, and also to compare olanzapine with risperidone. Sensitivity analyses were conducted for olanzapine and risperidone to determine the effects of altering drug cost and efficacy on total costs.
RESULTS: ICER for risperidone and olanzapine compared with haloperidol each indicated a dominant strategy over haloperidol (less costly and more effective). The ICER for risperidone was also dominant over olanzapine. A one-way sensitivity analysis for efficacy indicates that the efficacy of olanzapine must increase by at least 8% in order for olanzapine and risperidone to have equal total costs. In the base-case analysis, the cost differences between olanzapine and risperidone was $2.12/day with olanzapine being more expensive. In two-way sensitivity analyses varying both the cost of olanzapine and risperidone, the cost difference between them would have to increase to $11/day in order to have equal total costs.
CONCLUSION: Atypical antipsychotics were a dominant strategy over haloperidol in this analysis primarily because of lower re-hospitalizations in the atypical groups. The ICER indicated that risperidone was dominant over olanzapine because of lower drug costs and increased efficacy. The sensitivity analyses indicate that in order to have equal costs, olanzapine would have to either increase its effectiveness by 8% over risperidone or decrease its daily costs by $11/day. The atypical antipsychotics were more effective and had less total costs compared to haloperidol, and risperidone was more effective and had less total costs compared with olanzapine.

83. Cost savings resulting from a study on intravenous fluconazole prophylaxis in preterm infants. *Diane M. Tulio, RPh*, Juanice Colwell, Pharm.D; the Woman's Hospital of Texas, Houston, TX.

PURPOSE: Although still under investigation, prophylactic intravenous fluconazole administration during the first 6 weeks of life as been shown to effectively reduce central-line invasive fungal infections in low birth weight infants.
METHODS: Eligibility of infants into the protocol include birth weight less than 1000 g and the initiation of therapy to begin less than 5 days of life, ideally day of life 2. Baseline laboratory tests are performed on day of life 1 before therapy begun, and once weekly thereafter. The tests include BUN/creatinine, AST/ALT and a CBC with differential. Dosing is 3 mg/kg/dose every third day for two weeks, then every other day for two weeks, then daily for two weeks. Prophylaxis is discontinued if IV access is discontinued, invasive fungal disease occurs, or laborotory results are two to three times above baseline.
RESULTS: Since the implementation of this study in our facility, we have seen fungal infection rate drop significantly by at least 70%, leading to increased mortality and improved central line patency.
CONCLUSIONS: Cost savings occur as a result of less time and fewer resources needed to install and remove central lines and treat active infections. This includes nursing time to care and treat as well as pharmacy time to provide medication. In the span of 8 months, pharmacy had dispensed amphotericin courses for only two of 46 infants eligible for the study who developed active infections. Liposomal amphotericin has not been used in our facility for a 10-month period.

84. Health-related quality of life benefits of clinical pharmacy services: an update of the evidence. *A. Simon Pickard, Ph.D.*, Shih-Ying Hung, M.S.; University of Illinois at Chicago, College of Pharmacy, Chicago, IL.

PURPOSE: To summarize recent studies of clinical pharmacy services that have evaluated the impact of health-related quality of life (HRQL); to evaluate the extent to which recent literature addressed methodological and study design issues identified in a previous review; to determine whether studies that lacked a control group were more likely to report a statistically significant impact on HRQL.
METHODS: MEDLINE, EMBASE and IPA were searched from March 1999 to December 2004 using terms for health-related quality of life and clinical pharmacy services. Abstracts were screened by two reviewers, and studies were included if a clinical pharmacy service was evaluated and pre/post HRQL outcomes were reported.
RESULTS: Of 1152 citations identified, 36 articles met the inclusion criteria. Randomized pretest-posttest control group designs were employed in 22 studies. Twenty-three studies used a generic HRQL measure (primarily the SF-36), 21 studies used a condition-specific measure, and 8 studies included both. Significant impact on one or more domains of HRQL was predominantly demonstrated in interventions relating to asthma, hypertension and chronic heart failure. Statistically significant change in HRQL was reported by 8 of 21 studies that used a randomized control design (38%), 2 of 5 studies with a non-randomized design with control group (40%), and 6 of 8 studies without a control group (75%) (Chi-squares test, p-value=0.16).
CONCLUSIONS: Since 1999, published studies of clinical pharmacy services evaluating HRQL as an endpoint have tripled. Studies have improved in terms of longer length of follow-up, a wider breadth of clinical services has been evaluated, and several well-designed, methodologically rigorous studies have been published. Certain types of clinical services, such as asthma management, may be more likely to demonstrate short-term HRQL benefits. For those conditions, measurement of HRQL as an outcome may be particularly important in demonstrating the value of clinical pharmacy services.

Pharmacoepidemiology

85E. Impact of combined optimal lipid value achievement on risk of cardiovascular events in prevention, gender, and diabetes subgroups. *Eric J. Stanek, Pharm.D.*[1], Vincent J. Willey, Pharm.D.[2], Chaitanya Sarawate, M.S.[2], Mark J. Cziraky, Pharm.D.[2], Scott L. Charland, Pharm.D.[1]; (1)Kos Pharmaceuticals, Inc, Cranbury, NJ; (2)HealthCore, Wilmington, DE.

BACKGROUND: Patients not achieving combined optimal values for LDL-C, HDL-C, and triglycerides (TG) are at elevated risk for cardiovascular events (CVE). However, this has not been well characterized across patient subgroups.
METHODS: This was a retrospective, analysis of a 1.3 million member MCO database with 5-year follow-up. Patients had ≥ 1 lipid panel between 01/01/00-12/31/01, ≥ 12 months follow-up pre/post-lipid panel and were naive to lipid therapy. Patients were categorized as 1°/2° prevention, male/female, and diabetes mellitus (DM)/no DM. Optimal lipid values were defined using ATP III, AHA, and ADA guidelines. Combined achievement of LDL-C, HDL-C, and TG was determined. CV events were identified based on ICD-9/CPT codes in medical claims. The association between optimal lipid value achievement and CVE was evaluated by multivariate logistic regression.
RESULTS: Study included 44,351 patients with 30±12 months follow-up. Baseline lipids (mg/dL) were: TC 210±40; LDL-C 131±35; HDL-C 48±14; TG 159±77; nonHDL-C 163±39. There were 10,899 CVEs in 6,722 patients.
CONCLUSION: Optimal lipid values were achieved by <25% of patients across all subgroups, and only 1/3 received any lipid-altering therapy. Achievement of combined optimal lipids was associated with a significant 30% reduction in CVE risk. Treating the entire lipid panel may significantly improve outcomes.

Group	N	Age, mean±SD	M/F (%)	Combined optimal lipids (%) BL	F/U	Rx (%)	CVE Odds Ratio (95% CI); combined optimal lipids achieved: Y vs. N
All	44,351	64±13	50/50	11	18	30	0.70 (0.61, 0.81)
1∞ prev.	23,403	64±12	50/50	13	20	27	0.63 (0.50, 0.78)
2∞ prev.	20,948	65±14	51/49	9	18	33	0.75 (0.62, 0.90)
Men	22,345	62±13	100/0	11	21	30	0.75 (0.63, 0.90)
Women	22,006	66±13	0/100	11	17	29	0.67 (0.54, 0.84)
DM	8,164	62±14	53/47	8	18	36	0.72 (0.53, 0.99)
No DM	36,187	65±13	50/50	12	18	28	0.72 (0.61, 0.84)

Published in Circulation 2005;112:II-831.

86. The self-reported pharmaceutical industry interactions of Medicaid providers and subsequent correlations between their responses and perceptions of the pharmaceutical industry, including possible influences upon prescribing patterns. *Nicole Murdock, Pharm.D.*, Rex Force, Pharm.D.; Idaho State University, Pocatello, ID.

PURPOSE: Characterize the influence of self-reported pharmaceutical company interactions on prescribing in Medicaid providers.
METHODS: A query of a statewide Medicaid database identified eligible prescribers who then received a survey designed to determine the extent of interactions with the pharmaceutical industry. Pearson correlation coefficients were used to determine significant relationships between the survey responses and to identify trends in the providers' perception of the pharmaceutical industry and its possible influence on prescribing patterns.
RESULTS: A total of 1,244 surveys were mailed. The response rate was 48%

with 599 surveys returned. Family Practice was the major specialty group (36%). Of those polled, 81% believed that drug information provided by pharmaceutical representatives was biased. Approximately 47% of providers stated that time spent with pharmaceutical representatives did not influence their prescribing habits. Respondents reported one lunch/snack provided by, and 27.9 minutes of interaction with, pharmaceutical representatives per week. Providers and/or their groups reported dispensing 22.3 samples per week. All Pearson correlations reported below were significant at p<0.01. Providers who reported spending more time with pharmaceutical representatives were more likely to agree that time spent with them was burdensome and distracting (r=0.112). They were also more likely to disagree that representatives were a valid source of drug information (r=-0.167). Providers who disagreed that pharmaceutical representatives were burdensome and distracting were more likely to agree that they were a valid source of drug information (r=-0.347). They were also more likely to believe their prescribing patterns were influenced by the pharmaceutical industry (r=-0.250). On average, respondents indicated that there was one pharmaceutical representative interaction for every 13 patients seen in clinic. One in 3 patients received a sample prescription.
CONCLUSION: Respondents reporting extensive interactions with pharmaceutical representatives found this time burdensome and the information received biased. Providers spent considerable time with representatives and frequently dispensed samples.

Pharmacogenomics

87. Influence of resistin promoter polymorphisms on plasma resistin levels in nondiabetic subjects. *Christina L. Aquilante, Pharm.D.*[1], Amber L. Beitelshees, Pharm.D., M.P.H.[2], Lucille Capo Rome, M.S.N., APRN, BC, FNP[1], Lisa A. Kosmiski, M.D.[3]; (1)University of Colorado at Denver and Health Sciences Center, Denver, CO; (2)Washington University School of Medicine, St. Louis, MO; (3)University of Colorado at Denver and Health Sciences Center School of Medicine, Denver, CO.

PURPOSE: Resistin is an adipocyte-derived cytokine with a putative role in inflammation, obesity, and insulin resistance. Two common single nucleotide polymorphisms, -420 C/G and -537 A/C, exist in the promoter of the resistin gene. We sought to determine if these polymorphisms were associated with plasma resistin levels in nondiabetic subjects.
METHODS: A blood sample was obtained from 91 nondiabetic subjects without diagnosed cardiovascular disease. Resistin -420 C/G and -537 A/C genotypes were determined by PCR-pyrosequencing. Haplotypes were inferred using PHASE software. Plasma resistin levels were determined using an ELISA method. Baseline characteristics were compared between genotype groups by unpaired t tests (wild-type versus variant carriers) and between haplotype groups by ANOVA. Differences in plasma resistin levels were compared by genotype and haplotype using the GLM procedure, controlling for age, sex, race, BMI, and glucose.
RESULTS: We enrolled 62 women and 29 men (78 non-black; 13 black; mean age = 44 ± 7 years; mean body mass index=33 ± 5 kg/m^2; mean fasting plasma glucose = 92 ± 10 mg/dL). The -420G and -537C allele frequencies were 28.6% and 6%, respectively. The -420/-537 CA, GA, and GC haplotype frequencies were 71.4%, 22.5%, and 6.1%, respectively. Baseline characteristics were similar between genotype groups, with the exception of age, which was significantly higher in -420 G carriers (46 ± 7 vs. 42 ± 7 for the CC genotype, p=0.006). Mean plasma resistin levels did not differ significantly by -420 C/G genotype (CC=16.2 ± 6.7 ng/mL; G carriers=15.4 ± 6.9 ng/mL) or by -537 A/C genotype (AA=15.7 ± 6.4 ng/mL; C carriers=16.5 ± 10.1 ng/mL). Plasma resistin levels were not significantly different when analyzed according to the number of copies of the -420/-537 CA, GA, or GC haplotypes.
CONCLUSIONS: Our data suggest that resistin promoter polymorphisms do not influence plasma resistin levels in nondiabetic subjects without cardiovascular disease.

Pharmacokinetics/Pharmacodynamics/Drug Metabolism/Drug Delivery

88. Analysis of parenteral calcium gluconate administration and resulting ionized calcium levels in adult, hospitalized patients. *Kelli M. Lewandowski, Pharm.D.*, Lance J. Oyen, Pharm.D., Martin E. Kochevar, M.S., Mary F. Burritt, Ph.D.; Mayo Clinic Rochester, Rochester, MN.

PURPOSE: Ionized calcium levels (iCa) are a guide for identification and treatment of hypocalcemia, but low iCa may fail to normalize despite calcium supplementation. We retrospectively evaluated the response of iCa after 2 g IV calcium gluconate (CaGlc). The primary outcome was the change between pre-dose and post-dose iCa.
METHODS: The 34 hospitalized patients included were ≤ 22 years of age with two iCa levels within 12 hr of each other and CaGlc 2 g IV administered ≤ 6 hr but ≥ 2 hr before the post-dose iCa. Excluded patients had active disease states known to affect calcium levels or received a blood transfusion ≤ 2 hr or other calcium replacement ≤ 6 hr (excluding parenteral nutrition or dietary intake) before the pre-dose iCa level or between the two iCa levels. 34 patients were enrolled (p=0.8, α=0.05; two-sided, paired t-test), giving the ability to detect a difference of 0.325 mg/dL between pre- and post-dose iCa levels (SD of 0.65 mg/dL).
RESULTS: Thirty-two subjects were ICU and/or telemetry patients. There was an equal distribution of males and females, and the majority of patients were Caucasian. The mean change between iCa levels was 0.254 mg/dL (p<0.0001, 95% CI of 0.176-0.331). A significant relationship (p=0.0281) existed showing that the less time there was between pre- and post-dose iCa, the larger the change. Patients with lower pre-dose iCa showed a greater change in iCa levels (p=0.0033), and female patients showed a greater iCa change (p=0.0206). Laboratory variables (serum creatinine, phosphorus, magnesium, albumin, pH) and medications did not significantly affect iCa change.
CONCLUSION: CaGlc 2 g IV resulted in a statistically significant mean change from pre- to post-dose iCa. However, the clinical impact of the dose is less certain since the mean change was small (0.254 mg/dl).

89. Monte Carlo simulation for the determination of optimized population pharmacokinetic study design of hydrocortisone in neonates. *Varsha Bhatt-Mehta, M.S., Pharm.D.*[1], Paul Williams, Pharm, D, M.S., FCCP, FCP[2]; (1)University of Michigan, Ann Arbor, MI; (2)University of The Pacific, Stockton, CA.

PURPOSE: To investigate the competing study strategies for a population pharmacokinetic study (PPK) of exogenous hydrocortisone (HC) in neonates and pre-term infants. Issues addressed were: 1] minimum number of subjects to be included in the study, 2] could endogenous HC be modeled versus would it need to be included as study data, and 3] could a study strategy relating several covariates to both apparent volume and clearance be developed.
METHODS: 1] Templates of simulated data were constructed using random number generating tool ZRandom™ in conjunction with Microsoft XL, 2] Data (templates) were exported to be used in NONMEM, 3] NONMEM control streams were constructed to simulate data that would be representative of an executed study, 4] Models were estimated from each simulated data set, 5] Results were summarized and evaluated with respect to power, efficiency, and informativeness. Fifteen percent of samples were eliminated at random to simulate protocol deviations; Gestational age (GA), postnatal age (PNA), weight (wt-kg) and height (Ht-cm) were all simulated in ZRandom™ as log normal with mean (sd) of 33 (6), 7.6 (10), 2.8 (1.3), and 45 (6), respectively. For each study structure scenario 50 sets of data were generated.
RESULTS: Fourteen competing study structures were included in the final evaluation. A study structure that included 75 subjects with three targeted plasma samples for HC concentration determination, including endogenous HC, would have a power of greater than 0.95 when 2 covariates were included, estimating apparent volume of distribution and clearance within 20% of the true clearance, and the random effects in the model.
CONCLUSIONS: A study structure with 75 subjects with three opportunistic samples will be adequate for the execution of a PPK study in neonates. Monte Carlo simulation is a powerful tool for the evaluation of complex, competing study structures.

90. Pharmacokinetics of duloxetine in breast milk and plasma of healthy postpartum lactating women. Evelyn Lobo, Ph.D.[1], Corina Loghin, M.D.[1], Mary Pat Knadler, Ph.D.[1], Celedon Gonzales, M.S.[1], Lu Zhang, M.S.[1], Tonya Quinlan, B.A.[1], *Jill Chappell, Pharm.D.*[1], Joseph Chiesa, M.D.[2], Richard Bergstrom, Ph.D.[1]; (1)Eli Lilly and Company, Indianapolis, IN; (2)Veeda Clinical Research Ltd., Plymouth, United Kingdom.

PURPOSE: To evaluate the pharmacokinetics (PK) of duloxetine in breast milk and plasma in healthy women and to estimate the dose an infant might consume if breast fed.
METHODS: Single center, open-label study included 6 healthy women aged 22–35 years and at least 12 weeks postpartum, who stopped nursing during and after the study. Duloxetine 40 mg was given orally every 12 hr for 3.5 days; 7 samples of plasma and milk over 12 hr were obtained after the 7th dose. Breast milk samples were pooled at each time point. Plasma and breast milk samples were analyzed using validated LC/MS/MS methods. Mixed-effect ANOVA was used to determine breast milk to plasma exposure ratio. Safety measures included adverse event monitoring, vital signs, ECGs, lab tests, and depression rating scales.
RESULTS: The steady state breast milk to plasma exposure ratio is 0.25 (90% CI: 0.18 to 0.35). The estimated infant dose of duloxetine is about 7 µg/day (range 4 to 15 µg/day) or 2 µg/kg/day (range 0.6 to 3 µg/kg/day). The weight normalized infant dose is 0.14% of the maternal dose. Dizziness, nausea and fatigue were commonly reported. No clinically important changes in safety measures occurred.

CONCLUSIONS: Duloxetine is detected in breast milk and steady state concentrations in breast milk are one fourth those in plasma. As the safety of duloxetine in infants is unknown, prescribers should carefully assess potential risks of duloxetine exposure in infants and the benefits of nursing an infant when a mother is on duloxetine therapy.

91. In vitro modeling of intravenous meropenem (500 mg every 6 hours vs. 1 g every 8 hours) in *Acinetobacter bacteraemia*. *Romina Marchesano, B.Sc.Phm.*, Sandra Walker, Pharm.D., Scott Walker, M.Sc.Phm, Naveen Gnanabakthan, B.Sc. (Hon), Shirley Law, DipPharmTech, Christine Watt, B.Sc., Andrew Simor, M.D.; Sunnybrook and Women's Health Science Centre, Toronto, ON, Canada.

PURPOSE: The objective of this study was to determine, via an in vitro model of infection, whether the rate and extent of killing of a sensitive and multi-drug resistant strain of *Acinetobacter baumannii* differed when meropenem was administered at a dose and frequency modeling 500 mg IV q6h vs. 1 g IV q8h infused over 30 minutes.
METHODS: An in vitro model of infection using a 1-compartment model for meropenem was used. Two clinical isolates of *A. baumannii* were tested, a sensitive and multi-resistant strain (not resistant to meropenem and amikacin). 24-hour experiments were run using concentrations that resembled meropenem given by intravenous infusion over 30 minutes for 500 mg q6h and 1 g q8h regimens. Samples were taken throughout the 24 hours for quantification of meropenem and *A. baumannii* growth.
RESULTS: There was no statistically significant difference in % of time spent above the MIC (%T>MIC) between 500 mg q6h and 1 g q8h (p=0.48, 95% CI -34.94–52.38). When looking at the resistant strain only, meropenem remained above the MIC for a longer period of time in the 500mg q6h regimen compared to the 1 g q8h regimen (p=0.0004, 95% CI 9.95–23.43). No difference was found for the sensitive strain. The extent of kill of *A. baumannii* was not statistically different between the two regimens (p=0.85, 95% CI -2056.85 to 2405.59). The 500 mg q6h regimen achieved a 3 log reduction (99.9% kill) in less time than the 1 g q8h regimen (p=0.0006, 95% CI -131.70 – -60.43).
CONCLUSION: Meropenem 500 mg q6h has at least equal antimicrobial activity to 1 g q8h against a sensitive and multi-drug resistant strain of *A. baumanii*. Since the drug acquisition costs of meropenem 500 mg IV q6h are lower than 1 g IV q8h (~$100/day vs. $150/day), this dosing regimen may be preferred.

92. Determination of the correspondence of the root mean squared prediction error obtained via a traditional approach versus the bootstrap. *Amit Desai, B., Pharm*[1], James Uchizono, Ph., D.[1], Yousef Asiri, Ph. D.[1], Ene I. Ette, Ph., D.[2], Paul J. Williams, Pharm., D.[1]; (1)University of the Pacific, School of Pharmacy, Stockton, CA; (2)Vertex Pharmaceuticals, Cambridge, MA.

Objective: The purpose of this study was to determine whether there was a correspondence between the root mean squared prediction error for serum concentrations when estimated by the traditional external prediction method versus when estimated by the nonparametric bootstrap.
METHODS: Data was collected from 235 patients, 165 in the index population and 70 in the test population. A total of 437 concentrations measurements were measured. Previously, a population pharmacokinetic model was estimated. The final irreducible population pharmacokinetic model was determined. Predictions were made from the model into an external data set. The squared prediction errors were not normally distributed, and therefore the winsorized (W) mean squared error (WMSPE) was estimated. From the WMSPE the W-root mean squared prediction error (WRMSPE) was estimated and used as a prediction metric. Next, bootstrapping was used to estimate the optimism of the WRMSPE. The optimism was added to the WRMSPE when the original model was fitted to the original data to obtain the improved WRMSPE. The improved WRMSPE was compared to the WRMSPE from the external prediction.
RESULTS: The average optimism was very small (0.12) for the 200 bootstrap replicates of the original data. When the original model was used to predict into the external data, the WRMSPE was 10.44 mg/L, and from the bootstrap the improved WRMSPE was 9.35 mg/L. The means, median, and W-mean of the 200 WRMSPE values from the bootstrap were 12.22, 12.04, and 12.05.
CONCLUSIONS: These results indicate that the bootstrap provides estimates of the WRMSPE that have a high degree of correspondence to that obtained from the traditional method and serves as a confirmation that the bootstrap can be used as a validation method for population pharmacokinetic models. Given the data, any of the measures of central tendency would be appropriate to evaluate a population model.

93E. Posterior predictive check: a model checking tool. *Amit Desai, B.Pharm.*, James Uchizono, Ph.D., Paul Williams, Pharm, D, M.S., FCCP, FCP; University of the Pacific, Stockton, CA.

PURPOSE: The purpose of this work was to determine whether the statistical process called Posterior Predictive Check (PPC), under simulation conditions most favorable to achieve PPC's success, is able to identify model misspecification due to influenced data.
METHODS: We used a simple one–compartment disposition population pharmacokinetic model (PPK), applied to a population of 100 subjects, each with 4 time points. The simulated IV bolus dose of drug was 1000 units. Simulation of 50 non-influenced data sets and 50 influenced data sets, which were created by randomly substituting 10 subjects from documented influenced population data set, was executed using NONMEM (version V) on windows XP. PPC was performed on each data set (50 non-influenced and 50 influenced), and minimum concentration (Cmin) was calculated from the original and posterior distributions.
RESULTS: To test the performance characteristic of the PPC, simulated values from the posterior distribution of replicated data sets were compared to their respective initial data sets. The (Cmin) from the initial data sets were compared to their corresponding posterior distributions. In the case of non-influenced data sets the numbers of (Cmins) from the posterior distributions were in the range of 60% to 80% centered around the (Cmin) from the initial data set for different iterations. In case of influenced data sets the numbers of (Cmins) were in the range of 90%–100% centered around the (Cmin) from the initial data set for different iterations.
CONCLUSIONS: We concluded that in the case of non-influenced data, even though the numbers of (Cmins) below the initial observed data are > 50%, there is a corresponding difference between the models developed from influenced and non-influenced data. Therefore, we are hopeful that PPC can be used as a reliable model checking tool.
Presented at the Annual Meeting and Exposition of the American Association of Pharmaceutical Scientists, Baltimore, M.D., November 7-11, 2004.

94E. Pharmacokinetics of once-daily fosamprenavir 1400 mg plus atazanavir 400 mg without ritonavir in HIV negative subjects. *Patrick G. Clay, Pharm.D.*[1], Peter L. Anderson, Pharm.D.[2], Patrick F. Smith, Pharm.D[3], David Lein, Pharm.D.[4], Alan Glaros, Pharm.D.[1]; (1)Kansas City University of Medicine and Biosciences, Kansas City, MO; (2)University of Colorado Health Science Center, Denver, CO; (3)University at Buffalo, Buffalo, NY; (4)Kansas City Free Health Clinic, Kansas City, MO.

PURPOSE: Atazanavir (ATV) + fosamprenavir (FPV) is a potentially useful double-protease inhibitor (PI) combination with components that may offer a mutually beneficial resistance profile.
METHODS: COL100683 was a prospective, randomized, open-label, 3-way crossover study with 3-wk washout periods, in which 21 HIV (-) adults received, in random order: FPV 1400 mg, ATV 400 mg, or both PO once daily (QD) x 14 days. At the end of each period (Day 14), a 24-hr PK study (10 samples) was completed including standardized diets. Drug levels (FPV reported as APV) were assayed by a validated HPLC method. PK parameters were determined by standard noncompartmental methods and compared by paired t-test on log-transformed data. Bioequivalence was assessed by geometric mean ratios (GMR). Adverse event (AE) data were analyzed using student's t-test.
RESULTS: 21 subjects completed the study (11 men, 48% non-white) with a mean (SD) age of 31.7 (9.5) yr. PK parameters are reported below. No differences occurred with respect to periods or sequences.

	ATV	APV		
	ATV alone	ATV + FPV	GMR (90% CI)	% change
AUCss µg.h/mL	17.9 (65)	11.9 (54)	0.67 (0.51–0.88)	↓ 33%*
Cmax µg/mL	2.6 (59)	1.8 (54)	0.70 (0.53–0.93)	↓ 30%*
C24 µg/mL	0.14 (135)	0.06 (104)	0.43 (0.24– 0.56)	↓ 57%*

(continued)

	FPV alone	FPV + ATV	GMR (90% CI)	% change
AUCss µg.h/mL	21.7 (44)	38.7 (27)	1.78 (1.47–2.12)	78%*
Cmax µg/mL	4.8 (55)	6.5 (34)	1.36 (1.09– 1.72)	36%*
C24 µg/mL	0.06 (89)	0.23 (178)	3.83 (2.43– 6.76)	283%*

*p<0.05; data presented as geometric mean (CV%)

CONCLUSIONS: ATV+FPV was well tolerated. ATV significantly enhanced exposure of unboosted, once-daily FPV. ATV exposure was reduced when co-administered with FPV. The clinical relevance of these findings will remain unknown until controlled efficacy studies are completed.
Presented at the 13th Conference on Retroviruses and Opportunistic Infections, Denver, CO, February 5-9, 2006.

95E. Effects of age and gender on febuxostat pharmacokinetics, pharmacodynamics, and safety in healthy subjects. Michael Kukulka, BS, *Reza Khosravan, Ph.D.*, Jing-Tao Wu, Ph.D., Nancy Joseph-Ridge, M.D., Laurent Vernillet, Pharm.D., Ph.D.; TAP Pharmaceutical Products Inc., Lake Forest, IL.

PURPOSE: Febuxostat is a novel non-purine selective inhibitor of xanthine oxidase (NP-SIXO) being developed for the management of hyperuricemia in patients with gout. The effects of age and gender on the pharmacokinetics (PK), pharmacodynamics (PD), and safety of febuxostat were evaluated.
METHODS: In a phase-I, parallel-group, open-label, multiple-dose study, male (M) and female (F) subjects 19–40 years old [young, 12M/12F] and 65–76 years old [elderly, 12M/12F] received once daily 80–mg oral doses of febuxostat for 7 days. Blood samples were collected to assess the PK of febuxostat and its active metabolites (67M-1, 67M-2, 67M-4) and its effect on uric acid (PD marker). Protein binding and safety of febuxostat were also assessed.
RESULTS: The results are shown in the table.

Mean ± SD Plasma PK and Serum Uric Acid (sUA) Parameters on Day 7

Analyte	Parameter	Age Group		Gender	
		Y	E	M	F
Febuxostat	$C_{max,u}$ (ng/mL)	28±12	27±9	24±10	31±10[1,2]
$AUC_{24,u}$ (ng.h/mL)	56±19	61±20	54±23	63±15[1,2]	
f_u (%)	0.7±0.1	0.7±0.2	0.7±0.1	0.7±0.1	
67M-1	AUC_{24} (ng.h/mL)	225±63	265±84	224±68	265±80
67M-2	AUC_{24} (ng.h/mL)	229±76	243±69	240±81	232±63
67M-4	AUC_{24} (ng.h/mL)	235±77	270±125	223±70	281±125
sUA	$C_{mean,24}$ (%change)	-55±8	-56±9	-52±7	-59±8[1]

C_{max} or $AUC_{24,u}$: Unbound C_{max} or AUC_{24}; f_u: Unbound fraction; $C_{mean,24}$: sUA 24-hour mean concentration; [1]Statistically significantly different from M ($p \leq 0.05$); [2]Not statistically significantly different from M ($p > 0.05$) with weight as a covariate

The overall incidence of study drug-related adverse events (AEs) was lower in men than in women (13% vs 54%) and in young than in elderly (25% vs 42%). The most common AEs were headache and constipation. All AEs were mild or moderate in severity.
CONCLUSION: Neither age nor gender had any clinically significant effect on the PK, PD, and safety of febuxostat. Therefore, febuxostat does not require any dose adjustment based on age or gender.
Published in Clin Pharmacol Ther 2005;77(2):P50.

96E. Effect of food or antacid on febuxostat pharmacokinetics and pharmacodynamics in healthy subjects. *Reza Khosravan, Ph.D.*, Brian Grabowski, BA, Jing-Tao Wu, Ph.D., Nancy Joseph-Ridge, M.D., Laurent Vernillet, Pharm.D., Ph.D.; TAP Pharmaceutical Products Inc., Lake Forest, IL.

PURPOSE: Febuxostat is a novel non-purine selective inhibitor of xanthine oxidase (NP-SIXO) being developed for the management of hyperuricemia in patients with gout. Effects of food and antacid on oral febuxostat pharmacokinetics (PK) and pharmacodynamics (PD) were evaluated.
METHODS: In 4 two-period, crossover studies, male and female subjects received either a single dose (SD) of 40 mg (n=23) or 120 mg (n=19) or multiple dose (M.D.) daily 80 mg (n=23) of febuxostat under non-fasting [test (T)] and fasting [reference (R)] conditions; or received a single 40 mg dose with (T) and without (R) an antacid (800 mg $Mg(OH)_2$-900 mg $Al(OH)_3$). Plasma febuxostat (LC-MS/MS method) and serum uric acid (sUA, PD marker, enzymatic assay) concentrations were assessed.
RESULTS: A delay of t_{max} was observed with both food and antacid. Point estimates (PE) and confidence intervals (CI) for T and R ratios/differences are shown below for C_{max}, AUC and sUA 24-hour mean concentration ($C_{mean,24}$).

Febuxostat Dose	Febuxostat C_{max}	Febuxostat AUC[1]	$C_{mean,24}$ (%)
Food Effect			
40mg SD	0.54 (0.48-0.61)[2]	0.81 (0.77-0.85)[2]	-
80mg M.D.	0.51 (0.44-0.60)[2]	0.82 (0.78-0.87)[2]	6 (4-10)[3]
120mg SD	0.62 (0.52-0.74)[2]	0.84 (0.79-0.90)[2]	-
Antacid Effect			
80mg SD	0.68 (0.58-0.79)[2]	0.85 (0.81-0.90)[2]	-

[1]AUC∞ (SD) or AUC_{24} (M.D.); [2]T/R ratio PE (90% CI, log-transformed data) for febuxostat PK parameter ratios; [3]T-R difference PE (95% CI) for % change from baseline in $C_{mean,24}$.

Although food caused a decrease in absorption rate and extent of febuxostat in all food effect studies, this decrease was not associated with a decrease in febuxostat PD effect (sUA) when evaluated in the 80 mg M.D. study. Despite a decrease in the absorption rate of febuxostat, antacid had no effect on the extent of febuxostat absorption. Febuxostat was safe and well tolerated in all studies.
CONCLUSION: Febuxostat can be administered regardless of food or antacid intake.
Published in Clin Pharmacol Ther 2005;77(2):P50.

Psychiatry

97. Atypical antipsychotic monitoring in an outpatient clinic setting. Casey McCann, Pharm.D., Candidate, *Patricia Wigle, Pharm.D.*; University of Cincinnati College of Pharmacy, Cincinnati, OH.

PURPOSE: This study was designed to evaluate monitoring of patients on atypical antipychotic medications in an outpatient clinic setting.
METHODS: A retrospective analysis of 30 patients with bipolar disorder was performed. The evaluation criteria included monitoring for weight, serum glucose, blood pressure, serum cholesterol, and pregnancy tests, if applicable. Inclusion criteria included patients who had a diagnosis of bipolar disorder and had been seen in this clinic for at least a 12-month period of time. Exclusion criteria included patients who were seen by multiple psychiatrists or other health care providers, and patients whose medical record was unavailable.
RESULTS: Fifty-three percent of the patients were treated with both an antidepressant and a mood stabilizer. Of those patients, 24% were on an atypical antipsychotic medication. Fifty percent of patients on atypical antipsychotic medication had their weight, blood pressure, and serum glucose monitored at least 3 times in the past 12 months. Serum cholesterol, depression and mania scales and pregnancy tests were performed less frequently.
CONCLUSIONS: A small majority of patients on atypical antipsychotics were monitored appropriately for various metabolic changes during their course of therapy. However, improvements can be made in both the monitoring for metabolic changes and the disease process itself.

98. Novel antipsychotic use and its impact on the cost of care in a psychiatric hospital. *Suzanna Gim, Pharm.D.*, Kim Coley, Pharm.D., Robert J. Weber, M.Sc., F.A.S.H.P., Rohan Ganguli, M.D.; University of Pittsburgh Medical Center, Pittsburgh, PA.

PURPOSE: Costly novel antipsychotic (NA) prescribing has increased over the past few years. The NA class has continued to prosper, expanding in use beyond the FDA-approved indications. The objective of this study was to identify longitudinal prescribing patterns of NAs and determine the impact on pharmacy charges.
METHODS: Financial and clinical data was collected from 1999 through 2004, and grouped by fiscal year (FY). Pharmacy charges as a percent of total hospital charges, NA charges as a percent of total pharmacy charges, and the distribution of NA use by diagnoses treated were determined for each FY. Changes in percent contribution of pharmacy charges to hospital charges, utilization of NA compared to other drugs, and utilization of NA by selected psychiatric diagnoses were also compared.
RESULTS: Over the past five years, total hospital charges have increased by $54.6 million. The percentage of admissions associated with an NA charge increased from 40.5% in FY2000 to over half of all admissions in FY2004 (55.6%). Within the total hospital charges for each FY, the contribution of pharmacy charges has increased 4.9% (from 8.6% to 13.5%). NA contribution has increased to over one-third of pharmacy charges (28.5% to 36.7%). Olanzapine has contributed the most to NA charges. Olanzapine was also the most utilized NA, but dropped to second for quetiapine in FY2004. NA use outside of FDA-approved labeling has increased from FY2000 to FY2004 in the diagnoses analyzed; depression (25% to 40%), dementia (64% to 79%), neurotic disorders (31% to 41%), and childhood disorders including approved adult disorders as well as other childhood-specific disorders (34% to 61%).
CONCLUSION: The expanding use of NAs has affected the cost of care in this psychiatric facility. Substantive evidence is needed to clarify these increasingly common, inadequately researched, and increasingly costly psychopharmacological practices.

99. Implementation of a treatment algorithm for PTSD: reduction in atypical antipsychotic agent costs. Heather R. Hazeldine, Pharm.D., Zoran Urosevich, M.D., Herbert Nagamoto, M.D., *John J. Battisti, Ph.D.*; Univ Colorado Health Sciences Center, Eastern Colorado Health Care System, Denver, CO.

Despite their widespread use in PTSD, atypical antipsychotic agents have associated with them significant acquisition costs and safety and tolerability risks while having limited evidence of benefit. After a review of the published literature using Medline, a treatment algorithm for PTSD was created based on the VA *Pharmaceutical Use Outside of Approved Indications Guidance on "Off-label" Prescribing* guidelines for consideration of formulary inclusion to address this issue. The resulting treatment algorithm for PTSD restricted atypical antipsychotic availability to risperidone and quetiapine to patients who have refractory reexperiencing symptoms (distress with trauma-associated cues, memories, dreams, flashbacks, intrusive thoughts, paranoia, hallucinations, illusions, sleep disturbances) or hyperarousal symptoms (impulsivity, irritability, anger, sleep disturbances) who have had a trial of or have a contraindication to: (a) maximum tolerated dose of two formulary SSRIs (consider a trial of nefazodone or low-moderate dose mirtazapine [7.5 - 30mg/day, to avoid noradrenergic-associated hyperarousal and worsening of PTSD] for patients intolerant to an SSRI); (b) hydroxyzine, trazodone, and prazosin if patient has nightmares or sleep disturbances; (c) hydroxyzine for patients with general daytime anxiety; and (d) mood stabilizers (lithium,

carbamazepine, and valproic acid) for patients with refractory hyperarousal symptoms not requiring acute management. Six months after implementation of the algorithm, there was a significant reduction in total percentage of Mental Health Outpatient Clinic patients treated with atypicals, quetiapine, and risperidone and a reduction in total atypical, quetiapine, and risperidone acquisition cost, and cost per patient. Through evidence-based use of atypical antipsychotic agents in this population, we also expect to reduce adverse drug reactions and improve treatment of PTSD symptoms.

100E. Evaluation of long-acting injectable risperidone for older adult inpatients with psychosis. *Jose A. Rey, Pharm.D.*[1], Maria Rodil, M.D.[2], Maria D. Llorente, M.D.[2]; (1)Nova Southeastern University, Ft Lauderdale, FL; (2)University of Miami, Miami, FL.

PURPOSE: The treatment of the older adult patient with chronic psychosis with the long-acting formulation of risperidone in the inpatient setting has not been fully evaluated to date. The purpose of this study is to assess the effectiveness of long-acting injectable risperidone in an older adult inpatient population with psychosis.
METHODS: This is a retrospective assessment of patients aged 50 years and older admitted to an inpatient psychiatric facility for severe and unstable psychosis. Clinical judgment prompted the initiation of the long-acting injectable form of risperidone. Per hospital policy, baseline and follow-up assessments utilizing the Positive and Negative Syndrome Scale (PANSS) were done. Physician clinical assessment of response is reflected using the Clinical Global Impression Scales for Severity and Improvement (CGI-S/I).
RESULTS: These are the preliminary findings of 25 older adults who were treated with risperidone long-acting injection for at least 2 months in an inpatient setting. Schizophrenia was the diagnosis for 76% (n=19) of the patients. Other patients were diagnosed with either bipolar disorder with psychotic features or with schizo-affective disorder. The mean age was 59.5 years (range: 50–76 yrs). The mean of the total PANSS scores at baseline was 105 (SD +/- 28.3, range: 65–153, n=20). The mean total PANSS scores at last follow-up was 86.3 (SD +/- 27, range: 53–134, n=20). The difference in total PANSS scores was statistically significant ($p<0.01$). For the patients receiving a CGI-Improvement assessment (n=15), 67% were either much improved or very much improved at last follow-up. The mean dose of risperidone long-acting injection was 36.5 mg (n=25). Further descriptions and sub-analyses of this evaluation will be presented.
CONCLUSIONS: Long-acting risperidone was associated with clinically and statistically significant improvements in a group of older adults considered to be unstable inpatients with psychosis.
Presented at the 2006 Annual Meeting of the American Association for Geriatric Psychiatry, San Juan, Puerto Rico, March 10-13, 2006.

101. Eszopiclone coadministered with fluoxetine for insomnia coexisting with major depressive disorder (M.D.D): analysis by age. *John G. Karafilidis, Pharm.D.*[1], W. Vaughn McCall, M.D., M.S.[2], Mauricio Fava, M.D.[3], Thomas C. Wessel, M.D.[1], Robert Rubens, M.D.[1], Judy Caron, Ph.D.[1], Thomas Roth, Ph.D.[4], Andrea J. Anderson, Pharm.D.[1]; (1)Sepracor Inc., Marlborough, MA; (2)Wake Forest University Department of Psychiatry and Behavioral Medicine, Clinical Science Building, Winston-Salem, NC; (3)Massachusetts General Hospital, Boston, MA; (4)Henry Ford Hospital Sleep Disorders Center, Detroit, MI.

INTRODUCTION: Results of a study of eszopiclone and fluoxetine in co-existing insomnia and depression showed that initiation of co-therapy produced greater improvements in sleep and depression compared with fluoxetine monotherapy. Results of a post-hoc analysis of results by age are presented.
METHODS: Patients (aged 21–64 years) met DSM-IV criteria for M.D.D and insomnia, with screening 17-item Hamilton Depression Rating Scale (HAM.D.-17; excluding the sleep items) >14. All patients received fluoxetine QAM for 10 weeks. Patients were randomized to eszopiclone 3 mg (n=270) or placebo (n=275) QHS for 8 weeks, followed by a 2-week single-blind placebo run-out phase. Sleep and depressive symptom responses were evaluated in younger (<50 years; n=351) and older adults (≥ 50 years; n=136).
RESULTS: At baseline, older adults had greater difficulty with sleep indicated by longer sleep latency (SL), greater wake time after sleep onset (WASO) and less total sleep time (TST) compared with younger adults. Sleep quality, daytime alertness, and ability to function and concentrate in younger adults were either better than or the same as in older adults. Both age groups responded to eszopiclone/fluoxetine with statistically significant differences relative to fluoxetine alone in SL ($p\leq0.0042$), WASO ($p\leq0.0215$) and TST ($p\leq0.052$). Those in the older age group had greater changes in these parameters. Change from baseline HAM.D.-17 scores in the younger vs older group, respectively, were -12.01 vs -11.67 for co-therapy and -10.34 vs -8.95 with monotherapy. The percentage of responders (≥ 50% decrease in HAM.D.-17 score) was 59% vs. 65.8% in the younger vs. older group, respectively (monotherapy: 49.2% and 52.2%, respectively). Similarly, the percentage of remitters (HAM.D.-17 scores ≤ 7) was 42.9% vs. 46.3% in the younger and older group (monotherapy: 36.1% and 31.9%), respectively.
CONCLUSIONS: In this study, regardless of age, co-therapy provided significant improvements in both sleep and depression endpoints relative to monotherapy. Support: Sepracor Inc.

102. Eszopiclone coadministered with fluoxetine for insomnia coexisting with major depressive disorder (M.D.D): effects following eszopiclone discontinuation. *Andrea J. Anderson, Pharm.D.*[1], Andrew Krystal, M.D., M.S.[2], Robert Rubens, M.D.[1], Mauricio Fava, M.D.[3], W. Vaughn McCall, M.D., M.S.[4], Thomas C. Wessel, M.D.[1], Thomas Roth, Ph.D.[5]; (1)Sepracor Inc., Marlborough, MA; (2)Duke University Medical Center, Durham, NC; (3)Massachusetts General Hospital, Boston, MA; (4)Wake Forest University Department of Psychiatry and Behavioral Medicine, Clinical Science Building, Winston-Salem, NC; (5)Henry Ford Hospital Sleep Disorders Center, Detroit, MI.

INTRODUCTION: Insomnia and M.D.D may co-exist. The use of adjunctive hypnotics in this setting is controversial. We reported that eszopiclone/fluoxetine co-therapy significantly improved sleep and depression compared with fluoxetine monotherapy. Here we report data that further evaluated insomnia and M.D.D after discontinuation of eszopiclone due to concern that hypnotic discontinuation may undermine antidepressant response or hasten relapse.
METHODS: Patients met DSM-IV criteria for M.D.D and insomnia. All patients received fluoxetine QAM for 10 weeks. Patients were randomized to eszopiclone 3 mg (n=270) or placebo (n=275) QHS for 8 weeks, followed by a 2-week single-blind eszopiclone placebo discontinuation phase. During this discontinuation phase, subjective sleep was assessed daily; depression was assessed with the HAM.D.17 at the end of the phase (Week 10). Discontinuation effects were examined two ways: 1) change from baseline to Week 10; change from end of hypnotic treatment (EOT; Week 8) to Week 10.
RESULTS: During the discontinuation phase, the eszopiclone group maintained significant sleep improvements observed over the first 8 weeks (Week 8–10 average $p<0.05$ vs placebo). Relative to baseline, patients discontinued from eszopiclone continued to have significantly improved sleep ($p<0.05$) at each daily assessment for SL, WASO, and TST (average change -124.0, -68.67, and 154.96 minutes, respectively). Relative to EOT, patients discontinued from eszopiclone did not show significant decrements over the 2 weeks for SL, WASO, or TST (average change 1.72, 1.6, and 0.59 minutes, respectively). Improvements in HAM.D.17 scores relative to placebo observed at EOT (-14.6 vs. -12.3; $p=0.0005$) were maintained at Week 10 (-15.13 vs -12.70; $p<0.0001$).
CONCLUSIONS: In this study, sleep improvements associated with concomitant eszopiclone/fluoxetine were maintained after hypnotic discontinuation. Discontinuing eszopiclone was not associated with significant changes in measures of depression severity. No rebound insomnia was observed. Additional studies are needed to investigate the optimal duration of combination therapy.

Pulmonary

103. Impact of consensus guidelines for cystic fibrosis-related bone disease. Michelle L. Condren, Pharm.D.[1], *Lindsey D. Wilcox, Pharm.D.*[2]; (1)Texas Tech University School of Pharmacy, Amarillo, TX; (2)Texas Tech University School of Pharmacy, Port Neches, TX.

PURPOSE: In 2002, the Cystic Fibrosis (CF) Foundation developed guidelines for bone health screening. This pilot study will identify CF patients qualifying for bone densitometry, identify patients with bone disease, and determine the efficacy and applicability of the consensus guidelines.
METHODS: All charts were reviewed to identify patients qualifying for bone densitometry. After testing, charts were reviewed for the following data: age, height, weight, ideal body weight, presence of diabetes, pubertal status, pulmonary function, organ transplant status, corticosteroid use, medroxyprogesterone use, fracture history, calcium and vitamin D intake, caffeine and carbonated beverage intake, frequency of weight-bearing exercise, 25-OHD level, z and t scores, and absolute bone mineral density from Dual-energy X-ray Absorptiometry (DXA).
RESULTS: A total of 23 charts were reviewed. Of those, 15 (65%) qualified for bone densitometry. Ten patients completed a DXA scan. Four patients (40%), ages 14–21 years, were diagnosed with osteoporosis. Four patients (40%), ages 12–16 years, were diagnosed with osteopenia. Two patients qualifying for screening had normal bone density. Bisphosphonate therapy was initiated in 3 patients and all patients were started on appropriate dosages of calcium and vitamin D. The total number of risk factors for bone disease correlated with total body z-score ($p=0.018$) and lumbar z-score ($p=0.015$). Of the 2 patients with normal bone density, one was 18 years old with no additional risk factors, and the other was 16 years old with medroxyprogesterone use as the only risk factor.
CONCLUSIONS: In this population, implementation of the bone health screening guidelines was valuable, identifying that the majority of the patients

screened had abnormalities in bone density. Given the cost of DXA scans, larger studies are needed to determine whether certain risk factors or numbers of risk factors can be considered when determining a patient's need for bone density screening.

104E. A double-blind, placebo-controlled crossover comparison of the dose-response to levalbuterol for reversing methacholine-induced broncho-constriction with and without pretreatment with (S)-albuterol. *Hengameh H. Raissy, Pharm.D.*, Michelle Harkins, M.D., William Kelly, Pharm.D.; University of New Mexico, School of Medicine, Albuquerque, NM.

RATIONALE It has been suggested that high concentration of (S)-albuterol (SA) may mitigate the response to (R)-albuterol in acute bronchoconstriction, thus providing a possible mechanism for the greater response to levalbuterol in acute asthma. The objective of this study was to determine the effect of SA on the dose-response to levalbuterol in patients with moderate bronchoconstriction induced by methacholine.
METHODS: This was a double-blind, placebo-controlled, crossover study of 22 adults with mild stable asthma not receiving any long term control therapy with a positive methacholine challenge (FEV_1 PC 20< 8 mg/mL). Patients were started on ipratropium as needed at baseline visit. FEV_1 PC 30 was obtained and the patients were reversed with 0.625 mg, 0.625 mg, and 1.25 mg of albuterol nebulized at time 0, 5, and 10 minutes when PFT was measured at those times and at 15, 25, and 40 minutes to obtain the dose response curves. At visit 2 and 3, patients were randomly assigned to nebulize normal saline placebo (PB) or SA 5 mg before the methacholine PC 30 and were reversed with levalbuterol. The dose of levalbuterol was based on the first visit albuterol dose-response curve in order to enhance the sensitivity for detecting a difference in the levalbuterol dose-response curves. Five patients were excluded from the analysis because of albuterol use during the study. No difference was seen in FEV_1 PC 30, AUC 0-40 FEV_1 or the FEV_1 slope 0-40 following PB or SA.
CONCLUSION: Acute SA administration did not have a negative effect on bronchodilator response to levalbuterol. If accumulation of SA inhibits the response to (R)-albuterol, its mechanism requires more time than is apparent from a direct antagonistic effect.
Presented at the International Conference of the American Thoracic Society, San Diego, CA, May 2005.

Rheumatology

105E. The effect of eszopiclone 3 mg compared with placebo in patients with rheumatoid arthritis and coexisting insomnia. *Felda Relucio, Pharm.D.*[1], Thomas J. Schnitzer, M.D.[2], Robert Rubens, M.D.[1], Judy Caron, Ph.D.[1], David Amato, Ph.D.[1], Andrea J. Anderson, Pharm.D.[1]; (1)Sepracor Inc., Marlborough, MA; (2)Northwestern University, Chicago, IL.

INTRODUCTION: Patients with rheumatoid arthritis (RA) often report co-existing insomnia. This pilot study was conducted to evaluate the efficacy and safety of eszopiclone 3 mg in patients with RA and co-existing insomnia.
METHODS: This multicenter, double-blind, study enrolled patients aged 25–64 years with ACR-defined RA (receiving treatment for ≥ 3 months) who reported insomnia (wake time after sleep onset (WASO) ≥ 45 min and total sleep time (TST) ≤ 6.5 hr). After placebo run-in, patients were randomized to eszopiclone (n=77) or placebo (n=76) nightly for 4 weeks, followed by a 2-week run-out. Patient reports of sleep (sleep latency [SL], WASO, TST), Insomnia Severity Index (ISI), daytime function, pain, and RA assessments were evaluated.
RESULTS: Eszopiclone (vs. placebo) significantly reduced SL ($p<0.0001$), WASO ($p=0.0002$), and nocturnal awakenings ($p=0.0065$), and significantly increased TST ($p=0.0001$), sleep depth ($p=0.0003$), sleep quality ($p<0.0001$), daytime alertness, ability to function, and ability to concentrate (all $p<0.04$). ISI total scores were significantly better ($p<0.0001$) with eszopiclone vs. placebo, as were individual items of sleep quality, feeling rested, daytime fatigue, relationship enjoyment, and sleep difficulties (all $p<0.02$). Change scores on the Arthritis Self Efficacy Scale were clinically and statistically significant for overall score ($p=0.046$), pain ($p=0.0064$), and pain and other symptoms ($p=0.018$). No differences in duration or severity of morning stiffness were noted, although subjects' assessment of pain severity was significantly reduced with eszopiclone ($p=0.023$). Number of tender joints was also significantly reduced in the eszopiclone group ($p=0.035$). Subject global assessments were also better with eszopiclone, although not statistically significant ($p=0.072$).
CONCLUSION: In this pilot study of RA and co-existing insomnia, eszopiclone 3 mg improved all sleep efficacy measures and daytime function over the treatment period. In addition, patients treated with eszopiclone experienced reductions in some measures of pain and RA disease activity.
Support for this study provided by Sepracor Inc.
Presented at the Annual Meeting of the American College of Rheumatology, San Diego, CA, November 12-17, 2005.

Substance Abuse/Toxicology

106. The relationship of alcoholic blackouts to blood alcohol concentration. *Tami R. Argo, Pharm.D., M.S., BCPP*[1], Paul J. Perry, Ph.D.[2], Michael Trnka, Pharm.D., Student[3], Jillian Hernan, Pharm.D., Student[3], Mary Brabson, Pharm.D., Student[3]; (1)University of Texas at Austin, College of Pharmacy, Austin, TX; (2)Touro University - California College of Pharmacy, Vallejo, CA; (3)University of Iowa College of Pharmacy, Iowa City, IA.

PURPOSE: The primary aim of this study was to investigate the association between measured blood alcohol concentration (BAC) and the presence and degree of amnesia (no amnesia, grayout, or blackout) in actively drinking subjects. A secondary aim was to determine potential factors other than BAC that contribute to alcohol-induced memory loss.
METHODS: An interview questionnaire was administered to subjects regarding a recent alcohol-associated arrest with a documented blood alcohol concentration greater than 0.08 gm/dL for either public intoxication, driving under the influence, or under age drinking. Demographic variables collected included drinking history, family history of alcoholism, presence of previous alcohol-related memory loss during a drinking episode, and drinking behavior during the episode. Using self-described recall of timeline of events, memory of the drinking episode was evaluated to determine if either an alcohol-induced grayout (partial anterograde amnesia) or blackout (complete anterograde amnesia) had occurred.
RESULTS: A total of 65 subjects with a documented arrest were included. Twenty (31%) subjects described blackouts, 13 (20%) described grayouts, and 32 number (49%) reported no amnesic episode. A strong linear relationship between BAC and predicted probability of memory loss was determined for those having blackouts (R^2=0.54). Significant differences ($p<0.05$) were found in mean total number of drinks ingested prior to arrest, gulping of drinks, and blood alcohol concentration at arrest for those having blackouts compared to no amnesia. Differences in drinking more than planned were found between the no amnesia and grayout groups.
CONCLUSIONS: A significant association was found between the measured BAC and level of amnesia reported by the subject during a recent drinking episode. From a forensic perspective, it is reasonable to conclude that a subject with a BAC ≥ 0.310 gm/dl has a 50% probability of truthfully claiming that a blackout had occurred during an alleged incident.

Transplant/Immunology

107. Impact of a steroid withdrawal protocol on height and weight outcomes in pediatric renal transplant recipients. *Keri L. Roberts, Pharm.D.*, Lonnie D. Smith, Pharm.D., Jason Crompton, Pharm.D., Cynthia Terrill, RDCSRCD, Joseph Sherbotie, M.D.; University of Utah, Salt Lake City, UT.

PURPOSE: Chronic corticosteroid exposure is associated with weight gain and poor growth in pediatric renal transplant recipients (PRTR). We evaluated steroid withdrawal (SWD) efficacy in PRTR, focusing on height and weight outcomes.
METHODS: All PRTR transplanted from 1/2000-10/2005, undergoing SWD (4-days) were evaluated. Subgroup analysis by age was performed at 1, 2 and 3 years follow-up. Variables, including Scr, height and weight, were reviewed at baseline and every six months. Age-adjusted height and weight z-scores were calculated and compared with the 2005 North American Pediatric Renal Transplant Cooperative Study (NAPRTCS), as the majority of these patients received chronic corticosteroids.
RESULTS: Of patients transplanted, 28 met inclusion criteria. Reasons for exclusion: chronic steroids (13), <1 yr data (12), lost to f/u (3), primary allograft non-function (1) and restarting steroids following rejection (1). Comparison to NAPRTCS revealed higher mean delta height z-scores 2 years post-transplant across all age groups, with the greatest increase in ages 13–17. Mean weight z-scores from baseline also improved at 3 years. Interestingly, delta weight scores increased in ages 6–12 and 13–17 (1.39 vs. 1.13 and 0.8 vs. 0.7 respectively) upon comparison with NAPRTCS. BMI-Age% at 3 years increased from baseline in all patients. 22/28 pts (79%) remained within normal BMI range (5–85%), 1 remained underweight, 2 became at risk for overweight (BMI>85%) and 3 became overweight (BMI>95%).
CONCLUSIONS: SWD leads to improvement in mean height z-scores and demonstrates increased delta z-scores when compared to patients on chronic corticosteroids in NAPRTCS. PRTR are still at risk for becoming overweight despite withdrawal of corticosteroids.

Delta Height z-scores	Age 1	Ages 2-5	Ages 6-12	Ages 13-17
Baseline-1 YR	-0.32(n=1)	0.54(n=4)	0.9(n=11)	0.3(n=12)
Baseline-2 YR	(n=0)	0.61(n=2)	0.99(n=8)	0.56(n=8)
Baseline-3 YR	(n=0)	(n=0)	0.75(n=7)	0.61(n=6)
NAPRTCS-Baseline-2 YR	2.06	0.52	0.69	-0.02
Increase vs. NAPRTCS @ 2 YR	—	17%	32%	29-Fold

108E. Serial pharmacodynamic responses to anti-lymphocyte globulin. *Kathryn A. Gillis, Pharm.D.*[1], Yassa Qazi, M.D.[2], Jyotheen Karam, M.D.[2],

George Blessios, M.D.[2], Rocco C. Venuto, M.D.[2], Kathleen M. Tornatore, Pharm.D.[3]; (1)School of Pharmacy, Univeristy of North Carolina, Carrboro, NC; (2)Erie County Medicial Center, Division of Nephrology, School of Medicine, University at Buffalo, Buffalo, NY; (3) Department of Pharmacy Practice, School of Pharmacy & Pharmaceutical Sciences, Buffalo, NY.

PURPOSE: The cytokine receptor system {interleukin-2 (IL-2), Interleukin-2 receptor (IL-2R)} with stimulation of CD4 lymphocytes amplifies the immunologic response after transplantation. Serial assessment of IL-2, sIL-2R and CD4 lymphocytes was quantitated in ten renal transplant recipients (RTR){6 male;4 females} receiving live donor kidneys during induction therapy with anti-thymocyte globulin (ATG) up to 8 weeks post-transplant.
METHODS: Cytokines were quantitated during 5 phases: Phase I: before transplant; Phase II: 24 hr after intra-operative ALG induction at 15 mg/kg; Phase III: 24 hrs after last ALG dose; Phase IV: 4 weeks; Phase V: 8 weeks. All patients received prednisone, mycophenolate mofetil and cyclosporine with troughs targeted to 100-300 ng/ml. Serum and whole blood were collected for determination of cytokines by ELISA with CD4+ cells determined by flow cytometry.
RESULTS: Il-2 was below the limit of quantitation (<2.0 pg/ml) in all patients over all phases. However, sIL-2R was detectable in all patients during all phases. No significant change in sIL-2R was noted between any of the study phases, but a decline was observed in mean values from Phase I to Phase V (1436 ± 874 pg/ml to 693 ± 609). A nadir in CD4+ cells was noted in 60% of patients during Phase II (28 ± 28 cells/ml) compared with baseline. (515 ± 234 cells/ml) with a 94% percent change ($p<0.05$) attributed to the induction regimen. A significant recovery in CD4+ lymphocytes toward baseline was noted during Phases IV and V ($p<0.05$) with interpatient variability. A positive correlation was noted between sIL-2R and serum creatinine ($p=0.019$) with a negative correlation between sIL-2R and percent change in CD4 lymphocytes ($p=0.04$).
CONCLUSIONS: The inter-relationship between IL-2, sIL-2R, and CD4 lymphocytes during induction and maintenance immunosuppression may provide useful pharmacodynamic responses to serve as clinical monitoring parameters and complement therapeutic drug monitoring during the post-transplant period.
Published in J Am Soc Nephrol 2005;16:236A.

Urology

109. Persistence of medication therapy for overactive bladder in the Department of Defense. *Angela A. Allerman, Pharm.D., BCPS*, David R Bretzke, Pharm.D., Davd J Meade, Pharm.D., BCPS; Department of Defense Pharmacoeconomic Center, Fort Sam Houston, TX.

PURPOSE: Medication management of OAB is frequently complicated by suboptimal persistence with the muscarinic antagonists. Prescription claims were evaluated to determine persistence of OAB drug therapy in DoD beneficiaries.
METHODS: The study cohort was identified by querying the DoD Pharmacy Database Transaction Service, which serves as a repository for all prescriptions dispensed from Military Treatment Facilities, Retail Network, and Tricare Mail Order Pharmacy. Patients receiving initial therapy with a muscarinic antagonist between July 1, 2004, and September 30, 2004, were eligible for inclusion. Persistence with OAB therapy was defined as a prescription refill within 90 days from the date of the initial prescription fill. Assessment was carried out in quarterly periods from July 1, 2004, to October 30, 2005. Patients were excluded if OAB therapy was switched from one muscarinic antagonist to another at any time during the evaluation period.
RESULTS: Prescription profiles from a total of 17,435 patients receiving OAB therapy were available; 14,829 patients entered the persistence portion of the study, and 2,696 patients switched therapy. Patients receiving tolterodine extended release (ER) showed the highest persistence (34.7%) followed by oxybutynin ER (29.8%). The lowest persistence was with oxybutynin immediate release (18.5%). Persistence for all OAB drugs declined to 50% by the 1st quarterly assessment, and remained below 35% at study conclusion. There were an inadequate number of prescriptions for trospium, darifenacin, and solifenacin to assess persistence. These preliminary results validated the methodology, and the study will be updated to capture more data with the newer OAB drugs.
CONCLUSION: Persistence with OAB therapy is low in the DoD. More data are needed to determine the impact of newer muscarinic antagonists on persistence.

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.

110E. Effectiveness of interdisciplinary cardiovascular risk reduction for patients with coronary disease or diabetes. *Tracey H. Taveira, Pharm.D., CDOE*[1], Oanh J. Martin, Pharm.D., CDE[2], Peter N. Petropoulos, M.D.[2], Pranav M. Patel, M.D.[2], Satish C. Sharma, M.D.[2], Wen-Chih Wu, M.D., FCCP[2]; (1)University of Rhode Island, Kingston, RI; (2)Veterans Affairs Medical Center, Providence, RI.

CONTEXT: It is not known whether an approach to target different modifiable cardiovascular risk factors can further lower cardiovascular event risk as assessed by the Framingham Point Scores (FPS) beyond the usual care provided by primary care physicians in patients with CAD and/or diabetes. The Cardiovascular Risk Reduction Clinic (CRRC) is a practice model that integrates the management of the major modifiable risk factors into a single program.
OBJECTIVE: To assess the effectiveness of the CRRC model by comparing the FPS before and after CRRC intervention.
Design, Setting and Participants Baseline and last CRRC visit systolic blood pressure (SBP), HDL cholesterol (HDL-C), total cholesterol (Chol), and smoking status were abstracted from 375 patients referred by their primary care providers for secondary prevention who received at least one intervention by CRRC between January 2001-2002 at the Providence VA Medical Center.
INTERVENTION: The CRRC pharmacist coordinates an individualized diet and exercise program with the nutritionist and physical therapist and develops a pharmacotherapeutic plan to treat hypertension, dyslipidemia, diabetes, and tobacco use. Follow-up visits are scheduled every 6 weeks to monitor adherence and therapeutic effects, and to adjust medications.
RESULTS: The mean age of the patients was 65.1±10.5 years. Complete follow-up data was available on 84.8% of the patients with 79.7% diabetes, 37.7% with CAD, and 23.0% with both CAD and diabetes.
CONCLUSION: The CRRC model may reduce the long-term risk of cardiovascular events as assessed by FPS in patients with CAD and/or diabetes

Parameters	Pre-CRRC (SD)	Post-CRRC (SD)	P-value
Mean SBP (mm Hg)	134.4 (± 16.8)	126.9 (± 12.4)	<0.001
Mean Chol (mg/dL)	196.1 (± 47.2)	169.0 (± 38.9)	<0.001
Mean HDL-C (mg/dL)	39.3 (± 9.9)	39.4 (± 10.8)	0.888
Smoking (points)	0.65 (± 1.3)	0.42 (± 1.0)	<0.001
Total FPS (points)	14.5 (± 2.6)	13.5 (± 2.8)	<0.001

Published in Circulation 2003;107(19)e131,p4.

111E. Effect of baseline covariates on mortality risk in the VMAC trial. *William T. Abraham, M.D.*; Ohio State University, Columbus, OH.

INTRODUCTION: VMAC (N=489) was a randomized evaluation of nesiritide (NES) vs placebo for 3 h, and thereafter NES vs nitroglycerin (NTG) in the treatment of decompensated HF. Although not statistically significant, 30-day and 6-month mortality were greater for NES compared with NTG (30-day: 8.1 vs 5.1%, *P*=0.23; 6-month: 25.1% vs. 20.8%, *P*=0.32). Despite randomization, significant differences in baseline characteristics may have influenced these results.
OBJECTIVE: To determine the effect of differences in baseline characteristics on mortality risk in VMAC.
METHODS: The mortality effect of all variables with ≥ 3% absolute baseline differences between NES and NTG groups was assessed using univariate Cox regression models. Significant univariate mortality risk predictors were then evaluated using multivariate Cox regression models with a stepwise criterion of $P<0.05$ for entry and $P<0.10$ for retention. Separate models were developed for 30-day and 6-month mortality; these multivariate models were used to adjust mortality HRs for NES vs NTG.
RESULTS: Of the variables with baseline differences, creatinine clearance ≤ 60 mL/min, SBP ≤ 100 mmHg, prior dopamine or dobutamine use, and history of ventricular tachycardia were significant predictors of mortality. Adjusting for baseline differences in these variables reduced the mortality HR for NES vs. NTG: 1.56 to 1.17 at 30 days and 1.22 to 1.06 at 6 months.

VMAC Mortality Risk

	Hazard Ratio (95% CI)	*P*-value
30-Day		
Unadjusted	1.56 (0.75-3.24)	0.23
Adjusted	1.17 (0.55-2.49)	0.68
6-Month		
Unadjusted	1.22 (0.83-1.79)	0.32
Adjusted	1.06 (0.72-1.56)	0.78

CONCLUSIONS: Differences in baseline covariates may account for most of the apparent excess mortality observed in subjects receiving NES in VMAC. This analysis emphasizes the importance of using risk-adjusted mortality data in studies that are not designed to evaluate this endpoint.
Published in Circulation 2005;112(17, suppl II):II-589.

112E. Durability of guideline adherence in coronary disease and diabetic patients after discharge from a cardiovascular risk reduction clinic. Wen-

Chih Wu, M.D., FCCP[1], Oanh J. Martin, Pharm.D., CDE[1], *Tracey H. Taveira, Pharm.D., CDOE*[2], Mark D. Schleinitz, M.D.[3], Vincent Mor, Ph.D.[3], Satish C. Sharma, M.D.[1]; (1)Veterans Affairs Medical Center, Providence, RI; (2)University of Rhode Island, Kingston, RI; (3)Brown University, Providence, RI.

CONTEXT: Specialized clinics are effective strategies to improve guideline adherence in smoking cessation, and blood pressure and glycemic or lipid control. Little is known about the durability of guideline adherence after discharge from focused clinics. The Cardiovascular Risk Reduction Clinic (CRRC) is a pharmacist-led, multidisciplinary clinic that integrates the management of major modifiable risk factors into a single treatment program in accordance with the NCEP-ATP III and ADA guidelines in patients with diabetes or CAD. Patients are discharged to usual care when the guideline recommended goals are met.
OBJECTIVE: To evaluate the durability of guideline adherence in risk factor control after discharge from the CRRC.
DESIGN. SETTING AND PARTICIPANTS: 136 discharged patients were identified via chart review from 375 candidates enrolled in CRRC during 2001-2002. Guideline adherence rates for BP, A1c, smoking and LDL-Cholesterol were compared at baseline, discharge, 3–6, 6–9 and 9–12 months after discharge. Patients with absence of risk factor evaluation >6 months were judged to be non-adherent.
RESULTS: 89% of our sample patients had diabetes, 38% had CAD and 23% had CAD and diabetes. Mean age was 65.1 ± 10.5 years. Patients were discharged to standard care after 3.5 ± 1.5 CRRC visits (124 ± 88 days).

Guideline Adherence Rate

Compliance	Prior to CRRC (%)	At Discharge (%)	3-6 months post CRRC (%)	6-9 months post CRRC (%)	9-12 months post CRRC (%)
LDL	31.97*	72.73	60.94	58.46	57.52*
SBP	36.76*	75.74	30.15*	38.05*	33.33*
DBP	89.71*	95.59	74.26*	81.82*	81.68*
A1c	40.44*	66.18	72.79	69.12	55.88
Smoking	73.52*	86.80	-	-	81.62*

*P value <0.05 when compared to discharge

CONCLUSION: Guideline adherence is most durable for diabetes and smoking cessation, and least durable for blood pressure control. All risk factor compliance declined by 9–12 months. We are prospectively investigating the optimal means of maintaining guideline adherence after discharge.
Published in Circulation 2004;109(20):e285,p41.

113. Evaluation of a pharmacist-managed congestive heart failure clinic with adherence to the 2005 ACC/AHA guidelines for the management of chronic heart failure. *Timothy M. Murray, Pharm.D.*, Ryan Schupbach, Pharm.D.; University of Oklahoma College of Pharmacy, Tulsa, OK.

PURPOSE: In an effort to evaluate the current treatment of patients diagnosed with congestive heart failure (CHF) and seen in a pharmacy managed CHF clinic, adherence to the 2005 ACC/AHA CHF guidelines was evaluated.
METHODS: Several class I and II A recommendations were identified from the guidelines, and 40 charts were reviewed for adherence. Recommendations reviewed included: 1) documentation of heart failure stage, 2) correct classification of heart failure stage, 3) documentation of initial and serial clinical assessment, 4) documentation of assessment of smoking status, and 5) appropriate utilization of indicated medications. In addition hospital readmission rates at 30 days and 6 months were analyzed.
RESULTS: Each of the charts reviewed had documentation of a heart failure stage, and 89% of the patients were classified correctly. Documentation of initial and serial clinical assessment and assessment of smoking status was performed at each visit. Excluding patients with contraindications, those classified with heart failure stage C were found to be receiving ace-inhibitors 97%, beta blockers 92%, aldosterone antagonist 94%, digoxin 17%, and aspirin 95% of the time. Readmission rates for 30 days were 11%. Analyzing patients that had been seen in clinic at least 6 months from admission date resulted in a readmission rate of 26%.
CONCLUSIONS: In review of the 2005 CHF guideline recommendations, the pharmacy-managed CHF clinic's adherence rates were appropriate. The level of care patients within the clinic are receiving is in accordance with the national standards of care. Utilizing practice guidelines in a clinic setting enables pharmacists to practice evidence-based medicine, improve patient quality of care, and document relevant clinical outcomes.

114. Evaluation of the clinical and economic impact of clinical pharmacist participation on Intensivist rounds in a 42-bed intensive care unit. *Holly L. Monatt, Pharm.D.*; HealthONE Swedish Medical Center, Englewood, CO.

PURPOSE: Daily patient care rounds led by an Intensivist are an alternative to the Leapfrog Group's recommendation for 24-hour Intensivist coverage in the Intensive Care Unit. Pharmacist participation on these rounds is important due to the complexity and high cost of many therapies routinely used in the management of intensive care patients.
METHODS: Pharmacist interventions on Intensivist Rounds were tracked between January 3 and March 31, 2005. Cost-savings were assigned to each type of intervention if a specific therapy change was made. Direct drug cost-savings were assigned for the equivalent of only one day of therapy to avoid overestimating the impact of a recommendation. Other types of interventions that resulted in better quality care were tracked; but no cost-savings value was assigned to this type of intervention.
RESULTS: Changes in therapy recommended by the pharmacist that were successfully accepted and implemented by the prescriber resulted in total direct drug cost-savings of $26,803.16 Other interventions focused on preventing unnecessary pharmacy preparation of certain high-cost medications (savings of $1,601.97). Cost-savings for the avoidance of certain undesirable outcomes such as an adverse drug event (ADE), deep vein thrombosis (DVT), or ulcer were impossible to calculate.
CONCLUSIONS: Pharmacist participation on Intensivist rounds resulted in considerable cost-savings for the pharmacy department. Additionally, the pharmacist's recommendations resulted in the prevention of certain undesirable outcomes. The results of this program were shared with the hospital administration team, and approval was given for ongoing pharmacy participation on rounds.

Education/Training

115. Evaluating the impact of clinical interventions by Pharm.D. students on internal medicine clerkships: the results of a 3-year study. *David Q. Pham, Pharm.D.*; Arnold & Marie Schwartz College of Pharmacy and Health Sciences, Long Island University, Brooklyn, NY.

PURPOSE: As the practice of pharmacy continues to evolve to require more clinically oriented health care providers, Pharm.D. programs throughout the nation are continuing to expand their training to more hospital sites. These hospital sites often necessitate proof from pharmacy schools of the impact of Pharm.D. students on patient care. The primary purpose of this study is to evaluate the medical and economic impact of Pharm.D. students on internal medicine clerkships over a 3-year study period by assessing the usefulness, type, frequency, and acceptance rate of clinical interventions made and to specifically examine cost savings (or loss).
METHODS: During the orientation period for internal medicine clerkships, students are instructed to prospectively document utilizing hospital approved pharmacy intervention forms all clinical services and recommendations directed at improving patient care. One form is to be completed for each intervention made. Completed forms are submitted to the on-site faculty member on a daily basis to insure completeness, accuracy, and appropriateness. The preceptor then assesses the impact of the clinical intervention on a 1 to 3 rating scale: 1 defined as no to minimal impact on patient care, 2 defined as moderate impact on patient care, and 3 defined as significant impact on patient care. All interventions performed from January 2003 to January 2006 are recorded and analyzed. The study is conducted with students from the Arnold & Marie Schwartz College of Pharmacy at Kings County Hospital Center (KCHC). KCHC is a 627-bed, general medical and surgical county hospital with 10 internal medicine teams located in Brooklyn, New York.
CONCLUSION: The results from this study are ongoing until January 2006, at which time data will be computed and analyzed. The hypothesis is that Pharm.D. students would have a positive impact on medical staff education, and patient care, and prove to be cost effective.

116. Innovation in clinical pharmacy teaching in east Africa: spices versus tradition. *James N. Ombega, Pharm, D*; University of Nairobi, Nairrobi, Kenya
PURPOSE: The goal of this study was to assess the effectiveness, student acceptance and instructor atittude toward two newer and innovative methods (spices and cobes) of teaching in an African university.
METHODS: A student-centered,problem-solving, communication skills approach to teaching (spices) and community-oriented(cobes), methods of teaching were introduced and encouraged to be used during the teaching of clinical pharmacy course to third and fourth years, bacholor of pharmacy undergraduates in an African university, that over the years used the traditional way of delivery.This was done over a period of one year, and insruments of evaluation were administered to both the students and the instructors in order to determine instructor atittude and student perception and acceptability of this way of teaching.
RESULTS: It was observed that students prefered the newer, student/community-oriented methods. Furthermore, these students had enhanced problem-solving and reasoning skills. On the other hand, some members of the faculty,still preferred the teacher-centered methods.
CONCLUSIONS:It was concluded that the newer methods can enhance the teaching of clinical pharmacy in an African setting, but one has to be aware of obstacles, particularly from the faculty members.

Substance Abuse/Toxicology

117. Methanol poisoning in East Africa: racial implications. *James N. Ombega, Pharm, D*; University of Nairobi, Nairobi, Kenya.

PURPOSE: The purpose of this study was to determine if there was any variation in dose response to methanol poisoning antidote in patients of African origin.
METHODS: One hundred and sixty two patients, victims of massive accidental methanol poisoning due to contaminated African alcoholic beverage, usually consumed by the urban poor, were treated for methanol poisoning using intravenous ethanol drip. The dose of ethanol was individualized and titrated against clinical response and biochemical data of each patient.
RESULTS: The dose responses of these patients were pooled together and statistically compered to those used mainly by the caucasian population.
CONCLUSION: It was observed that the dose response of ethanol as an antidote for methanol poisoning among African populations was significantly different from the Caucasians.These findings imply that due to massive poisoning in many communities in East Africa and often massive deaths, the antidote studies in this populations ought to be given some international attention.

118. Prospective identification of hospitalized patients with diabetes using electronic data. *Terry L. Seaton, Pharm.D.*[1], Richard M. Reichley, R.Ph.[2], Laura A. Noirot, B.S.[3], Brian F. Gage, M.D.[3], Wm. Claiborne Dunagan, M.D.[4], Thomas C. Bailey, M.D.[4]; (1)St. Louis College of Pharmacy, St. Louis, MO; (2)BJC HealthCare, St. Louis, MO; (3)Washington University School of Medicine, St. Louis, MO; (4)BJC HealthCare and Washington University School of Medicine, St. Louis, MO.

PURPOSE: Diabetic drug orders do not reliably predict a diagnosis of diabetes. For quality improvement initiatives, we developed and validated a clinical prediction rule to prospectively identify patients with diabetes using electronically available data.
METHODS: The derivation study sample comprised admissions from Quarter-2 of 2004. We used ICD-9 codes for diabetes mellitus as the outcome variable in a forward stepwise logistic regression model with entry/keep probability criteria of 0.5. Independent variables included prior diabetes ICD-9, current/past hypoglycemic drug orders, presence/absence of an A1c result, and current/past glucose at or above the 75th percentile. ROC analysis of the final model was used to optimize sensitivity and specificity. We then validated the model using an independent sample of all admissions from the Quarter-4 of 2004.
RESULTS: The study sample included 11,462 admissions, of which 1,980 (17.3%) had an ICD-9 code for diabetes. Prior diabetes diagnosis was present in 1,479 (12.9%) of the subjects. The best fit log regression model included the variables shown in the Table.

Variable	Odds Ratio	P value
Current insulin daily charge	12.498	<0.001
Current oral hypoglycemic order	26.711	<0.001
Current long-acting insulin order	5.491	<0.001
No. of prior ICD-9 codes	0.988	<0.001
No. of prior DM ICD-9 codes	1.144	<0.001
A1c determination	3.896	<0.001
Prior diabetes ICD-9	5.720	<0.001
Prior oral hypoglycemic order	1.632	0.0054
Glucose > 75th percentile	1.938	<0.001

The c-statistic for the derivation sample was 0.958. Accuracy was optimized at a predicted probability of 0.15, with 92.2% of admissions correctly classified, 91.6% sensitivity, 92.3% specificity, 28.7% false positives and 1.9% false negatives. The c-statistic for the validation set, with 11,567 unique patient admissions, and 2,073 (17.9%) patients with diabetes, was 0.958.
CONCLUSION: Using electronically available administrative and clinical data, it is possible to prospectively identify patients with diabetes early and reliably for quality improvement initiatives.

119. Acceptance of medication recommendations from a pharmacist-run diabetes clinic in a rural community pharmacy. *Marianne McCollum, Ph.D., R.Ph.*[1], Samuel L. Ellis, Pharm.D.[1], Jenae Lorenzo, RPh[2], Christoper J. Turner, Ph.D.[1]; (1)University of Colorado School of Pharmacy, Denver, CO; (2)Barnes Pharmacy, Sterling, CO.

PURPOSE: This study evaluated acceptance rates for recommendations from a rural, community pharmacy-based diabetes program involving collaboration between the community pharmacy, pharmacy students receiving advanced experiential training in the 4th (P4) academic year, and faculty members from the school of pharmacy.
METHODS: Under the direction of pharmacist preceptors, P4 students met with patients for 6 monthly visits to conduct diabetes education and clinical monitoring. Laboratory assessments included hemoglobin A1c, blood pressure, and fasting lipid profiles. Clinical notes with medication recommendations (start/stop or dose change) were faxed to the patient's physician following each visit. Repeated recommendations were considered to be independent recommendations in these analyses, as each represented an opportunity for a physician to take action. Acceptance (yes/no) for each recommendation was noted in the patient record.
RESULTS: A total of 52 patients enrolled in the clinic, for whom 533 medication recommendations were faxed to 29 physicians. The overall acceptance rate was 32% (35% for dose changes, 28% to start or stop a medication). The most common recommendations were for medications to treat cholesterol (134), followed by oral diabetes medications (131), blood pressure medications (129), and insulin (89). Acceptance rates were highest for aspirin (61%), followed by pain medications (40%) and insulin (34%). All 7 recommendations for pneumococcal and influenza vaccinations were accepted. Three physicians accepted more than half of the recommendations they received (55%, 56%, and 59%); four accepted no recommendations.
CONCLUSIONS: Medication management recommendations from a pharmacist-run diabetes care clinic in a rural community pharmacy setting were accepted by physicians 32% of the time. Acceptance rates varied greatly by physician, perhaps indicating different levels of buy-in from different physicians serving this patient community. Further investigations involving physician surveys are planned to determine factors affecting physician attitudes toward the clinic and their influence on recommendation acceptance rates.

120. Clinical outcomes associated with a rural community pharmacy diabetes program developed in collaboration with the University of Colorado School of Pharmacy. *Samuel L. Ellis, Pharm.D.*[1], Marianne McCollum, Ph.D.[1], Jenae Lorenzo, RPh[2], Christopher J. Turner, Ph.D.[1]; (1)University of Colorado School of Pharmacy, Denver, CO; (2)Barnes Pharmacy, Sterling, CO.

PURPOSE : This study evaluated the clinical outcomes associated with a rural diabetes program that was developed and administered in collaboration between the community pharmacy, fourth year (P4) pharmacy students receiving experiential training, and a faculty member from the University of Colorado School of Pharmacy.
METHODS: A retrospective analysis was done on patients completing the 6-month diabetes self-management education program between January 2004 and June 2005. Patients were assessed by the community pharmacist and fourth-year pharmacy students at each visit. Data collected included BMI, blood pressure, hemoglobin A1c, and fasting lipid profile. A pharmacotherapy plan was developed and faxed to the provider after each patient visit.
RESULTS: A total of 53 patients completed six monthly diabetes self-management education visits. Eighteen patients entered the program but did not complete all 6 visits and were not included in this analysis. Mean reductions in hemoglobin A1c (0.8%; p <0.001), LDL-cholesterol (21.8 mg/dL; p <0.001), weight (5.5 pounds; p=0.006), and systolic (4.9 mmHg; p=0.03) and diastolic (6.6 mmHg; p<0.001) blood pressure were all statistically significant at 6 months compared to baseline. The number of patients achieving ADA recommended treatment goals were also significantly increased at 6 months for A1c (39% vs 66%; p=0.006), LDL-Cholesterol (31% vs 66%; p=0.01), and blood pressure (19% vs. 40%; p=0.02)
CONCLUSION: A rural, community pharmacy-managed diabetes program developed in collaboration with the University of Colorado School of Pharmacy was able to significantly improve the number of patients with type 2 diabetes reaching American Diabetes Association standards of care for hemoglobin A1C, LDL-cholesterol, and blood pressure. As a result of these findings, future collaborative projects between community pharmacies and the school of pharmacy are under way.

121. Medication assessment of geriatric inpatients by clinical pharmacists (MAGIC). *Kerry Wilbur, B.Sc.Pharm., ACPR, Pharm.D.*[1], Anna Liu, Pharmacy, Student[2], Roger YM Wong, BM.Sc., M.D.[3]; (1)Vancouver General Hospital - CSU Pharmaceutical Sciences, Vancouver, BC, Canada; (2)Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada; (3)Faculty of Medicine, University of British Columbia, Vancouver, BC, Canada.

PURPOSE: Early discharge from hospital has increased patients' self-responsibility role in medication management at a time when community health resources are diminishing. The aging population has been associated with rising numbers of elderly who manage drug therapy on their own. Many drug packagings in use significantly impede access by elderly patients to their medication. Pharmacists are most likely to discover obstacles to geriatric self-medication and make interventions to ameliorate these barriers. The objective of this study was to develop an objective screening tool for pharmacist assessment of geriatric patients' functional ability to take medications.
METHODS: Geriatric patients admitted to a Canadian tertiary care hospital were prospectively screened. Pharmacist researchers administered a medication skills assessment tool to consenting patients who managed their

own medications at home prior to admission. Intervention was implemented prior to discharge to support those elderly subjects who demonstrated functional inability to manage their medication regimen.
RESULTS: Sixty patients were enrolled (mean age 83, female 77%). Forty three percent lived home alone. Twenty-four patients were excluded due to cognitive impairment; 10 of these patients lived home alone prior to admission. Average number of total medications was 7 (range 1–16). Twenty percent self-reported some degree of difficulty managing medications. Impaired ability to functionally manage medication regimen as determined by performance on the skills assessment tool was demonstrated by 28%. No specific patient characteristics predictive of poor performance were identified, although those who were unsuccessful completing the skills assessment were slightly older (86 vs. 82 years, $p<0.05$). Discharge intervention plans were initiated for 25% patients.
CONCLUSIONS: A number of geriatric patients managing medication independently at home demonstrated impaired ability to functionally manage their regimen. Our efficient screening assessment tool can help hospital pharmacists assume a greater role in identifying these patients and participating in discharge medication planning.

122. Can the Australian model for home medicine reviews prove useful in the United States? *Deane Dight, BPharm, M.P.H.*; University of Canberra, Bruce ACT, Australia.

BACKGROUND: Because Australia has a population less than one-tenth that of the United States, innovation in health care is more feasible on a smaller scale. Medicare Australia pays physicians and surgeons a fee-for-service, and Australia has achieved low medication prices through the Pharmaceutical Benefits Scheme (PBS) for which the general population and pensioners pay a standard contribution fee for each item. Through innovative thinkers in the late 1980s, a system by which cognitive skills of pharmacists could be funded by the federal government was developed and came to fruition in the mid-1990s. Accredited pharmacists were able to contract with aged-care facilities to perform Residential Medication Management Reviews (RMMRs) and be remunerated by the Commonwealth Department of Health and Ageing. In the new millenium Home Medicines Reviews (HMRs) were formally introduced.
Accreditation process: Both workshops and distance learning options were available for practicing pharmacists to progress to the case-based accreditation assessment. In 1996 a small group of practicing clinical pharmacists were chosen to act as assessors. From 1996 until 2003 the assessment process was a series of 10 cases in hardcopy. Since 2004 this process has been computer-based.
The current situation: There are currently over 1500 accredited pharmacists in Australia who provide both RMMRs and HMRs and are remunerated by the federal government. Between July 2004 and June 2005 more than 23,000 Home Medicines Reviews (HMRs) had been completed*.
The fourth community pharmacy/government agreement: A new agreement has just been ratified and includes far-reaching expansion of Medication Management Reviews.
*I anticipate being able to provide the latest figures to hand, probably February or March 2006 for the April Spring Practice and Research Forum.

123. Clinical pharmacy specialist leads creation and implementation of a comprehensive venous thromboembolism prevention program for the Hospital Corporation of America. *L. Hayley Burgess, Pharm.D., BCPP*, Alicia H Perry, Pharm.D., Jane Englebright, R.N., Ph.D., Frank Houser, M.D.; The Hospital Corporation of America, Nashville, TN.

Venous thromboembolism (VTE) is a significant national health problem. Resulting from clot formation within the venous circulation, VTE is manifested as deep vein thrombosis (DVT) and pulmonary embolism (PE). The American Heart Association reported that each year approximately 2 million Americans are afflicted with DVT, up to 600,000 of these patients subsequently develop a PE, and as many as 200,000 will die of PE.
The Hospital Corporation of America owns and operates over 180 hospitals in the United States and Europe. To determine the extent of DVT and PE primary and secondary diagnoses within HCA, data analysis from October 2003 to September 2004 was conducted, resulting in 1.8 million discharges, including 18,850 DVT and 10,000 PE diagnoses. Our risk management database from 1995 to 2005 reported 495 VTE claims. The highest incidence of claims originated in the medical unit (179), operating room (96), and emergency department (85).
VTE is a preventable cause of hospital death, where published literature suggests only 30% of patients at risk actually received prophylaxis. OU Medical Center and St. David's Partnership found this statistic to be consistent within HCA facility practice. Senior leadership within the HCA Corporate quality department supported a company-wide VTE prevention program and joined the Coalition to Prevent DVT. Led by a clinical pharmacy specialist, an interdisciplinary team was formed to create an implementation toolkit. The toolkit included educational materials, standardized risk assessment and prophylaxis order sets, data collection strategies, and examples of successful implementations of VTE prophylaxis programs within the company. These tools reside on the HCA internal medication safety Web site. Educational efforts have included 2 company-wide implementation Webcasts, each with participation of 800+ clinicians. HCA is conducting a research protocol to evaluate our success of VTE risk assessment screening, appropriate prophylaxis use, and cost effectiveness of this program.

124. Evaluation of cost-effective treatment options for heparin-induced thrombocytopenia. *Trupti Mehta, Pharm.D., BCPS*, Jian Fan, Pharm.D. Candidate, Chin Y. Liu, M.S., Pharm.D., BCOP; Harper University Hospital, Detroit Medical Center, Detroit, MI.

PURPOSE: Current treatment options for the management of heparin-induced thrombocytopenia (HIT) include direct thrombin inhibitors, such as lepirudin and argatroban. Fondaparinux is a factor-Xa inhibitor approved for the treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE) as well as thromboprophylaxis in a post-surgery setting. Fondaparinux has no known effect on platelet factor 4 and theoretically may be useful for treating patients with HIT. The use of direct thrombin inhibitors require scontinuous intravenous infusion and labor-intensive monitoring whereas fondaparinux dosing is weight-based and administered subcutaneously once daily with less intensive monitoring. The objective of this study is to identify the potential role for fondaparinux in the management of HIT, develop an algorithm to guide treatment, and determine the estimated cost-savings with its use as an alternative to lepirudin or argatroban.
METHODS: This study is a retrospective chart review. Inclusion criteria are the following: patients with suspected or confirmed HIT without evidence of acute thrombosis requiring thromboprophylaxis or continuation of anticoagulation for history of DVT or PE. Patients who received lepirudin or argatroban from July 2004 through June 2005 at Harper University Hospital (HUH) will be identified through a pharmacy database. The following information will be obtained: number of patients with HIT, antithrombotic treatment, duration of treatment, indication, platelet counts, presence of HIT antibody, and cost of therapy.
RESULTS: Data collection is ongoing. The Detroit Medical Center Pharmacy and Therapeutics Committee approved the algorithm for management of HIT in October 2005.
CONCLUSION: The results of this study will help evaluate the incidence of HIT at HUH and the estimated cost-savings associated with utilization of the algorithm defining the role of fondaparinux in the management of HIT.

125. Evaluation of lipid monitoring in treatment-experienced HIV-infected patients. *Kelly Hester, Pharm.D., BCPS*, Pamela Stamm, Pharm.D.; Auburn University Harrison School of Pharmacy, Auburn, AL.

PURPOSE: To compare lipid monitoring in HIV-infected patients receiving highly active antiretroviral therapy (HAART) compared with Infectious Diseases Society of America (IDSA) clinical guidelines
METHODS: It is estimated that elevations in cholesterol and triglycerides occur in over 50% of patients receiving therapy with protease inhibitors. Because the general population of HIV-infected patients is typically younger than the population traditionally at risk for cardiovascular disease, the need for screening for lipid abnormalities may not be fully appreciated. The IDSA primary care guidelines for persons infected with HIV recommend a fasting cholesterol panel prior to initiation of HIV treatment, 4–6 weeks following initiation, and at least annually thereafter. A retrospective chart review was conducted on 100 randomly selected HIV-treated patients to evaluate lipid monitoring. Data regarding cardiovascular risk factors, lipid panels throughout treatment, lipid lowering therapy, length of HAART, current and past antiretroviral use, duration of HIV diagnosis, age, gender, race, viral load, and CD4 counts were collected.
RESULTS: Ninety seven percent were taking at least one antiretroviral agent known to cause dyslipidemia. Sixty-seven percent had received at least 1 year of HAART, and 64% had protease-inhibitor experience. Forty-two percent had at least 2 risk factors for cardiovascular disease. As a group, 81% did not have a lipid panel ordered for evaluation for the duration of treatments and only 5% had baseline labs evaluated. Total cholesterol was evaluated in 73% of patients, but lipid panels were evluated in 19% and revealed 28% with total cholesterol > 200 mg/dL, 4% with HDL < 40 mg/dL, and 9% with LDL > 130 mg/dL.
CONCLUSION: Results of this study reflect suboptimal adherence to the IDSA standards of care for lipid evaluation in treatment-experienced HIV-infected patients. However, it suggests there is significant opportunity to provide pharmaceutical care to evaluate cardiovascular risk in this population.

126. Impact of a multidisciplinary infectious disease management team on the prevalence of extended spectrum beta-lactamase enzymes in a tertiary care teaching hospital. *Roy Guharoy, Pharm.D.*, Donald Blair, M.D., Win Myat, M.D., Madhuchanda Chowdhury, M.D., Shelley Gilroy, M.D., Fred Rose, M.D.; SUNY-Upstate Medical University, Syracuse, NY.

PURPOSE: Infections caused by multidrug resistant Gram negative bacilli that produce extended spectrum beta lactamase enzymes (ESBL) have been reported with alarming frequency. The objective of our presentation is to describe the impact of our multidisciplinary infectious disease (ID) management team on the prevalence of ESBL enzymes in our tertiary care teaching hospital.The ID team was formed in 2000, and utilization indicators were reformulated. All broad spectrum formulary agents require ID approval unless the indication documented on the order form meets the release indicator. Pharmacists review clinical justification of all hospital-wide restricted antimicrobial usage with the ID team daily, and interventions are made, if needed.
METHODS: Klebsiella pneumoniae was chosen as the surrogate marker for identifying resistance secondary to ESBL. Defined daily dose and resistance trends were compared.
RESULTS: Defined daily dose utilization of 3rd-generation cephalosporins during 2000-2004 were as follows: 13,647 (2000); 11,921(2002); 12,874 (2002); 10,388(2003), and 10,346(2004).Third generation cephalosporin sensitivity against *K.pneumoniae* ranged from 96%–99%. Patient days increased by 7% during the time period.
CONCLUSIONS: Third-generation cephalosporin sensitivity against *K. pneumoniae* was reported as 89% by the National Nosocomial Surveillance report in 2003. Our pro-active multidisciplinary ID team-managed intiatives led to decreased use of 3rd-generation cephalosporins and lower resistance in our institution.

127. To err is human: result of a computerized physician order entry system on patient safety in a tertiary care teaching hospital. *Roy Guharoy, Pharm.D.*, Neal Seidberg, M.D., Nancy Page, M.S., John Degrazio, B.S., Barbara Bennett, B.S., Maureen Cummings, M.S., Theresa Wagner, B.S., Karen Hirschman, M.S., Joy Ganley, B.S.; SUNY-Upstate Medical University, Syracuse, NY.

PURPOSE: The Institute of Medicine reported 98,000 avoidable patient deaths each year secondary to medication errors. Computerized Provider Order Entry (CPOE) is the best available tool that can greatly reduce the adverse events. We describe the impact of a multidisciplinary team-led CPOE implementation on patient safety at our tertiary care teaching institution.
METHODS: Our team decided to interface between all ancillary systems, finance, and CPOE. Newly developed order sets were based on the feedback from expert users, pharmacy, and nursing. CPOE pilot implementation was completed in rehabilitation, pediatrics, and orthopedics service areas. Experiences from specific areas were utilized for CPOE implementation at other areas. A rapid cycle implementation process was utilized to implement the CPOE system hospitalwide within a 3-month period.
RESULTS: Adverse event data base was reviewed for pre and post CPOE implementation in the pilot units. Prescribing related adverse events were reduced by 51% (214 vs. 105). Patient allergy related adverse events were reduced by 35% (40 vs. 26). In addition, the CPOE order sets are leading to optimal use of evidence-based drug regimens for specific disease states. Our satellite pharmacists are now able to spend more time with various medical teams via utilization of tablet personal computers during rounds.
CONCLUSIONS: CPOE implementation has resulted in improved patient safety of our patients. Expanded pharmacist participation in direct patient care has resulted in increased therpaeutic interventions. Our strategy was to implement the basic version of CPOE in the first phase. A plan for implementation of advanced search engine and decision support-based rules for optimization of individual patient therapy over the next 9-month period has been developed. The step will lead to prospective avoidance of many potential adverse drug events and make our institution a safer place for our patients.

128. Clinical pharmacist intervention to promote use of inhaled corticosteroids in persistent asthmatics. *Vanessa Smith, Pharm.D.*[1], Samuel Moss, M.D.[2]; (1)Kaiser Permanente, Atlanta, GA; (2)Kaiser Permanente, Alpharetta, GA.

PURPOSE: This project evaluated educational intervention by a clinical pharmacist in patients diagnosed with persistent asthma with a HEDIS (Health Employer Data Information Set) inhaled corticosteroid ratio to short-acting [beta]$_2$- agonist (SABA) of less than 0.5 (calculated by the number of ICS/ICS + SABA refills in 1 year) who filled at least five prescriptions for a SABA in the past 6 months to 1) compare patients' use of inhaled corticosteroids (ICS) after the intervention through refill rates and HEDIS ICS to short-acting [beta]$_2$-agonist (SABA) ratios, and 2) evaluate asthma control before and after the intervention.
METHODS: Fifteen patients were identified as persistent asthmatics. Starting September 1, 2004, patients were contacted by telephone to assess current ICS and SABA use and symptoms through the Asthma Control Test™ and to educate on the importance of ICS use in management of asthma. Patients were reevaluated four months after the intervention.
RESULTS: Four of the 15 patients (26.7%) refilled an ICS prescription the month prior to the intervention compared to 4 months after the intervention, when 11 of the 15 patients (73.3%) refilled an ICS prescription. Improvement in HEDIS ICS to SABA ratio (indicated by increase or no change) occurred in 11 of the 15 patients (73.3%). Based on the Asthma Control Test, 10 of the 15 patients (66.7%) at the start of the study and 4 out of the 15 (26.7%) 4 months after the intervention were considered not well controlled.
CONCLUSION: Educational intervention by a clinical pharmacist showed to increase the likelihood of persistent asthmatics to refill an ICS prescription. Increased ICS use correlated with improvement in asthma control. Utilization of a clinical pharmacist in education of persistent asthmatics appears to improve ICS use and asthma control.

129E. Pharmacist-acquired medication histories in an emergency department. *Melinda K. Carter, Pharm.D.*, Dennis Allin, M.D., FASHP, Leigh Anne Scott, Pharm.D., M.B.A.; The University of Kansas Hospital, Kansas City, KS.

PURPOSE: To identify discrepancies between medication histories taken by Emergency Medicine providers and medication histories obtained by a clinical pharmacist.
METHODS: During a 3-month period a pharmacist was assigned to the Emergency Department in a 420-bed, tertiary care teaching facility that serves as a Level I Trauma Center. Upon arrival, Emergency Department providers completed a standard assessment including patient's medication history. Patients to be admitted through the Emergency Department were interviewed by the pharmacist. Height, weight, immunization history, and allergy information were collected by the pharmacist in addition to the medical history. Sources of information included the patient, caregivers, family members, prescription vials, medication lists from nursing facilities, and follow-up telephone conversations with community pharmacies and physician's offices. The medication history obtained by the Emergency Department personnel was compared to the history obtained by the pharmacist and discrepancies documented.
RESULTS: 286 medication histories were performed by the clinical pharmacist in the Emergency Department. 34 (12%) were excluded due to inability to compare with medication history performed by the Emergency Department staff. 252 (88%) histories were included in the study. Clinical pharmacists identified 1096 medications versus 817 by Emergency Department providers. 637 of 817 (78%) medications documented by ED personnel were incomplete and supplemented with dosing information by the pharmacist. Clinical pharmacists reported 375 medication allergies versus 350 for Emergency Department personnel with corresponding manner of allergic reaction reported in 200 of 375 (53%) by the pharmacists versus 8 of 350 (2%) by the ED personnel. Immunization history was obtained in 252 of 252 (100%) by the pharmacists versus 45 of 252(17%) by ED personnel.
CONCLUSION: Pharmacy services in the Emergency Department facilitated and improved the process for obtaining and documenting a complete medication history in admitted patients.
Presented at the Midwest Residency Conference, Omaha, NE, May 6-7, 2005.

130. Discrepancies between medication lists in the electronic medical record and actual medication use in a survey of patients with diabetes: implications for medication reconciliation systems. *Philip T. Rodgers, Pharm.D, BCPS, CDE, CPP*, Scott V Joy, M.D., CDE; Duke University Medical Center, Durham, NC.

PURPOSE: New regulations for medication reconciliation in health systems require consistency in medication use and documentation between the health care settings. The outpatient medication list is often consulted. However, the accuracy of these medication lists may be questionable. Appropriate pharmacotherapy relies on accurate documentation of the patient's daily medication regimen. This study evaluated the frequency and types of errors in the documentation of medication lists and drug allergies for a group of patients with diabetes in a primary care setting.
METHODS: Patients with diabetes in a primary care practice were identified and contacted by telephone. Consenting patients were asked to state all prescription, over-the-counter, and herbal medications they were currently taking, and all known drug allergies. This information was compared to the medication and allergy list in the patient's electronic medical record. The frequency of discrepancies between the patients' verbal record and the electronic medical record were noted.
RESULTS: A total of 128 patients participated. Overall, discrepancies in medication documentation were noted in 69.5% of the patients contacted. A total of 37.5% were on fewer medications than recorded, 30.5% were on different doses than recorded, and 25.8% were on more medications than recorded. Discrepancies specifically in diabetes medications were noted in 7% of patients. Regarding OTC medications, 35% were on more medications than listed, with aspirin being the most common. Herbal medications, notably glucosamine and ginko, were not recorded in 6% of the medical records, and recorded allergies were erroneous in 11%.
CONCLUSIONS: Documentation errors regarding medications were common in this population of patients with diabetes. Practitioners should use caution

in utilizing information relating to drug therapy from medical records, and should verify medication use with patients verbally to ensure accuracy. Medication reconciliation systems need to recognize some of the common limitations of the outpatient electronic medication list.

131E. Opportunities and barriers to the implementation of pharmacist-provided admission medication histories and discharge counseling services: a pilot program. *Suzanne M. Rabi, Pharm.D.*, Wafa Y. Dahdal, Pharm.D., BCPS; Midwestern University, Chicago College of Pharmacy, Downers Grove, IL.

PURPOSE: Research demonstrates that pharmacist admission history and discharge counseling improves patient care, decreases healthcare costs and noncompliance, and increases patients' knowledge of their medications. The objective of this study was to describe opportunities and barriers to establishing a patient education program operated by a college-based pharmacy resident at a tertiary hospital.
METHODS: A pharmacy resident rotating on the telemetry floor at a tertiary institution piloted the program by providing services 2–3 days/week for 4 weeks. The resident participated on medical rounds with the cardiology consult service. All patients were offered the education program. Medication histories were initiated by the pharmacy resident from the institution's list of admissions; discharge counseling services were initiated by the resident, medical team, or nursing. The number and type of interventions rendered as well as challenges to the implementation are described.
RESULTS: Fifty-six admission histories and 40 discharge counseling sessions were provided; 56 interventions were made (~6 interventions/day). The most frequent interventions were improper documentation of allergies or medications (N=26, 46.4%) and not starting a previous medication (N=20, 35.7%). Non-cardiac medications accounted for 67.9% of interventions. Barriers included: (1) pharmacy resident provided part-time coverage; therefore, not all patients were educated and fewer interventions were made, (2) health literacy; over 80% of patients did not have a medication list and did not know their medications.
CONCLUSIONS: Pharmacists have many opportunities to affect patient care by conducting admission medication histories and discharge counseling services. The demand for such services may increase as pharmacist-provided medication therapy management programs are becoming increasingly valued and reimbursed. Given the limited resources, collaborations between college- and hospital-based pharmacy personnel are essential to optimize the services. To effectively influence health literacy, pharmacists should conduct a thorough evaluation of patients' level of education, knowledge of their diseases, medications, and involvement in self-care.
Presented at the Annual Midyear Meeting of the American Society of Health-System Pharmacists, Las Vegas, NV, December 7, 2005.

132. Medication reconciliation: a multidisciplinary approach to implementation across the continuum of care. *Jenester P. Mostella, Pharm.D.*, Pamela K. Throgmorton, Pharm. D., Patrick Ellis, Pharm.D.; Huntsville Hospital, Huntsville, AL.

PURPOSE: Reconciling patient medications across the continuum of care is a crucial component in improving the quality of patient care and in preventing medication errors. Medication reconciliation (MR) is one of the 2005-2006 National Patient Safety Goals and part of the Institute for Healthcare Improvement's 100,000 Lives Campaign. This multidisciplinary approach to MR process is part of an ongoing effort to meet regulatory requirements, pharmacy departmental goals, and the hospital's quality initiatives.
METHODS: A multidisciplinary team's review of a pilot study of pharmacist conducted medication histories, completed in 2005, indicated that although pharmacists were more effective than nurses in obtaining an accurate and complete history, it would be more feasible to educate nurses to complete the history, with pharmacists providing verification. The Pharmacy and Therapeutics Committee approved new policies and procedures and MR forms. The Information Technology Department provided software support for changes to documentation and reporting processes across the continuum of care. Pharmacists trained nurses to obtain an accurate medication history. Pharmacy students participated in the follow-up of MR issues.
RESULTS: Interdisciplinary MR policies and procedures were implemented. Admission MR process included nurse-conducted interviews, pharmacist verification, student follow-up, and documentation in the patient's permanent record. Transfer MR process consisted of a computer-generated report, reviewed by physicians. Discharge MR process incorporated a review to prevent therapeutic duplication, a computer-generated list of medications for the next provider, and a pocket home medication card for the patient.
CONCLUSION: A systematic, multidisciplinary approach to the MR process provides a mechanism to reduce the potential for adverse drug events and is an effective solution to providing MR across the continuum of care.

133. The complex logistics and potential errors in the daily use of intravenous patient-controlled analgesia (IV PCA). *Rolin Wade, RPh, M.S.*[1], Rob W. Hutchison, Pharm.D.[2], Mark J. Cziraky, Pharm.D., FAHA[1], Sue Vallow, Pharm.D.[3]; (1)HealthCore, Inc., Wilmington, DE; (2)Presbyterian Hospital, Dallas, TX; (3)PriCara Pharmaceuticals Inc., Raritan, NJ.

PURPOSE: This qualitative cross-sectional hospital study evaluates the IV PCA utilization process and identifies the potential errors in the complex logistics of daily IV PCA administration.
METHODS: The staff at 11 US hospitals were interviewed onsite by a research pharmacist for the daily IV PCA logistics (ordering, pump procurement and programming, analgesic preparation and storage, staff education and competency, IV PCA administration, and pump maintenance and repair). The investigator also collected data through observation of the complete IV PCA logistical process. Study design was informed by a literature review and an IV PCA failure mode and effects analysis (FMEA) published by The Institute for Safe Medication Practices (ISMP). Intra and inter-hospital variations were then studied to identify potential medication errors and adverse events within each process step.
RESULTS: The possibility of 28 major (permanent lessening of sensory, motor, physiologic, or intellectual function), and 34 catastrophic (death or major permanent loss of function) error points were identified in relation to the prescription-ordering process, IV PCA pump, analgesic cartridge, and IV tubing. A composite flow chart of IV PCA logistics revealed the involvement of eight people and a minimum of 70 decision points (action steps) and a maximum of 104 per patient per course of therapy. There was significant variation observed within and between hospitals in the daily administration process.
CONCLUSIONS: This study documented the complexity of IV PCA logistics and identified 28 major and 34 catastrophic potential error points associated with the process. When applying the concept of providing patient demand dose and patient-controlled delivery of analgesia, these results highlight the need to develop improved methods of reducing medication errors and adverse events related to IV PCA.

134. Clinical utility of pharmacist medication intervention documentation data. *Laura C. Hobbs, Pharm.D.*, Elizabeth C. Udeh, Pharm.D., Robert A. Quercia, M.S., RPh., Lisa Allen, Ph.D.., Michael E. Dziok, B.S.; Hartford Hospital, Hartford, CT.

PURPOSE: Our goal is to effectively use data collected from our pharmacist medication intervention documentation program. At our institution, intervention data is used for three clinical functions. The first function is to focus education and training for prescribers, nurses, and pharmacists. Second is to help improve computer prescriber order entry (CPOE) processes, and third is to supplement the medication event reporting system.
METHODS: A new pharmacist intervention documentation program was implemented at our institution summer of 2004 in collaboration with the quality management department. Reports about the interventions were developed and shared with pharmacy clinical support team, Therapeutics Committee, Medication Error Reduction Group, and Hospital Quality Council. These forums suggested effective uses of this information for providing education to different disciplines. Reports from the intervention database were being used to tailor alerts in the CPOE system. The intervention program was further designed to populate the hospital medication event reporting system without duplicate documentation by the pharmacists.
RESULTS: To provide feedback to the prescribers, department specific reports with clinical vignettes about high-risk orders on which pharmacists intervened were developed and shared at well-attended monthly meetings. In addition, department-specific interventions are used to supplement nursing in-service material. Interventions are shared periodically at pharmacist in-services to provide examples of excellent patient care. A report on the medications most frequently intervened on for renal dose adjustment is being used for additional alerts in our CPOE system. Capturing of selected interventions significantly increased the number of medication errors submitted by pharmacists into the hospital medication event reporting system.
CONCLUSION: Our intervention program has been well received by administration, pharmacy, medical, and nursing staff. Data from our intervention reports have been used successfully in educating pharmacy, medical, and nursing staff. This program has also been valuable in enhancing our CPOE system and hospital event reporting system.

135. Assessment of the impact of pharmacist-provided medication reconciliation services in the emergency department of a teaching institution. *Lyle Kolnik, Pharm.D.*, Stacey Mayes, Pharm.D., M.S.; St. Luke's Hospital/Mayo Clinic Jacksonville, Jacksonville, FL.

INTRODUCTION: The Joint Commission on Accreditation of Healthcare Organizations has listed medication reconciliation as one of the National Patient Safety Goals of 2005-2006. Medication reconciliation is a method by which healthcare practitioners ensure the completeness of a patient's

medication profile from admission to discharge. Presently, pharmacist-driven medication reconciliation programs are limited in hospitals throughout the country. This study will explore this opportunity by assessing the impact of pharmacist-provided medication reconciliation services in the Emergency Department of a teaching institution.
METHODS: This two-armed study will be conducted prospectively for 3 months during which the pharmacist will be responsible for obtaining medication histories, reconciling medications, differentiating medication allergies from side effects, and identifying drug interactions. This evaluation will be quantified by comparing the total number of order medication clarifications required prior to order entry after nursing/physician-completed medication histories versus pharmacist-completed medication histories. A completely reconciled medication profile contains a comparison of outpatient medications, admission medication history, and inpatient admission orders, and includes an explanation of omitted medications.
RESULTS: The results of both phases will then be analyzed in order to compare consistency and ascertain the impact of pharmacist-provided medication reconciliation services in the ED as it relates to patient safety. A cost savings analysis will be completed to assess potential savings based upon the average cost of an injury resulting from an adverse drug event.
CONCLUSION: Study in progress.

136. Allergy misclassification in three urban academic medical centers. *Michael Gonyeau, Pharm.D., BCPS*, Margarita DiVall, Pharm.D., BCPS, Jennifer Trujillo, Pharm.D., BCPS; Northeastern University School of Pharmacy, Boston, MA.

BACKGROUND: Healthcare workers who obtain medication histories from hospitalized patients frequently do not ascertain the nature of reported drug allergies and reactions nor record such in the medical record. Inaccurate allergy documentation may then be automatically transmitted from record to record without verification. This inappropriate information may result in alterations in prescribing patterns and the use of sub-optimal therapy if the unclarified drug allergy is the gold standard or most effective therapy.
Objectives: To determine the nature of drug allergies in a group of medical inpatients, and to evaluate the accuracy and completeness of allergy documentation by healthcare workers.
METHODS: Patients on medical wards were interviewed by a clinical pharmacist or pharmacy student using a pre-specified interview form to ascertain patient perceived allergies and reactions. This information was then compared with allergies listed in the hospital computer system and the patient's medical record.
RESULTS: Five hundred twenty seven patients were interviewed. The average age of patients was 66 ± 27 years and 45% were men. 238 (45%) patients had ≥ 1 allergy documented in the medical record, while 252 (48%) had ≥ 1 allergy documented in the hospital computer system. However, allergy reactions were listed in only 7% and 5% respectively. One hundred sixty seven patients stated a medication allergy upon interview ($p<0.001$ vs. medical record and $p<0.001$ vs. hospital computer system). Upon further questioning, pharmacists determined that only 67 (40%) of the stated reactions were true allergies ($p<0.001$). There were 104 instances of treatment alteration based on documented patient allergy, with the most common alterations in antibiotic therapy.
CONCLUSION: Medication allergy documentation in patients on medical wards is inaccurate. Patient interview by a clinical pharmacist with pre-specified interview questions resulted in a more accurate patient allergy history. This may translate into decreased medication errors and preserve drug treatment options.

137E. Zonisamide disposition and dosage adjustment when given with phenytoin. *Wesley J. Poynor, Ph.D.*, William R. Garnett, Pharm.D., FCCP; Virginia Commonwealth University Medical Center, Box 980533, Richmond, VA.

PURPOSE: Zonisamide (ZNS) is a broad spectrum antiepileptic drug that exhibits a significant interaction with phenytoin (PHT): the half-life of ZNS is decreased by 60% (from 69 hours to 28 hours) due to the induction of enzymatic metabolic activity by PHT. We explored this interaction and the withdrawal of PHT therapy and its clinical implications for ZNS dosing.
METHODS: Using a pharmacokinetic multiple-dosing model, we simulated the addition of PHT to ZNS monotherapy. We also simulated the withdrawal of PHT from binary therapy. We made reasonable assumptions about the time course of PHT induction and de-induction of oxidative enzyme activity.
RESULTS: The decline in ZNS plasma levels upon adding PHT was 60%; perhaps more significantly, the ZNS plasma levels seen on monotherapy were more than double those seen with PHT co-therapy. We note that in co-therapy with PHT, ZNS dosing levels could easily be pushed from 200 mg BID to as high as 400 mg BID and still have plasma levels in the therapeutic range of 15–30 µg/ml. After withdrawing PHT, the ZNS dose must be decreased to a target level of 200 mg BID. We make recommendations on decreasing the ZNS dose in a stepwise fashion beginning 7 days after discontinuing PHT therapy.
CONCLUSIONS: ZNS dosing when given with PHT can be rationally elevated from the monotherapy dose recommendation of 200 mg BID up to a 400 mg BID level. The adherence to a 200 mg BID dose in co-therapy with PHT may explain apparent failure to achieve additional antiepileptic activity when adding ZNS. The reverse drug interaction occurs when PHT is withdrawn from ZNS therapy. Because of the dramatic effect of PHT on ZNS half-life, dose adjustments are necessary when PHT is withdrawn.
Presented at the Annual Meeting of the American Epilepsy Society, Washington, D.C., December 2-6, 2005.

138. Medication use evaluation and pharmacoeconomic impact of zoledronic acid formulary restriction policy. *Carisa J. Masek, Pharm.D.*, Erin J. Iselin, Pharm.D., Lisa J. Killam-Worrall, Pharm.D., BCPS; The Nebraska Medical Center, Omaha, NE.

PURPOSE: This medication use evaluation (MUE) examined the impact of a Medical Staff/Pharmacy and Therapeutics restriction policy designed to 1) manage the location of administration of intravenous zoledronic acid, 2) monitor adverse events occurring as a result of zoledronic acid administration, 3) evaluate the therapeutic recommendations resulting from the MUE, and 4) evaluate the potential pharmacoeconomic impact of the administration policy.
METHODS: Medical records of patients that received intravenous zoledronic acid in an outpatient cancer care center or the hospital between June 1, 2004, and June 30, 2005, were reviewed. Indication for use of zoledronic acid, location of infusion, dose, dosage schedule, baseline and consequent serum creatinine and serum calcium levels, and presence of adverse events were collected and evaluated.
RESULTS: During the 13-month study period, 98 patients received zoledronic acid. All of the zoledronic acid doses were administered in the outpatient cancer care center. A majority of the patients received zoledronic acid for bone metastases (53%), followed by a diagnosis of multiple myeloma (30%), and hypercalcemia of malignancy (9%). Out of the 419 doses given, 15% required a renal adjustment, and of these 48% were not renally adjusted. For the 9 patients that received zoledronic acid for hypercalcemia of malignancy, 78% experienced a normalization of serum calcium level. Out of the 98 patients receiving zoledronic acid, 2% experienced a rise in serum creatinine, and 30% of patients experienced hypocalcemia. Four patients were switched to pamidronate upon hospital admission, resulting in a potential cost-savings of approximately $5000.
CONCLUSION: The results of the MUE show that the zoledronic acid formulary restriction policy was effective in managing the use of zoledronic acid in the outpatient cancer care center and inpatient setting. The results highlighted areas of education for pharmacy and medical staff. The policy resulted in a potential cost-savings for the institution.

139. Evaluating the safety and cost of bevacizumab use. *Jacqueline K. Schneider, Pharm.D.*, Erin Iselin, Pharm.D., Lisa Killam-Worrall, Pharm.D., BCPS; The Nebraska Medical Center, Omaha, NE.

PURPOSE: A Medication Use Evaluation (MUE) was conducted at The Nebraska Medical Center to monitor the use of bevacizumab in the infusion centers since its addition to the formulary in September of 2004.
METHODS: Medical records of 13 patients who received at least one dose of bevacizumab between September 2004 and August 2005 were reviewed to determine appropriateness of use, safety, and cost. Each chart was reviewed for source of malignancy, administration, monitoring, and adverse drug events associated with bevacizumab, as well as patient history of thromboembolism and hypertension.
RESULTS: The majority of patients received bevacizumab for the approved indication of metastatic colorectal cancer treatment (85%). An adverse drug event was noted in seven patients receiving bevacizumab: an increase in blood pressure (2), proteinuria (2), and thromboembolic event(s) (3). The thromboembolic events were deep venous thromboses with one patient developing a pulmonary embolism as well. One of the two patients who developed hypertension was placed on antihypertensive therapy. During this monitoring period, 3 patients discontinued therapy due to an adverse effect they experienced (thromboembolism (2), proteinuria (1)). The cost of the 81 doses administered during the study time frame was $162,000.
CONCLUSION: The overall use of bevacizumab was appropriate. Due to the high percentage of patients (54%) who experienced an adverse event, monitoring of bevacizumab's use will continue. Another medication use evaluation is scheduled to be conducted in approximately 12 months at The Nebraska Medical Center.

140E. Randomized, double-blind, placebo-controlled study of darbepoetin alfa every 3 weeks for the treatment of chemotherapy-induced anemia. Kerry Taylor, M.D.[1], Peter Ganly, B.M.B.Ch., Ph.D., F.R.C.Path., F.R.C.P.Edin.[2], Veena Charu, M.D.[3], Joseph DiBenedetto Jr., M.D.[4], Karolyn Kracht, Ph.D.[5], *Thomas Lillie, M.B., Ph.D.*[5], Enrique Hernandez, M.D., FACOG, FACS[6];

(1)Mater Hospital, South Brisbane, Queensland, Australia; (2)Canterbury District Health Board, Christchurch, New Zealand; (3)Pacific Cancer Medical Center, Inc., Anaheim, CA; (4)Oncology Hematology Associates, Providence, RI; (5)Amgen Inc., Thousand Oaks, CA; (6)Temple University Hospital, Philadelphia, PA.

BACKGROUND: The ability to administer darbepoetin alfa (DA) every 3 weeks (Q3W) (coincident with chemotherapy) would simplify the treatment of chemotherapy-induced anemia (CIA). We report results from the first multicenter, randomized, double-blind, placebo-controlled, phase 3 clinical trial evaluating efficacy and safety of fixed-dose DA Q3W.
METHODS: This study enrolled patients ≥ 18 years old, anemic (hemoglobin [Hb]<11g/dL), diagnosed with a nonmyeloid malignancy, and scheduled for ≥ 12 weeks of chemotherapy. Patients (N=391) were randomized 1:1 to receive DA 300 µg or placebo Q3W for 15 weeks. DA dose could have been increased or decreased depending on response. Efficacy assessment included incidence of red blood cell transfusions and achievement of target Hb of ≥ 11 g/dL (not ≥ 13g/dL), consistent with evidence-based practice guidelines.
RESULTS: 386 randomized patients were included. Demographic characteristics were similar between the 2 groups. Mean (SD) baseline Hb was 10.03 (0.86) and 10.05 (0.92) g/dL in the placebo and DA groups, respectively. Most common tumor types were breast (23%), colon (11%), nonsmall-cell-lung cancer (10%), and hematologic malignancies (11%). Incidence of RBC transfusions (week 5 to end of treatment phase [EOTP]) was significantly lower with DA (24%; 95%CL:18-30) than with placebo (41%; 95%CL:34-49) (P<0.001). Hb rose steadily in the DA group through approximately week 9, increasing by a mean (SD) of 1.08 (1.28) g/dL from baseline, and then remained relatively stable. The proportion of patients achieving target Hb from week 5 to EOTP was significantly higher with DA (82%; 95%CI:76-88) than with placebo (48%; 95%CI:41-56) (P<0.001). Dose adjustment rules helped to maintain Hb levels within target range. The safety profile of DA was consistent with that observed in previous studies. Rapid increases in Hb concentration or increases to ≥ 13 g/dL were not associated with adverse events.
CONCLUSIONS: Fixed Q3W administration of DA is well tolerated and effective for the treatment of CIA.
Presented at the 47th Annual Meeting and Exposition of the American Society of Hematology, Atlanta, GA, December 10-13, 2005.

141E. Synchronicity: evaluating darbepoetin alfa administered at 300 µg every 3 weeks to treat chemotherapy-induced anemia in breast cancer patients. Peter Silberstein, M.D.[1], Ralph Boccia, M.D.[2], Delong Liu, M.D.[3], N. Simon Tchekmedyian, M.D.[4], Charles Holladay, M.D.[5], Dianne Tomita, M.S.[6], *Thomas Lillie, MB, Ph.D.*[6], Gregory A. Otterson, M.D.[7]; (1)Creighton Cancer Center, Omaha, NE; (2)Center for Cancer and Blood Disorders, Bethesda, M.D.; (3)New York Medical College, Valhalla, NY; (4)Pacific Shores Medical Group, Long Beach, CA; (5)Charleston Cancer Center, Charleston, SC; (6)Amgen Inc., Thousand Oaks, CA; (7)Ohio State University, Columbus, OH.

BACKGROUND: Breast cancer chemotherapies are highly myelosuppressive, often resulting in anemia and reduced quality of life. Darbepoetin alfa (DA) can effectively treat chemotherapy-induced anemia in breast cancer patients (Schwartzberg et al, 2004). DA can be administered at extended intervals, offering the possibility of synchronizing DA dosing with an every 3-week (Q3W) chemotherapy schedule.
METHODS: This 16-week, open label, single-arm study evaluated DA 300 µg Q3W in achieving and maintaining hemoglobin in a target range (11–13 g/dL, consistent with evidence based guidelines) in anemic patients (hemoglobin < 11 g/dL) undergoing chemotherapy. Secondary endpoints included transfusion requirements, incidence of a hematopoietic response, and the mean changes in hemoglobin and FACT-F scores from baseline at the end of study (EOS). Proportion endpoints were analyzed using Kaplan-Meier (KM) methods. The analysis was stratified by baseline hemoglobin (<10 g/dL or ≥ 10 g/dL).
RESULTS: Data from the breast cancer subset are presented (n=354; 29% of all pts). DA 300 µg Q3W effectively alleviated anemia. More patients with baseline hemoglobin ≥ 10g/dL than those with baseline hemoglobin <10g/dL reached target hemoglobin (92% [88–95] vs. 80% [71–89]) and achieved a hematopoietic response (74% [68–80] vs. 72% [62–82]); patients with baseline hemoglobin ≥ 10g/dL also required fewer transfusions (10% [6–14] vs. 25% [16–34]). Hemoglobin increases correlated with clinically significant improvements in quality of life as measured by the FACT-F scale. Safety results were consistent with those reported for this population in other DA studies.
CONCLUSION: DA 300 µg Q3W effectively achieved and maintained hemoglobin in target range. The possibility of increased convenience created by synchronizing DA therapy with common chemotherapy regimens may be important for breast cancer pts who are often younger than pts with other tumor types, more likely to be working, and are often the primary caregivers for their families.
Presented at the 28th Annual San Antonio Breast Cancer Symposium, San Antonio, TX, December 8-11, 2005.

142E. A phase 2, single-arm, open-label trial to evaluate the effectiveness of darbepoetin alfa for the treatment of anemia in patients with low-risk myelodysplastic syndrome. Janice Gabrilove, M.D.[1], Ronald Paquette, M.D.[2], Roger M. Lyons, M.D.[3], Chaudry Mushtaq, M.D.[4], Jan Montgomery, Pharm.D.[4], Mikkael Sekeres, M.D.[5], Hung Lam, Ph.D.[6], *Lyndah Dreiling, M.D.*[6]; (1)Mt Sinai School of Medicine, New York, NY; (2)UCLA Medical School-Hemat & Onc, Los Angeles, CA; (3)US Oncology-Hematology/ Oncology Associates of South Texas, San Antonio, TX; (4)South Carolina Oncology Associates, Columbia, SC; (5)The Cleveland Clinic Foundation, Cleveland, OH; (6)Amgen Inc., Thousand Oaks, CA.

BACKGROUND: Patients with myelodysplastic syndromes (M.D.S) often develop clinically significant anemia due to ineffective hematopoiesis. Erythropoiesis-stimulating proteins (ESPs) like darbepoetin alfa (DA) (150–300 µg/week) can increase hemoglobin concentrations, thereby reducing transfusion requirements.
METHODS: This phase 2, single-arm, open-label trial (planned n=200) is evaluating the efficacy of DA 500 µg given SC every 3 weeks (Q3W) in anemic (hemoglobin ≤ 11g/dL), low-risk M.D.S patients. Eligible patients had low or intermediate-1 risk M.D.S (IPSS/FAB criteria) and no previous/ongoing chemotherapy or biologic response modifiers (except for ESPs [stopped ≥ 7days and ≤ 1month before enrollment] and G-CSF [allowed for infection before enrollment]). Endpoints included proportion of patients achieving an erythroid response during the test period (primary), change in hemoglobin (baseline to wk 13), transfusion incidence, and impact on patient-reported fatigue.
RESULTS: This study has completed enrollment; data are available from a planned interim analysis of the first 100 patients. Of 63 patients who never received an ESP before enrollment (ESP-naive), 51% were female, 81% were white, 73% had low-risk M.D.S, and 22% had intermediate-1 risk M.D.S. 37 patients had previously received ESPs (ESP-treated). Presented as ESP-naive versus E-treated, the crude percentages (95% CI) were 77% (66–88) vs 36% (20–53) for an overall (major plus minor) erythroid response, 47% (34–60) vs 21% (7–35) for a major erythroid response, and 17% (8–27) vs 32% (17–48) for those who required transfusions during wks 1–13. 16% of all patients reported a serious adverse event (none were considered treatment-related). Injection site pain (4% of patients) was the most common treatment-related adverse event. No thromboembolic events have been reported.
CONCLUSION: Interim results from this fully-enrolled study indicate that DA 500 µg Q3W appears to be well tolerated and capable of increasing hemoglobin levels in low-risk M.D.S patients. Final results for the primary endpoint will be presented.
Presented at the 47th Annual Meeting and Exposition of the American Society of Hematology, Atlanta, GA, December 10-13, 2005.

143. Venous thromboembolism prophylaxis: experience with a preprinted risk assessment and prophylaxis order form in a population of family medicine inpatients. *Gary N. Elsasser, Pharm.D.*, Christopher J. Destache, Pharm.D., Mark Goodman, M.D., Donald R. Frey, M.D.; Creighton University School of Pharmacy and Health Professions, Omaha, NE

An informal evaluation of venous thromboembolism (VTE) prophylaxis practices in a population of family medicine inpatients revealed less than optimal use of American College of Chest Physician (ACCP) guidelines. As a result, a preprinted risk assessment and order form was developed for all adult, non-obstetrical admissions whose predicted length of stay was to exceed 24 hours. The project goals were: 1) to increase the awareness among family medicine staff and residents of the risks for VTE in medical patients; 2) assist in identifying those patients who may benefit from VTE prophylaxis; and 3) to increase the utilization of ACCP supported regimens to optimize prophylaxis practices. The VTE risk assessment and order form was approved at a faculty meeting, the Forms Committee and Pharmacy and Therapeutics of the hospital. A presentation to family medicine staff and residents preceded the implementation of the form on February 15, 2005. Approximately every 2 weeks thereafter, reinforcing presentations were provided along with reminder notes and signs distributed throughout the department encouraging residents and staff to use the form. The form was used in 43 of 210 (20.5%) eligible patients from March 1, 2005 to May 31, 2005. An in-depth retrospective chart review is currently under way intended to compare the utilization of VTE prophylaxis practices before and after initiation of the form and secondarily to determine if there is an improvement in the rate of adherence to ACCP guidelines. We will present data comparing the two populations reviewed for demographics, VTE risks, and prophylactic measures utilized.

144. Retrospective comparison of flunisolide and formoterol versus fluticasone/salmeterol for chronic obstructive pulmonary disease in a veterans affairs medical center. *Christopher Degenkolb, Pharm.D.*, Melanie Kuester, Pharm.D.; Richard L. Roudebush Veterans Affairs Medical Center, Indianapolis, IN.

Based on the current Global Initiative for Chronic Obstructive Lung Disease

guidelines for management of chronic obstructive pulmonary disease (COPD), patients with an FEV_1 of less than 50% of predicted value who are started on an inhaled corticosteroid have been shown to have decreased exacerbations and thus improved health status. The combination of an inhaled corticosteroid with a long-acting beta-2 agonist is more effective than either therapy alone. The Roudebush VA Medical Center has multiple inhaled corticosteroids as well as two long-acting beta-2 agonists on formulary. Although the preferred formulary agents have been the flunisolide and formoterol inhalers, the fluticasone and salmeterol combination inhaler has been the most frequently used at a significantly higher cost to the institution. The objective of this analysis is to determine whether the two treatment options are similar in efficacy as well as patient compliance in order to aid in the selection of a preferred regimen. Patients with a diagnosis of COPD, who were prescribed a combination of flunisolide and formoterol inhalers or a fluticasone/salmeterol inhaler within the past two fiscal years, have been selected via a computerized database. In addition to baseline characteristics, charts will be reviewed and data collected to determine the number of COPD exacerbations, refill history, and adverse drug reactions. Finally a cost-effectiveness analysis will be performed to determine the most appropriate regimen based on the information collected. Upon final analysis, a recommendation of the most cost-effective corticosteroid and long-acting beta-2 agonist combination will be made to the Pharmacy, Nutrition and Therapeutics committee of the institution for preferred status on the formulary.

145. Economic impact of pharmaceutical intervention in the care of human immunodeficiency virus patients. *Branca S. Teixeira, Dr.*, Barbara G. Santos, Dr., Teresa Cunha, Dr., Gustavo Dias, Dr., José Neves, Dr., Jorge Brochado, Dr.; Pharmacy Department St Antonio General Hospital, Porto, Portugal.

PURPOSE: Determine the adherence of human immunodeficiency virus (HIV) patients to the antiretroviral regiments treated in St. Antonio General Hospital during 2004 and the direct costs of the non-adherence. Identify the possible causes of non-adherence to antiretroviral treatment. Establish guidelines on the pharmacist's role in the care of patients with HIV infection.
METHODS: Retrospective analysis of HIV patients' pharmaceutical records. Literature review.
RESULTS: HIV patient records (316 records) were analysed between January and December 2004, 35.74 % of these were non-compliant, which directly implied a cost of 557147.12 Euros. We were able to identify the following possible factors associated with non-adherence to antiretroviral therapies: mental illness, unstable housing, active substance abuse, antiretroviral adverse effects, dietary, pill burden, and inconvenient frequency of drug administration.
CONCLUSIONS: Pharmacists have a role in the care of HIV patients. Clinical pharmacists who provide these services are responsible for the quality of care, the satisfaction of patients and the efficient use of resources. The potential benefits to patients include access to medication information, the prevention and resolution of medication-related problems, improved outcomes and increased satisfaction. This study demonstrates the importance and effectiveness with respect to disease outcomes of the pharmacist's role in educating the patient about his or her disease and medications and the economic and professional credit for value-added services.

146. Evaluating the efficacy and tolerability of ketolide and macrolide antibiotics at a large managed care organization. *David Feng, Pharm, D*[1], Saira Jan, Pharm, D[1], Daniel Flores, Pharm, D[2]; (1)Horizon Blue Cross Blue Shield of New Jersey, Newark, NJ; (2)Pfizer Inc., Morris Plains, NJ.

PURPOSE: Macrolides are commonly prescribed antibiotics, often used in the outpatient treatment of upper respiratory infections (URI's).[1, 2] Telithromycin is the first of a new class of antibiotics, the ketolides, which are structurally similar to the macrolides. The FDA has approved telithromycin for the treatment of community acquired pneumonia (CAP), acute exacerbation of chronic bronchitis (AECB), and acute bacterial sinusitis (ABS) in adults.[3] In-vivo studies demonstrate efficacy of telithromycin equal to other commonly prescribed outpatient antibiotics; however, in-vitro studies have shown improved effectiveness in eradicating strains of penicillin-resistant streptococcus pneumoniae (PRSP), a common URI pathogen.[6–9] The purpose of this analysis is to compare telithromycin to macrolide antibiotics and to determine whether differences in the efficacy and/or tolerability can be identified in the setting of a large Managed Care Organization (MCO).
METHODS: A retrospective pharmacy claims analysis of MCO plan members receiving a prescription for a macrolide, or ketolide antibiotic during the 2004-05 flu season. Patients were included if they had a corresponding diagnosis code for CAP, ABS, or AECB within ±15 days of the index prescription. Treatment failures were defined as the filling of a second oral antibiotic (ketolide, macrolide, fluoroquinolone, or beta-lactam antibiotic) prior to the anticipated completion, or within 10 days of the anticipated end of therapy of the index treatment. Statistical analysis was performed using a Chi-Square test of independence.
RESULTS: A total of 13,709 patients were included in the study, with the majority receiving a macrolide antibiotic (90.5% vs. 9.5%). Overall failure rates were highest in the telithromycin group (13.11%), compared with either clarithromycin (11.96%) or azithromycin (9.65%). Higher telithromycin failure rates were evident, both for failures due to lack of efficacy or tolerability.
CONCLUSIONS: We find no evidence to suggest that first-line use of telithromycin results in improved outcomes in an outpatient real world setting.

147. Implementation of a clinical documentation system with PDA capability at a large academic medical center. *Morton P. Goldman, Pharm.D., BCPS*, Michael A. Militello, Pharm.D., Michael Adams, B.S., Brad Main, R.Ph.; The Cleveland Clinic Foundation, Cleveland, OH.

PURPOSE: Documenting interventions is important for justification of clinical pharmacy services. A commercial documentation system that had been utilized at our institution was upgraded in a manner that was not compatible with our existing hardware. It was determined that it would be most cost effective to develop an institution-specific documentation system that could be customized to our specifications and incorporate PDA technology.
METHODS: A committee was convened to determine the key components for an effective system. These included speed and ease of use, complete array of intervention and outcomes choices with drop-down boxes to minimize free text, patient information from our ADT system, our formulary with associated costs, ability to calculate direct cost savings, data entry via desktop or PDA, and flexible report-generating capability.
RESULTS: The internally developed Clinical Documentation System was implemented in the fall of 2003. Fifteen different types of interventions can be documented including drug information, discontinuation of drug, changing dose or drug, drug interactions, initiating therapy, IV to PO, etc. Clinical impact is documented as preventing toxicity or side effect, improved efficacy, unnecessary therapy, facilitating continuity of care, cost effectiveness, and improved compliance. Direct cost savings is automatically calculated utilizing both AWP and institution specific data. Activities outside and within the institution such as presentations, publications, etc., are also documented. Clinical Specialists use both desktop and PDA applications and are satisfied with the speed and ease of data entry. More than 19,000 interventions were documented in this system in 2004..
CONCLUSION: The implementation of an internally developed Clinical Documentation system allowed us the flexibility to establish a method of documentation that is customized to our exact specifications. A number of changes will be implemented by the end of 2005 to upgrade the system. Overall satisfaction among users is excellent.

148. Documentation of clinical interventions and activities using a Web-based tool within a psychiatric facility. Indu Lew, Pharm.D.[1], *Krina Patel, Pharm.D.*[2], Robert T. Adamson, Pharm.D.[1], Kim Walsh, R.Ph.[2]; (1)Saint Barnabas Health Care System, West Orange, NJ; (2)Saint Barnabas Behavioral Health Center, Toms River, NJ.

PURPOSE: Hospital pharmacists have demonstrated their importance in improving patient care by intervening in the medication use process and educating health care professionals and patients. In this era of fiscal constraints, documentation of clinical interventions and activities is essential to the practice of pharmacy. Objective is to document the clinical interventions, activities, cost savings and revenue-generating services of pharmacists and residents in a psychiatric facility.
METHODS: All clinical interventions and activities performed in a 1-year period by pharmacists and residents were documented in HealthProLinkÆ, a commercially available, Web-based documentation software. Documentation involved the following global categories: automatic therapeutic substitutions (ATS), committee work, order clarification, education, laboratory analysis, quality assurance, renal dose adjustment, inpatient and outpatient group counseling, therapeutic interventions, and pain consultations. Associated cost savings for each intervention was determined using actual contract pricing. Each pharmacist-managed pain consultation resulted in a cost savings of $100 per patient, which would have been charged to the facility as a physician-managed consult. Revenue generation for outpatient group counseling ranged between $120 and $180 per patient, per session.
RESULTS: A total of 4,292 interventions and activities with a corresponding cost savings and revenue generation of $88,388 were documented in the study period. Documented clinical interventions and activities by global categories were: ATS (n=65), committee work (n=13), order clarification (n=894), laboratory analysis (n=724), quality assurance (n=570), renal dose adjustment (n=542), education (n=359), group counseling (n=508), therapeutic interventions (n=484), and pain consultations (n=133). The cost savings by global categories were: ATS ($308), renal dose adjustment ($31), therapeutic interventions ($13,789), and pain consultations ($13,300). The revenue generated by outpatient group counseling was $60,960.

CONCLUSIONS: This tool serves as an effective method for documenting clinical activities and interventions in real time with corresponding cost savings.

149. Enhancements of the physician-directed, pharmacy-managed intravenous to oral conversion program at a large metropolitan teaching hospital. *Erin J. Iselin, Pharm.D.*; The Nebraska Medical Center, Omaha, NE.

PURPOSE: Recent enhancements to an existing intravenous (IV) to oral (PO) program include expansion of the program to all inpatient populations, including neonate and pediatric populations, and implementation of documentation of IV to PO interventions in a clinical pharmacy database. The clinical tool was designed to help 1) establish an accurate conversion rate, 2) obtain cost savings information, and 3) show possible barriers to the conversion process.
METHODS: The clinical tool was queried for data collected between April 1, 2005, and September 30, 2005, at one large metropolitan teaching hospital. Data queried for analysis was the date a specified IV medication was initiated, date criteria was met for conversion to PO medication, physician acceptance of the conversion, length of therapy, and the specified hospital unit.
RESULTS: Sixteen approved IV medications were analyzed for conversion to a therapeutic PO alternative medication for two quarters. The IV medications eligible for conversion during the reported period were 2,238 and 2,492 respectively. These opportunities produced conversion rates of 35% and 28.5% respectively. Declination of the conversion by a physician did not play a significant role. Barriers to the conversion process included IV medications being discontinued before the patient was identified as meeting criteria and absent pursuits to identify medications to convert. Cost savings with oral therapy for the reported period was estimated at $51,000.
CONCLUSION: The analysis of the intravenous to oral program illustrated that the conversion rate was below the desired goal of 80%, but was making better strides than the previous program. The enhancements to the program documented all possible opportunities and successful conversions in addition to enabling cost savings to be calculated. Barriers to the conversion process have been identified and are being assessed to ultimately increase future conversion rates and subsequently increase cost savings and produce a positive patient outcome.

150. Use of a tablet personal computer to enhance patient care on patient care rounds on a bone marrow transplant unit. *Michael Cockerham, M.S., Pharm.D., BCOP*; ULM College of Pharmacy, Shreveport, LA.

PURPOSE: Clinical pharmacists have demonstrated a positive impact on patient care; however, critical to the effectiveness of the pharmacist is the ability to access patient and pharmaceutical databases in a timely manner. The purpose of this project was to demonstrate the usefulness of a light-weight, portable Tablet PC system to access hospital patient databases, pharmacy medication profiles, and Internet accessible pharmaceutical databases while on patient care rounds and to demonstrate the feasibility of collecting data for clinical trials, medication use evaluations and adverse drug reaction reporting.
METHODS: A Motion Computing LE1600 Tablet PC was purchased, with wireless and Bluetooth technology, Integrated Fingerprint Reader, and Microsoft Office 2003 Professional Edition software. The study consisted of two study periods. The first 2 months data were prior to use of the Tablet PC in clinical practice. The second 2-month period data will be collected using the Tablet PC on patient care rounds. Data were collected on the numbers of Adverse Drug Events reported, pharmacy orders processed, databases accessed, progress notes written, and an objective evaluation of the computers' usefulness.
RESULTS: Data are still being collected, and the evaluation period will be completed in February 2006. Systems accessed via the Tablet PC include: oncology patient data, NetAccess with multiple patient databases, Seimans Pharmacy System, the LSUHSC Shreveport Library with 53 online databases, 1850 electronic journals and 235 electronic textbooks, MicroMedex, Lexi-Drugs Online, M.D. Consult, hospital formulary, and oncology clinical practice guidelines.
CONCLUSIONS: It is essential that pharmacists have the necessary resources to be able to administer pharmaceutical care. Personal Digital Assistants (PDAs) have significantly improved the portability and availability of medical references to health care providers. The advantages of a portable PC with access to greater numbers of databases and references are a step forward in patient therapeutic efficacy, safety, and confidentiality.

151. Impact of a pharmacy-managed medication reconciliation program. *Sanjeev K. Bhanot, Pharm.D.*, James Fuller, Pharm.D., Steven R. Abel, Pharm.D., Sharon M. Erdman, Pharm.D.; Wishard Health Services and Purdue University School of Pharmacy, Indianapolis, IN.

PURPOSE: The Joint Commission on Accreditation of Healthcare Organizations has identified medication reconciliation as a 2006 national patient safety goal. The purpose of this study was to evaluate the impact of pharmacy-managed medication reconciliation at a county teaching hospital in Indianapolis.
METHODS: Fourth professional year pharmacy students conducted medication histories on hospitalized adult patients to identify medications taken prior to admission for comparison to admission medication orders. A pharmacist evaluated any identified discrepancies, and the pharmacy student communicated recommendations to the primary medical service. The frequency and nature of the pharmacy interventions were collected. Interventions were defined by type of error (omission, incorrect order, or duplicate therapy) or other therapeutic recommendation.
RESULTS: In a 4-month period, 1753 medications were evaluated for reconciliation in 316 patients. Overall, 1708 (97.4%) of the medications were reconciled. The remaining 45 (3.6%) medications were not reconciled as a result of patient discharge prior to follow-up. Of the 1753 medications, 97 (5.5%) required a pharmacist intervention to become reconciled. The types of interventions included: omission of an outpatient medication on admission orders (61.9%); incorrect medication order such as wrong dose or schedule (26.8%); duplicate therapy (2.1%); and other therapeutic recommendation (10.3%). A pharmacist intervention was required in 46 (14.6%) patients in order to reconcile their medications.
CONCLUSIONS: A considerable number of pharmacist interventions were required to reconcile medications for hospitalized patients through a pharmacy-managed medication reconciliation program at a county teaching hospital.

152. Pharmacist-provided bone density screenings in the female population. *Kimberly D. Mitchell, Pharm.D.*[1], Kimberly M. Crosby, Pharm.D.[2]; (1)Southwestern Oklahoma State University College of Pharmacy and May's Drug Stores, Inc., Tulsa, OK; (2)The University of Oklahoma College of Pharmacy and May's Drug Stores, Inc., Tulsa, OK.

PURPOSE: Pharmacist-provided community bone density screenings may help to target sub-populations at risk for premature bone loss. Current guidelines from the U.S. Preventive Services Task Force recommend that all women 65 years of age and older and women 60 years of age and older with one or more risk factors for osteoporosis receive bone density screening. Screening women who fall outside this guideline may identify 1) women who are at increased risk for osteopenia/osteoporosis, and 2) risk factors that are common among this younger population.
METHODS: Ultrasound bone density measurements were recorded from women 18 years of age and older participating in community health screening events. Each subject was asked to complete an osteoporosis questionnaire, which included questions regarding age, exercise habits, personal fracture history, dietary calcium intake, and other osteoporosis risk factors. All subjects received counseling regarding lifestyle and risk factor modification.
RESULTS: Between August 2004 and November 2005, 759 subjects received bone density screenings. Subject data were analyzed to identify sub-populations with reduced bone density as measured by T-score. Forty-five percent of smokers, 40% of women with a body weight less than 70 kilograms, and 26% of women who reported > 8 hours of exercise per week had an abnormal T-score less than -1.0.
CONCLUSIONS: Women with dietary and lifestyle risk factors related to osteoporosis often fall outside current recommended screening range by age. These women may benefit early in the disease process from pharmacist-provided education in the community setting.

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.

153. Effect of antifibrinolytic prophylaxis on transfusion rates for on-pump cardiac surgeries. *Evan Z. Ramsey, Pharm.D.*[1], Wendell S. Akers, Pharm.D., Ph.D.[2], Douglas T. Steinke, Ph.D.[2], Kelly M. Smith, Pharm.D.[2], John A. Armitstead, M.S., FASHP[1], Phillip C. Camp, M.D.[1], Chandrashekar Ramaiah, M.D.[1], Victor Ferraris, M.D., Ph.D.[1], Jeremy D. Flynn, Pharm.D.[1]; (1)University of Kentucky Chandler Medical Center, Lexington, KY; (2)University of Kentucky College of Pharmacy, 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, such as aprotinin and ε-aminocaproic acid, have been shown to decrease blood loss and transfusion requirements. The purpose of this study is to compare the outcomes associated with the use of aprotinin and ε-aminocaproic acid in on-pump cardiac surgeries at our 473-bed teaching hospital.

METHODS: A billing database was utilized to identify cases that met inclusion criteria [age>18 years, cardiothoracic surgery (not transplant or congenital in nature) requiring CPB]. A retrospective chart review of each patient's medical record was conducted to ascertain demographic data and antifibrinolytic prophylaxis used, and stratify severity of disease. Primary end points investigated were amount of blood products transfused following surgery, chest tube drainage in the first 24 hours following surgery, need for re-exploration, and adverse events. Upon completion of the study, we plan to include data from approximately 50 patients who received no prophylaxis for comparison with the antifibrinolytic agents. A regression analysis will be conducted to identify predictors and evaluate the risk of bleeding with each antifibrinolytic agent used.
RESULTS: Data collection has been completed for 39 of 300 patients, 97% (38/39) of which received antifibrinolytic prophylaxis: 63% (24/39) aprotinin and 37% (14/39) ϵ-aminocaproic acid. Of those receiving aprotinin, 54% (13/24) required blood products and experienced an average 24-hour chest tube output of 801.3 mL; 8% (2/24) needed surgical re-exploration. Among the ϵ-aminocaproic acid patients, the average 24-hour chest tube output was 557.8 mL, and 38.5% received blood products; 0 required re-exploration. No allergic reactions or thrombotic events were noted. Final data will be presented to our Cardiothoracic surgery faculty in an effort to standardize our approach to antifibrinolytic prophylaxis based upon procedure and risk.

154. An evaluation of potassium and magnesium replacement nomograms in the heart failure special care unit (HFSCU). *Tyrone Lin, Pharm.D.*, Jodie M. Fink, Pharm.D., Michael A. Militello, Pharm.D.; The Cleveland Clinic Foundation, Cleveland, OH.

PURPOSE: Potassium and magnesium replacement nomograms were developed for patients in the heart failure special care unit at risk of hypokalemia, hypomagnesemia, and ventricular arrhythmias. The goal of this study is to evaluate the efficacy and safety of both nomograms.
METHODS: A medical chart review was conducted in all patients initiated on the nomograms in the HFSCU over a 3-month period. The primary objective was to assess the percent of patients who reached goal potassium (4.0 to 5.0 mmol/L) and magnesium (2.0–2.4 mg/dL) during the first 24 hours of nomogram initiation. Secondarily, the length of time to goal potassium and magnesium, concomitant medications that may affect potassium and magnesium levels, and safety of the nomograms were assessed. Patients with renal dysfunction were evaluated separately.
RESULTS: Fifty patients (mean age: 54 years, 60% male) were analyzed. 74% (34/46) reached goal potassium within 24 hours (mean 18 hours). Key factors affecting time to goal potassium were urine output, potassium level at initiation, and medications. Goal magnesium within 24 hours occurred in 71% (24/34) of patients. As a function of the nomogram, the mean time to goal was longer with magnesium than potassium. In patients with renal dysfunction, 91% (10/11) and 43% (3/7) reached goal potassium and magnesium within 24 hours, respectively. No patients developed hyperkalemia (>5.0 mmol/L) or hypermagnesemia (>3.0 mg/dL).
CONCLUSION: The potassium and magnesium nomograms are effective and safe in heart failure patients. Goal potassium was achieved more frequently in patients with renal dysfunction due to decreased potassium elimination. Improvements to both nomograms should be focused on patients who take > 24 hours to reach goal.

155. An evaluation of anticoagulation control in heart failure: a descriptive assessment of the quality of anticoagulation control and the risks of adverse events in heart failure patients on warfarin. *Katherine W. Phillips, Pharm.D.*, Toby Trujillo, Pharm.D., BCPS; Boston Medical Center, Boston, MA.

PURPOSE: Patients with heart failure due to systolic dysfunction (EF < 40%) are at an increased risk of thromboembolism, and many physicians routinely anticoagulate these patients even in the absence of other indications for warfarin (atrial fibrillation, mechanical heart valves, etc.) However, the yearly incidence of thromboembolic events in heart failure patients is lower (1.8–2.5%) as compared to patients with atrial fibrillation (5%) or with mechanical heart valves (12–22%). Consequently, one may question whether the absolute benefit of warfarin outweighs the potential risks in the heart failure population. Available literature does not suggest that warfarin improves outcomes in heart failure, and limited information exists regarding the risks of anticoagulation with warfarin in these patients. The purpose of this study is to assess the risks of anticoagulation in group of cardiomyopathy patients anticoagulated with warfarin.
METHODS: A retrospective, observational chart review will be conducted evaluating patients followed at the Boston Medical Center cardiomyopathy clinic. Patients will be included if they have systolic dysfunction and received anticoagulation with warfarin for at least 3 months. The primary end point will be to describe the quality of INR control in this population. Secondary end points will include the incidence of bleeding and thromboembolic events.
RESULTS: 215 patients have been identified for inclusion. Current interim analysis includes 7664 total patient days and an average ejection fraction of 14%. 51.9% of all INR values are within the goal INR range. As assessed through linear interpolation, only 41.1% of total patient days were within the goal INR range.
CONCLUSION: Quality of anticoagulation in this heart failure population is substandard compared with the current standard of practice in national guidelines, potentially indicating that heart failure patients are more difficult to control. Full results, including the incidence of bleeding and thromboembolic events, will be presented.

156. Evaluation of current preventive regimens for contrast-induced nephropathy in patients undergoing cardiac catheterizations. *William Alvarez, Jr., Pharm.D., BCPS*, Steven Schulman, M.D., Keri Hyde, R.N., M.S.N., M.P.H., Amy Entis, R.N., M.S.,; The Johns Hopkins Hospital, Baltimore, M.D.

PURPOSE: This retrospective chart review was conducted to determine the incidence of CIN in patients receiving oral n-acetylcysteine plus IV hydration (Group I), IV sodium bicarbonate (Group II) or oral n-acetylcysteine plus IV sodium bicarbonate (Group III).
METHODS: Medical records of patients admitted to the coronary care unit that received one of the aforementioned preventive regimens and underwent cardiac catheterization between September 1, 2004 and July 31, 2005, were reviewed. Exclusion criteria selected were similar to other larger randomized controlled clinical trials evaluating CIN. Patients' demographics, risk factors for CIN, medications administered pre-catheterization, and preventive regimens were documented.
RESULTS: Medical records from 232 patients receiving one of the preventive regimens were reviewed. Fifty-two patients met inclusion criteria (30 Group I, 5 Group II, and 17 Group III). All patients received the isoosmolar contrast media iodixanol. The average amount of iodixanol administered was 214 mL. Overall, 14 patients (27%) developed CIN following cardiac catheterization. Eight patients (57%) in Group I, 1 (7%) in Group II, and 5 (36%) in Group III developed CIN. At least one CIN risk factor was found in 38 (73%) of the patients. The most common risk factor was heart failure (average ejection fraction of 22%).
CONCLUSION: Among the groups, the incidence of CIN was similar. However, a larger prospective trial with equal numbers of patients is needed to confirm these results. It was also found that the combination of oral acetylcysteine plus IV sodium bicarbonate was frequently used. It is unknown whether or not this combination has additional protection against the development of CIN.

157. Assessment of relationships between antibiotic use and susceptibility of microorganisms in a surgical trauma intensive care unit. *Brian P. Anger, Pharm.D.*, Cathy L. Worrall, Pharm.D., BCPS, BCNSP, FAPhA, Nicole A. Weimert, Pharm.D., John A. Bosso, Pharm.D., BCPS, FCCP; Medical University of South Carolina, PO Box 250132, Charleston, SC.

PURPOSE: A relationship between antibiotic use and bacterial susceptibility is thought to exist. Realizing that unit-specific susceptibility and prescribing patterns may vary from hospital-wide data, we began tracking these data in our surgical trauma intensive care unit (STICU) in 2002. Over time, this information may affect empiric antimicrobial therapy decisions.
METHODS: Census, antibiotic usage, and microbiology data were obtained from the admissions, pharmacy, and microbiology departments, respectively. Defined daily dose per 1000 patient days (DDD/1000 PD) was used as the marker of drug usage. Percent susceptibility (%S) for gram positive and gram negative organisms was considered versus DDD/1000 PD for organisms with at least 10 isolates per year after duplicate isolates were eliminated. Duplicate isolates were defined as any organism with the same susceptibility pattern from the same site in the same patient.
RESULTS: Among 20 genera of organisms isolated, six met our criterion for inclusion: *Pseudomonas aeruginosa*, *Acinetobacter* spp., *Enterobacter* spp., coagulase (-) *staphylococci*, methicillin-susceptible *Staphylococcus aureus*, and methicillin-resistant *S. aureus*. An outbreak of unit-specific multidrug-resistant *Enterobacter* and *Acinetobacter* species occurred in 2004 that did not appear to be related to antibiotic usage patterns. For *P. aeruginosa*, the expected inverse relationship between drug usage and susceptibility occurred for certain antibiotics. For example, our unit-specific cefepime and ciprofloxacin susceptibilities have increased to 66% and 82% with declining drug use compared to susceptibilities of 55% and 64% institution-wide, respectively. In contrast, piperacillin/tazobactam susceptibility has not changed despite increased empiric use in our unit. Tobramycin displayed an unexpected increase in susceptibility from 85% to 100% with increased drug usage.
CONCLUSIONS: Further data are needed to determine the statistical and clinical significance of drug prescribing and antimicrobial susceptibility patterns in our STICU. The 2005 data will be added to the database in early 2006.

158. Incidence of venous thromboembolism in neurocritical care patients. *Keri S. Kim, Pharm.D.*[1], Gretchen M. Brophy, Pharm.D., BCPS[2]; (1)University

of Illinois Medical Center at Chicago, Chicago, IL; (2)Virginia Commonwealth University, Medical College of Virginia Campus, Richmond, VA.

INTRODUCTION: Neurosurgical patients may be categorized as a high-risk group for developing venous thromboembolism (VTE); however, there is a concern about administering anticoagulant agents for thromboprophylaxis in patients with intracerebral hemorrhage due to potential cerebral bleeding complications. This study describes the incidence of VTE in the neurocritical care patient population at a level I trauma center.
METHODS: This retrospective, descriptive study evaluated neuroscience intensive care unit patients admitted between January 2001 and July 2004 with an ICD-9 code for one of the following disease states: traumatic brain injury, subarachnoid hemorrhage, and intracranial hemorrhage. Then, a database search was done to determine which of these patients were also diagnosed with a VTE during their hospital stay, and a chart review was then conducted on these patients.
RESULTS: 1199 subjects met the inclusion criteria and 39 of these patients were diagnosed with VTE. Currently, 33 of the 39 subjects have been evaluated and data collection will soon be completed. The incidence of new onset VTE was 3.3%. Venous thromboembolic events occurred in 17 patients with traumatic brain injury, 10 patients with subarachnoid hemorrhage, and 12 patients with intracranial hemorrhage. All patients were started on intermittent pneumonic compression devices on the day of admission and the majority of the subjects received unfractionated heparin 5000 units subcutaneously every 12 hours within 24 hours of admission (19 out of 33 subjects). DVT accounted for 95% VTE events and the median hospital day of diagnosis was day 19 (range 4–51 days). Computed tomography scans confirmed no hematoma growth in any of the VTE patients during their hospital stay.
CONCLUSIONS: The incidence of VTE in patients with intracerebral hemorrhage was 3.3%, with a majority of patients experiencing DVTs. Pharmacologic prophylaxis of VTE can be administered within 24 hours of injury without evidence of further cerebral complications.

159. Pharmacy resident attitudes toward pharmaceutical promotion. *Sumer L. Ashker, Pharm.D.*, Jill S. Burkiewicz, Pharm.D.; Midwestern University Chicago College of Pharmacy, Downers Grove, IL.

PURPOSE: Pharmaceutical industry promotional activities involving healthcare professionals are extremely prevalent. Research shows that physician-industry interactions are likely to influence physicians' prescribing and professional behaviors. Industry-sponsored educational events have been associated with increased prescription rates. For this reason, some medical residency programs have developed educational programs that train medical residents to critically evaluate pharmaceutical promotion. Research concerning pharmacist-industry interactions is less common than research concerning physician-industry interactions. Little is known regarding the effects of these interactions on the knowledge and practice of pharmacy residents. However, interactions between the pharmaceutical industry and pharmacy residents are growing. This study will investigate the opinions of pharmacy residents toward pharmaceutical promotion, and the effects it has on their attitudes and professional practice.
METHODS: An electronic, anonymous, multiple choice survey will be distributed to 500 general and specialty pharmacy residents via electronic means. Questions will investigate opinions regarding ethics and appropriateness of pharmaceutical industry promotion. They will also investigate opinions regarding industry-sponsored meals, educational events, gifts, and pharmaceutical sales representatives. In addition, questions will investigate the perceived influence that pharmaceutical promotion has on the professional knowledge and practice of pharmacy residents. Other questions will inquire whether pharmacy residency programs have policies or offer training regarding resident-industry interactions. Descriptive statistics and the Mann-Whitney U test will be used to report results.
RESULTS: Results are pending.
CONCLUSIONS: Information regarding pharmaceutical industry influence on pharmacy residents may help to determine whether educational intervention is necessary during pharmacy residency programs.

160. Effects on the lipid profile after conversion from rosiglitazone to pioglitazone in Native American, type 2 diabetic patients. *Jodi N. Sparkman, Pharm.D.*[1], Ryan R. Schupbach, Pharm.D.[1], Jeffrey Stroup, Pharm.D.[2], David Wilkett, D.O.[1]; (1)Claremore Indian Hospital, Claremore, OK; (2)University of Oklahoma College of Pharmacy, Tulsa, OK.

OBJECTIVE: Thiazolidinediones regulate the body's response by altering the transcription of genes controlling glucose and lipid metabolism. Recent literature has shown a more favorable lipid profile with the use of pioglitazone versus rosiglitazone, resulting in an increase in HDL-C, decrease in triglycerides, and no change in LDL-C and total cholesterol. The objective of this study is to identify whether there is a difference in the lipid profile in the Native American population, when rosiglitazone is replaced with pioglitazone.
METHODOLOGY: The conversion of rosiglitazone to pioglitazone is as follows per P&T committee: 2 mg rosi daily to 15 mg pio daily (group 1), 4 mg rosi daily to 15mg pio daily (group 2), 8 mg rosi daily to 30 mg pio daily (group 3), and 4 mg rosi twice daily to 45 mg pio daily (group 4). Electronic chart review will identify patients diagnosed with type 2 diabetes currently treated with pioglitazone. The primary outcome will be change in the fasting lipid panel. The following data will be collected: lipid levels including total cholesterol (TC), LDL-C, HDL-C, and triglycerides (TG) while taking rosiglitazone and after a minimum of 12 weeks of pioglitazone therapy. Secondary outcomes measured will be change in weight, BMI, ALT, AST, and HbA1c.
RESULTS: Baseline data as mean (mg/dL) as follows: Group 1 TC = 163.95, LDL-C = 87.98, HDL-C = 38.55, TG = 187.15; Group 2 TC = 175.20, LDL-C = 99.76, HDL-C = 34.70, TG = 205.10; Group 3 TC = 185.83, LDL-C = 104.78, HDL-C = 38.52, TG = 232.40; Group 4 TC = 182.17, LDL-C = 99.73, HDL-C = 36.79, TG = 223.19.

161. Pharmacy resident participation in cardiopulmonary resuscitation events. *Meredith B. Toma, Pharm.D.*[1], P. Shane Winstead, Pharm.D.[1], Kelly M. Smith, Pharm.D.[2], Daniel A. Lewis, Pharm.D.[1], Timothy Clifford, Pharm.D.[1]; (1)University of Kentucky Chandler Medical Center, Lexington, KY; (2)University of Kentucky College of Pharmacy, Lexington, KY.

PURPOSE: Little data are available describing the role of pharmacists in cardiopulmonary resuscitation (CPR) events. Most publications indicate that pharmacists are responsible for drug admixture and provision of drug information. However, there are no data specifically describing pharmacy resident participation in CPR events. A survey of accredited pharmacy residency programs was conducted to determine the participation of pharmacy residents in CPR situations. Secondary objectives include identification of pharmacy staff responsibilities, educational methods used to train pharmacy staff and residents, and evaluation methods used to assess competency for personnel that respond to CPR events.
METHODS: A 46-question survey was developed, and IRB approval obtained. The survey was tested internally and externally prior to final distribution. The survey was sent to all residency program directors at ASHP-accredited residency programs via Survey Monkey, a Web-based distribution tool. A total of 720 residency program directors were contacted via e-mail, as listed in the ASHP online residency directory. Respondents were asked to complete the survey within 3 weeks of the invitation, with two electronic reminders sent to prompt response.
RESULTS: Survey response is ongoing. Currently, 15% of program directors have responded (108/720). Approximately 30% of survey respondents require resident participation in CPR events, while roughly 40% state that resident response to CPR events is optional and dependent on rotation. Eighty-two percent of respondents indicate that there is a formal CPR team at their institution, with pharmacy staff included 84% of the time. The primary duties of responding pharmacy personnel have been listed as drug admixture (89%) and provision of drug information (94%).
CONCLUSIONS: Final results of this survey will help to categorize the level of involvement of pharmacy residents in CPR events, describe their assigned roles, ascertain training methods, and determine assessment methods for pharmacy staff that respond to CPR events.

162. Antiretroviral resistance patterns in a rural southern state. *Molly E. Kent, Pharm.D.*[1], David J. Feola, Pharm.D., Ph.D., BCPS[2], Kelly M. Smith, Pharm.D.[2], Ardis Hoven, M.D.[1], Frank Romanelli, Pharm.D., BCPS[2]; (1)University of Kentucky Chandler Medical Center, Lexington, KY; (2)University of Kentucky College of Pharmacy, Lexington, KY.

PURPOSE: To document the rate of antiretroviral resistance at an infectious diseases clinic in a rural southern state in order to 1) establish baseline antiretroviral resistance rates and 2) compare resistance rates for the time periods of January 1, 2003, to December 31, 2003, and January 1, 2004, to June 30, 2005.
METHODS: Medical records of therapy-naïve and treatment-experienced patients (n=200) with human immunodeficiency virus (HIV) who underwent genotypic or phenotypic resistance testing between January 1, 2003, and June 30, 2005, at an infectious diseases clinic of an academic medical institution were identified for review. Demographic data, viral load, $CD4^+$ cell count, and genotypic (mutations) and phenotypic (IC_{50}) resistance testing results are being collected. Data stratified by patient treatment type (treatment-experienced vs. therapy-naive) and by resistance testing modality (genotypic vs. phenotypic) will be analyzed using the chi-square test to compare mean rates of resistance between the two cohorts (2003 vs. 2004 to June 30, 2005). It is anticipated that final research results will be completed by March of 2005.
RESULTS: To date, medical records were analyzed from treatment-experienced patients (n=21) in the January 1, 2004, to June 30, 2005, cohort

only. Phenotypic resistance (defined as resistance to one or more agents within a drug class) for nucleoside reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), and protease inhibitors (PIs) was 71% (15/21), 76% (16/21), and 67% (14/21), respectively. Phenotypic multi-drug resistance (defined as resistance to three or more drug classes) occurred in 43% (9/21) of treatment-experienced patients.
CONCLUSION: Knowledge of local antiretroviral resistance patterns may enhance antiretroviral drug selection and improve patient care.

163. The development of a pharmacy-based infectious disease Web site and its impact on patient care. *Jason J. Schafer, Pharm.D.*, Debra A. Goff, Pharm.D., Kurt B. Stevenson, M.D., M.P.H., Julie E. Mangino, M.D., Kim D. Hawksworth, R.Ph.; The Ohio State University Medical Center, Columbus, OH.

PURPOSE: Evaluate a new pharmacy-based infectious diseases (ID) Web site's impact on patient care and the exchange of ID knowledge among pharmacists.
METHODS: A custom-made ID Web site was designed for the inpatient pharmacy department in a large academic teaching hospital employing 106 pharmacists who provide uninterrupted pharmacy services. 2 ID pharmacists, 2 ID physicians, and 1 information technology pharmacist created the Web site. Three pharmacists were randomly selected to pilot the Web site for 3 weeks. They could post questions as patient specific with a medical record number or as general infectious diseases inquiries. Questions were answered by the ID specialists who received e-mail notification each time a question was posted. The impact on patient care was measured for patient-specific questions. Data collected from the posted questions included the medical record number and whether an ID consult was present or recommended. Electronic charts were reviewed to determine whether the ID Web site recommendation was followed and how it changed patient care. Questions were answered using evidence-based medical literature linked as PDF articles. The impact of general knowledge questions is assessed by monitoring Web site viewing frequency and evaluating satisfaction surveys designed to measure ID knowledge enhancement.
RESULTS: During the 3-week pilot, 10 questions were submitted by 3 pharmacists. 3 questions were patient specific: 1 had an ID consult, and 2 had recommendations to change therapy for which both were subsequently followed. The satisfaction survey for the 7 general knowledge questions confirmed that all 3 pharmacists increased their ID knowledge.
CONCLUSION: This pilot study demonstrates that a pharmacy-based ID Web site has the potential to affect patient care and improve the efficiency of ID knowledge distribution in a large pharmacy department. Full implementation by the pharmacy department is under way, and its impact will continue to be measured.

164. Does prescriber compliance with a prospective approval procedure of an antibiotic management program affect medication-ordering process time? *Patricia L. Saunders, Pharm.D.*, Blair Capitano, Pharm.D., David L. Paterson, M.D., Ph.D., Brian A. Potoski, Pharm.D.; University of Pittsburgh Medical Center, Pittsburgh, PA.

PURPOSE: A criticism of antibiotic management programs that require prospective antibiotic approval is that they may delay the patient's receipt of antibiotic therapy through impedance of the medication ordering process. However, it can be postulated that such a delay occurs only when the prescriber is non-compliant with the procedure, thus necessitating an additional pharmacist intervention. The objective of this study was to determine the impact of prescriber non-compliance with the antibiotic management program (AMP) procedure on the medication ordering process time.
METHODS: Antibiotic orders will be collected in the central pharmacies of the two academic medical centers where the AMP currently operates. Orders should be received by the pharmacy with an approval number to indicate prescriber compliance with the prospective antibiotic approval procedure. The orders received without an approval number denote prescriber non-compliance with the procedure. The medication-ordering process time will be measured based on the following: the time the medication order is received by the pharmacist, the time needed to contact the physician regarding antibiotic approval, the time needed for the AMP approval call, and the time the antibiotic is entered into the pharmacy system. The average time of the medication-ordering process for antibiotics ordered by compliant prescribers will be compared to that ordered by non-compliant prescribers. These times will then be compared to the average time of the medication-ordering process of a random sample of orders for unrestricted antibiotics, which will serve as a control group. The student's t-test will be used to assess for differences of medication-ordering process time between groups.
RESULTS: Data collection is currently ongoing.

165. Pharmacist's impact on the adherence to JCAHO medication management standards. *Kimberly Tallian, Pharm.D.*, Joyce Leung, Pharm.D.; University of California, San Diego Medical Center, San Diego, CA.

BACKGROUND: The medication management standards are a new chapter introduced by the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) in 2004. These medication management activities involve systems and processes that an organization uses to provide medication-related therapies to patients, which are critical to the safety and care of these patients. As part of the JCAHO's new continued readiness accreditation process, the tracer methodology is used to look at performance with respect to services provided as viewed by the patient.
PURPOSE: To assess whether the spot tracer methodology conducted by pharmacists on high-risk medications was able to identify opportunities for improvement and provide a valid mechanism to track compliance with the medication management standards over time.
METHOD: This was a retrospective study conducted in the inpatient setting between August 2004 and April 2005. Spot tracers were conducted by the pharmacist on high-risk medications, which focused on medication management standards related to prescribing, ordering, preparation, dispensing, and administration.
RESULTS: Fifty-two high-risk medication spot tracers were completed (chemotherapy (n=4), heparin (n=15), insulin (n=9), narcotic (n=15), anticoagulant (n=7), vasoactive agent (n=2)). Compliance in legibility, indication, and signature were found. Improvement in correct order written (80% vs. 96%), pump settings (95% vs. 100%), and MAR documentation (84% vs. 93%) were seen. Lack of compliance with double checks of high risk medications (90% vs. 35%) prompted an educational effort and biweekly audits. This intervention provided nurses with a greater awareness of the standard and showed that the compliance level surpassed the baseline level when reassessed.
CONCLUSIONS: Spot tracers conducted by pharmacists can identify areas of noncompliance with the JCAHO medication standards. These areas of noncompliance can be used as opportunities for improvement to not only positively affect patient safety but also build important new collaborative relationships between pharmacists and nurses at the bedside.

166. Clinical efficacy of darbepoetin versus erythropoietin in adult end-stage renal disease. *Theresa Breithaupt, Pharm.D.*, Julie Barnes, Pharm.D., BCPS; Medical University of South Carolina, P.O. Box 250132, Charleston, SC.

BACKGROUND: End-stage renal disease (ESRD) is associated with anemia due to decreased erythropoiesis. Treatment with erythropoietin has been used to increase the production of erythrocytes and improve hemoglobin levels, which in turn improves quality of life and overall health. On an outpatient basis, treatment with erythropoietin is given 3 times/week as maintenance therapy, and prior to the initiation of the darbepoetin protocol, this therapy was continued at our institution on an inpatient basis.
PURPOSE: Due to contractual issues, darbepoetin is less expensive for our institution to procure. Therefore, a protocol was developed to convert patients from 3 times/week erythropoietin to once-weekly darbepoetin on an inpatient basis. Previous studies have shown effectiveness when using darbepoetin to increase hemoglobin. However, ensuring the clinical effectiveness of using darbepoetin over erythropoietin in the inpatient setting needs more investigation.
METHODS: This will be a retrospective chart review assessing the efficacy of darbepoetin compared to erythropoietin in maintaining hemoglobin levels. All patients with ESRD admitted to the nephrology service and receiving erythropoietin between October and November 2004 or receiving darbepoetin between August and September 2005 will be included. The primary outcome will be the difference in hemoglobin between admission and discharge. Secondary outcomes include cost savings, FDA-approved dosing conversion from erythropoietin to darbepoetin, admission diagnosis, and incidence of transfusion.
RESULTS: Initial analysis of the erythropoietin arm included 11 patients with ESRD. The mean length of stay was 40 days. The mean admission hemoglobin was 10.2 mg/dL, and the mean discharge hemoglobin was 10.3 mg/dL.
CONCLUSION: Complete results will be presented at the ACCP Spring meeting, Monterey, CA.

167. Impact of permissive underfeeding on outcomes in surgical-trauma patients. *Kelly M. Goodson, Pharm.D.*, Cathy Worrall, Pharm.D., BCPS, BCNSP, FAPhA, English F. Barbour, R.D., CNSD, Kit N. Simpson, D.P.H., Mark H. DeLegge, M.D.; Medical University of South Carolina, Charleston, SC.

PURPOSE: Intensive glycemic control in critically ill patients improves clinical outcomes by reducing morbidity and mortality. Studies are beginning to suggest that hypocaloric feeds improve mortality at discharge, shorten both hospital and intensive care unit lengths of stay, and decrease need for mechanical ventilation by improving glycemic control. The primary objective of this study is optimal blood glucose control. Secondary objectives include reduction in hospital and intensive care unit lengths of stay, days of mechanical ventilation, infectious complications, and all-cause mortality.

METHODS: Patients > 18 years of age admitted to the surgical trauma intensive care unit will be candidates for the permissive underfeeding protocol. Patients receiving specialized nutrition support who have ≥ 2 blood glucose measurements > 150 mg/dL will be eligible for study enrollment. After collecting data for 30 patients in the control group, study patients will be initiated on the permissive underfeeding protocol. The primary end point is mean blood glucose control score for the four worst measures daily for the first five days. The possible range for the glucose control score is 20–80. The expected range is 26–52 with an expected standard deviation of 4. The criteria for scoring are provided in the table below.

Glucose Levels	Control	Score
> 181 mg/dl	Very Hyperglycemic	4
151-180 mg/dl	Hyperglycemic	3
121-150 mg/dl	High Control	2
101-120 mg/dl	In Control	1
71-100 mg/dl	Low Control	2
51- 70 mg/dl	Hypoglycemic	3
< 50 mg/dl	Very Hypoglycemic	4

RESULTS: To date, nine patients have been enrolled in the control arm. The mean baseline blood glucose was 160 mg/dL, with all patients requiring insulin therapy at baseline according to the institutional standards for treatment of hyperglycemia. The mean blood glucose control score was 50.7.
CONCLUSION: Complete results will be presented at the ACCP Spring meeting, Monterey, CA.

168. Evaluation of the relationship between serum total and ionized magnesium concentrations. *Caren Hughes, Pharm.D.*, Marcus Ferrone, Pharm.D., BCNSP; Mayo Clinic/St. Luke's Hospital, Jacksonville, FL.

PURPOSE: A significant amount of time and money is spent at many institutions analyzing blood samples for ionized magnesium levels. Tremendous cost savings are possible if a clinician could recognize the appropriate circumstance under which an ionized magnesium level should be obtained to accurately evaluate the magnesium stores of a patient. Incidental reports in the literature have also suggested a potential link of ionized magnesium levels to that of other regularly measured serum values. The primary objective of this study is to describe the correlation of serum total and ionized magnesium levels in relationship to serum pH, albumin, triglycerides, and total cholesterol concentrations.
METHODS: Medical records from approximately 403 total parenteral nutrition patients between January 2004 and December 2005 were reviewed for availability of concomitant measurements of serum total and ionized magnesium, pH, albumin, triglycerides and total cholesterol concentrations. Those patients possessing this complete set of serum values will be included for analysis. A scatter plot will be created to informally explore the correlation between ionized and total magnesium values and their relationship to the other serum measurements. Linear regression will then be used to further explore the relationship between the two magnesium variables.
RESULTS: To date, 213 patient charts have been reviewed, and 37 meet inclusion criteria for analysis. It is expected that approximately 75 patients will have concomitant measurements of the variables desired for this study. With this sample size, the Kendall rank correlation test will have a 90% power to detect a correlation of 0.25 or greater based on simulations with normally distributed data.
CONCLUSION: Initial results from the data obtained indicate a weak correlation between ionized and total serum magnesium values. Further analysis of the data with respect to the other measured serum variables will follow and be available at the time of presentation.

169. Collaborative anemia management in an outpatient oncology clinic. *Deborah M. McNutt, Pharm.D.*, James A. Trovato, Pharm.D., M.B.A., BCOP; University of Maryland School of Pharmacy, Baltimore, M.D.

PURPOSE: The intent of this study is to prospectively evaluate the role of the clinical pharmacist in treating breast cancer patients with anemia compared with a retrospective control and establish pharmacist-provided anemia management services in our oncology clinic. We hypothesize that collaboration between the physician and pharmacist in the management of anemia results in optimal darbepoetin alfa utilization and decreased drug cost. The primary objective of this study is to measure the change in patient's hemoglobin from baseline and the number of blood transfusions required compared to the retrospective control. Secondary objectives include documenting the potential cost savings in terms of drug cost and describing the dose and schedule of darbepoetin alfa compared with the retrospective control.
METHODS: A retrospective review of breast cancer patients who received darbepoetin alfa for the treatment of their anemia in our outpatient clinic during the time period of 06/01/04 to 05/31/05 will be conducted. These patients will be compared to a prospective group of breast cancer patients who have been diagnosed with anemia and are candidates to receive darbepoetin alfa. Patients will be excluded if they have received prior erythropoietin therapy within two weeks of screening, uncontrolled hypertension, or an active gastrointestinal bleed. Informed consent will be obtained from patients who meet the eligibility criteria for study entry. In collaboration with the physician, the pharmacist(s) will initiate, monitor, and adjust darbepoetin alfa therapy, according to laboratory findings. We will document and describe the usage, monitoring parameters, response, and drug cost associated with darbepoetin alfa first 12 weeks of therapy.
RESULTS: Pending results of the retrospective control arm will be reported at the 2006 ACCP Spring Practice and Research Forum. In addition, descriptive preliminary data from the prospective arm is anticipated.

170. Adverse events associated with vaccination of infants in the neonatal intensive care unit at sixty days of life. *Jacquelyn D. Kamm, Pharm.D.*, Debra K. Gardner, Pharm.D.; The Ohio State University Medical Center, Columbus, OH.

PURPOSE: The administration of diphtheria-tetanus-acellular pertussis-inactivated polio-Haemophilus influenzae type B (DTaP-IPV-HIB) to preterm infants has been associated with an increase in cardiorespiratory events (apnea, bradycardia, and/or desaturation). The purpose of this study is to assess whether treatment changes made near the time of vaccine administration contribute to these adverse events.
METHODS: A retrospective chart review of 70 preterm infants who received DTap-IPV-HIB while hospitalized between January 1, 2004, and October 31, 2005, was conducted. Adverse events defined as apnea, bradycardia, and desaturation measured pre and post vaccine administration were documented. Recent changes in medical management with regard to oxygen requirement, caffeine administration, formula or feeding route, and environment (open crib versus heated isolette) were recorded. The infants were divided into two groups: those who exhibited an increase in cardiorespiratory events and those who did not. Statistical analysis was performed using Fisher's Exact Test to compare the frequency of changes in medical management between the two groups.
RESULTS: Thirty-nine medical records have been reviewed. Thirteen of the 39 infants (33%) had an increase in apnea, bradycardia, and/or desaturation. Of those 13 subjects, 11 had at least one recent change in medical management (85%). In the group that did not have an increase in cardiorespiratory events, 18 of 26 patients had at least one recent change to therapy (69%), p=0.45.
CONCLUSION: Interim results indicate there is not a statistically significant difference of change in medical management between infants who experienced an increase in cardiorespiratory events versus those that did not after DTaP-IPV-HIB administration.

171. Caspofungin use at an urban tertiary-care center: outcomes and opportunities for cost reduction. *Nadia Z. Haque, Pharm.D.*[1], Susan L. Davis, Pharm.D.[2]; (1)Henry Ford Hospital, Detroit, MI; (2)Henry Ford Hospital and Wayne State University, Detroit, MI.

PURPOSE: We conducted a retrospective review of caspofungin use at an inner-city tertiary-care teaching hospital in Detroit, Michigan.
METHODS: All patients receiving caspofungin were evaluated for indication, clinical and microbiological characteristics, outcomes, and cost.
RESULTS: 118 orders were written for caspofungin in 2005, 56% approved by Infectious Diseases, average duration 10.2 days (95%CI 7.2–13.3). Services prescribing caspofungin were medical intensive care unit (ICU) (33%), transplant (19%), internal medicine (19%), hematology/oncology/ BMT (9%), and surgery (11%). Characteristics of 90 clinically evaluable patients (initial course of caspofungin, receiving ≥ 3 days): 53% male; APACHE II score 12.4 (95%CI 10.5-14.3); 88% hospitalized > 72 hours; 42% prior ICU admission; 84% prior antibacterial use, 45% prior antifungal use, and 19% recent surgery. Comorbid conditions included: 16% transplant, 19% diabetes, 42% central venous catheters, and 53% immunosuppressed (including HIV, malignancy, or medications). Indications: 34% empiric therapy in sepsis, 23.4% documented candidemia, 14% febrile neutropenia, 8% documented *aspergillosis*, 6% esophageal candidiasis, and 14% other. Microbiology: 46% no fungal organisms isolated, 21% *C. albicans*, 14% *C. glabrata*, 12% multiple *Candida* spp, 7% moulds. Five cases of *C. glabrata* demonstrated resistance to fluconazole. 9% of patients had their therapy de-escalated after cultures reported, and 9% had oral stepdown therapy to azoles. Clinical success was achieved in 73% of empiric uses and 62% of definitive therapy; 9% of patients had infection-related readmissions. Crude mortality was 27%. Overall caspofungin cost was $614,000/12 months. Average cost/patient was $2600 for empiric and $4500 for definitive therapy, highest cost observed in mould infections (e.g. *aspergillosis*). A broad prospective restriction program would potentially avoid 16% of doses, saving $98,000 annually.
CONCLUSION: Use of caspofungin requires prospective monitoring for appropriate indication and duration. Additional outcomes and cases from 2004 will also be presented.

172. Gestational diabetes in a Medicaid population: 10-year trends in incidence and medication usage. *Brooke Pugmire, Pharm.D.*, Rex W. Force, Pharm.D., FCCP, BCPS; Departments of Family Medicine and Pharmacy Practice, Idaho State University, Pocatello, ID.

PURPOSE: The goal of this study was to examine Medicaid claims data to describe the incidence of and evaluate prescribing trends in gestational diabetes mellitus (GDM).
METHODS: This retrospective, observational study reviewed Medicaid claims among pregnant women between January 1, 1995, and September 30, 2005 to identify those with GDM and describe the yearly incidence. Ethnicity and age were determined. The prescription claims database was queried to evaluate hypoglycemic drug utilization by obtaining yearly counts of claims for these agents and number of patients using them. Diagnoses of diabetes after delivery and gestational diabetes in subsequent pregnancies were determined. Rates of maternal complications including hypertensive disorders and cesarean deliveries were also assessed.
RESULTS: Preliminary results indicate that during the study period 87,546 pregnancies were identified in 61,553 women. The number of pregnancies complicated by GDM was 4,639 (5.3%) in 4,233 women. The incidence of GDM was 3.87% in 1995 and 7.25% in 2005. The average age was 27 and 24 in the pregnancy groups with and without GDM, respectively. Of the pregnancies complicated by GDM, 762 (16%) were treated with a hypoglycemic agent. There were 4,112 prescription claims among the 762 pregnancies treated with hypoglycemic agents. Insulins accounted for 84% of claims. Metformin, sulfonylureas, glitazones, and combination drugs accounted for 8.8%, 5.2%, 1.6%, and 0.4% of claims, respectively. Claims for oral agents indicate increasing rates of use during the study period.
CONCLUSIONS: These data indicate increasing rates of GDM and use of oral hypoglycemic agents in a Medicaid population. Completed analysis of the data will be available at the time of presentation.

173. Examining the incidence of fungal infections in heart and lung transplant recipients receiving itraconazole prophylaxis. *Amanda M. Ball, Pharm.D.*, Craig A. Martin, Pharm.D., Kelly M. Smith, Pharm.D., Phillip C. Camp, M.D., Timothy Mullett, M.D., Jeremy D. Flynn, Pharm.D.; University of Kentucky Chandler Medical Center, Lexington, KY.

PURPOSE: Invasive fungal infections are a significant source of morbidity and mortality in heart and lung transplant recipients. Antifungal prophylaxis is common practice, but antifungal management strategies vary among institutions. At our institution oral itraconazole is the prophylactic antifungal of choice. The study objective is to examine the incidence of fungal infections in heart and lung transplant recipients receiving itraconazole prophylaxis at our institution. This incidence will be compared to those reported in the literature to gain insight into the efficacy of our antifungal management strategy. We hypothesize that our fungal infection incidence is similar to those reported in current literature.
METHODS: Observational, retrospective chart review of adults receiving a heart or lung transplant, from January 2001 until May 2005, who received itraconazole for prophylaxis. The study protocol was approved by the Institutional Review Board. Transplant databases were utilized to screen all heart or lung transplant patients meeting inclusion criteria. The medical records of all eligible patients were reviewed for demographics, risk factors for fungal infections, duration of antifungal prophylaxis, rejection episodes, bacterial/viral infections, and mortality. Pharmacy and microbiology databases were reviewed for patients meeting inclusion criteria who also received an antifungal agent for treatment of documented or suspected infection, or positive fungal cultures. The medical records of patients with a possible, probable, or proven fungal infection were further evaluated for causative pathogen, site of infection, treatment, and outcome.
RESULTS: 87 patients met inclusion criteria, 44 heart and 43 lung transplants. To date 14 patients (16.3%) have a documented fungal infection, 11 (78.6%) of which are lung transplant recipients. *Aspergillus* spp. account for 73% of these infections and 82% of those were lung transplant recipients. *Candida* spp. account for 13% of infections. Final study results will be utilized by our Transplant Steering Committee to reassess current antifungal prophylaxis practice.

174. Involvement of a clinical pharmacist in a post-transplant outpatient clinic. *Erin M. Megerle, Pharm.D.*, Holli A. Winters, Pharm.D., Shiv K. Seth, Ph.D.; The Ohio State University Medical Center, Columbus, OH.

PURPOSE: Clinical pharmacy services have been shown to greatly affect patient care in many areas of medicine such as transplantation. Transplant patients are often maintained on complex medication regimens that put them at risk for adverse drug reactions and harmful drug interactions. The purpose of this study is to report the types of drug therapy interventions made by a clinical pharmacist in a post-transplant clinic.
METHODS: This is an observational study of all solid organ transplant patients followed by a clinical pharmacist in an outpatient transplant clinic from July 2004 to March 2006. Data were taken from pharmacy monitoring forms. All pharmacy recommendations and interventions were documented, including medication and allergy list reconciliation, potential drug interaction recognition, dosage adjustment recommendations, and patient counseling.
RESULTS: Fifty-seven transplant patients (45 kidney and 12 kidney/pancreas) have been analyzed to date. Preliminary results show that 19% of the patient medical records contained incomplete or incorrect allergy lists. Eighty-one percent of the patient medication profiles required reconciliation by the clinical pharmacist. A major drug interaction was identified in over half (52%) of the medication profiles. Ninety-three percent of the drug interactions involved one of the patient's immunosuppressant medications. A potential adverse drug reaction was recognized in 44% of the patients. A recommendation to the physician was made for 63% of the patients. The most common recommendations included the adjustment of antihypertensive medications, suggestions for over-the-counter products, laboratory monitoring of side effects, bone density surveillance, and lipid management. Following the initial medication history interview with the clinical pharmacist, 28% of patients were revisited for patient counseling.
CONCLUSION: A clinical pharmacist is an integral member of the outpatient transplant team. Clinical pharmacy involvement in a post-transplant clinic improves the quality, accuracy, and safety of patient care.

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.

175. Gender differences in blood pressure control in an outpatient family medicine clinic. Michelle Kender, Pharm.D., Candidate, *Patricia Wigle, Pharm.D.*; University of Cincinnati College of Pharmacy, Cincinnati, OH.

PURPOSE: This study was conducted to evaluate the level of blood pressure control in male and female patients in an outpatient family medicine clinic.
METHODS: A retrospective chart review of 40 patients was performed. Inclusion criteria included patients who had a hypertension diagnosis and had at least 3 office visits in the past 6 months. Exclusion criteria included patients who were in acute pain and patients whose medical record was unavailable. Eighteen male and 22 female patients were included.
RESULTS: Forty percent of the patients had Stage 2 hypertension. Fifty-three percent of patients (38% female, 62% male) were at their blood pressure goal at the last clinic visit. Forty-seven percent of the patients (74% female, 26% male) were not at their goal blood pressure. Other parameters assessed included social history, current drug therapy, and whether the blood pressure was stable or recently controlled.
CONCLUSIONS: In this sample of patients, there was a difference in blood pressure control between male and female patients.

176. Methods for dosing digoxin in heart failure in the modern era. *Melissa Fitch, BS*, Robert J. DiDomenico, Pharm.D., Marlos Viana, Ph.D., Jerry Bauman, Pharm.D.; University of Illinois at Chicago, Chicago, IL.

PURPOSE: The therapeutic range of digoxin (Dig) for heart failure (HF) has changed to become more narrow but older dosing methods have not been modified to reflect this change. We sought to compare the Jelliffe and Jusko-Koup methods of choosing an initial dose of Dig using the newer therapeutic range in order to offer simple dosing guidelines for patients (pts) with HF in the modern era.
METHODS: Laboratory records over a 6-month period were screened for hospitalized pts who had Dig levels. Pt medical records were then reviewed for those who had post-distributive, steady-state levels for inclusion into the study (N=54 pts). Pts with drug interactions (e.g., amiodarone) were excluded. Pt-specific data was collected and used to calculate expected Dig level by both the Jelliffe and Jusko-Koup methods.
RESULTS: Of the 54 pts, 30 were male and 24 were female, aged 68+15yrs. Dig levels ranged from 0.4 to 2.4 ng/ml and creatinine clearance (Clcr, Cockcroft and Gault) ranged from 8 to 132 ml/min. Using the Jelliffe method, there was a significant correlation between expected and observed Dig levels ($r2=0.23$, $p<0.01$). Using the Jusko-Koup method there was a similar significant correlation ($r2=0.24$, $p<0.01$). However, measurement of agreement between expected and observed Dig levels as described by the root mean square error (MSE) revealed more accurate performance for the Jusko-Koup method (MSE=0.40) compared with the Jelliffe method (MSE=0.81).
CONCLUSIONS: The Jusko-Koup method is a more accurate method to estimate the initial dose of Dig. Using this method and a target Dig level of 0.7 ng/mL, initial dosing recommendations for pts with HF are as follows: for Clcr<30 mL/min start 0.125 mg qod; for Clcr 30–80 mL/min start 0.125 mg qd; for Clcr 80–120 mL/min start 0.125 alternate with 0.25 mg qd and for Clcr>120 mL/min start 0.25 qd.

177. Exploring patients' knowledge about therapeutic lifestyle changes for hypertension. *Bryan Meriwether, Pharm.D., candidate*, Kristal L. Williams, Pharm.D.; Butler University College of Pharmacy and Health Sciences/IU Methodist Family Practice Center, Indianapolis, IN.

PURPOSE: The objective of this study is 1) to evaluate the level of knowledge about specific therapeutic lifestyle changes and the DASH diet among patients with hypertension and 2) to increase the awareness among healthcare professionals of the need to provide patient education on lifestyle modifications for hypertension.
METHODS: A 9-item questionnaire about the DASH diet and JNC-VII recommendations was designed by the principal investigators. The questionnaire will be randomly administered to consenting, English-speaking and English-reading, adult (18 years or older) patients with hypertension, as identified by ICD-9 code 401, who present to the family medicine center for primary healthcare services between December 2005 and March 2006. Patient responses will be stratified based on demographics to explored relationships between questionnaire scores and demographic information. Results will be presented to the family practitioners, and a patient counseling training session on lifestyle modifications for hypertension will be given.
RESULTS: In progress. To date, 15 patients have completed the questionnaire. The average age of the participants was 55.7 years. Eighty percent of the participants were female. Sixty-six percent were Caucasian. All patients reported completing some college courses. All patients reported having hypertension for more than 5 years, and all had at least one co-morbid condition. Sixty percent of the participants stated they had some form of nutritional and lifestyle counseling by a healthcare professional. Only 2 patients reported previously hearing of the DASH diet. The most common incorrectly answered questions were related to recommendations on daily intake of fruits and vegetables, definition of low sodium, the allotted daily sodium intake for patients with hypertension, and the recommendation for physical activity.
CONCLUSION: More emphasis needs to be given to providing specific lifestyle and dietary recommendations to patients with hypertension. Pharmacists have a vital role in providing counseling on the DASH diet and JNC guidelines.

178. Comparing two methods for assessment of adrenal function in critically ill patients. *Mallika P. Patel, Pharm.D., Candidate*[1], Aaron M. Cook, Pharm.D.[2], David M. Hiestand, M.D.[2], P. Shane Winstead, Pharm.D.[2]; (1)University of Kentucky College of Pharmacy, Lexington, KY; (2)University of Kentucky Chandler Medical Center, Lexington, KY.

PURPOSE: Currently, the most common method at our institution to determine appropriateness of steroid treatment in the critically ill adult patient population is to perform a corticotropin stimulation test to assess patient's response. An alternative method of using a baseline cortisol level < 25 mcg/dL may indicate patients with adrenal insufficiency, and therefore those who would benefit from treatment with steroids. The purpose of this study is to determine if the rate in which patients that had a baseline cortisol level < 25 µg/dL could be diagnosed with adrenal insufficiency without having a stimulation test performed for the diagnosis.
METHODS: Medical records of 58 adult patients admitted to the Intensive Care Units at the University of Kentucky Chandler Medical Center who were administered a dose of cosyntropin were reviewed. Patient's baseline cortisol levels, results of corticotropin stimulation test, and date of steroid initiation were documented as primary endpoints. Secondary data obtained included length of steroid treatment, appropriateness of steroid taper, duration of vasopressor therapy, length of stay (hospital and ICU), survival data, and use of drotrecogin alfa.
RESULTS: Data will be reported based on the patient population identified between the time period of July 1, 2004 and June 30, 2005 who were administered a dose of cosyntropin for use in diagnosis of cortical response. The retrospective data collection and analysis will be completed by April.
CONCLUSION: This data may provide rationale to support using a single baseline cortisol level to predict adrenal insufficiency and responsiveness to corticosteroids in critically ill adult patients.

179. Antibiotic administration times in a septic population from a multidiscipline perspective. *Jeffrey G. Biermann, B.S., Pharm*; Midwestern University, Downers Grove, IL.

PURPOSE: Severe sepsis, with an incidence of 300 cases per 100,000 in the United States, will become an ever increasing dynamic problem. Appropriate treatment with and early initiation of antibiotics has been shown to decrease death rate among patients admitted for severe infections. Appropriate initiation of antibiotics has been defined as treatment initiated within 24 hours of established sepsis onset. To our knowledge, no study has been published which examines the interacting role of physician ordering, pharmacy data entry, and drug availability in the administration of antibiotics to the septic population. This study will examine various processes in the continuum of ordering to administration of antibiotics from a physician, nursing, and pharmacy prospective in a population of severe sepsis and septic shock patients.
METHODS: Retrospective chart review will be conducted on 100 patients (planned) at Northwest Community Hospital admitted with sepsis who are enrolled as part of the CHASE (Community Hospitals Against the Sepsis Epidemic) study.
RESULTS: The results of this study will primarily be descriptive in nature. Various analysis are planned, including time to first dose of antibiotic based on location of order (e.g., ER, ICU, floor), time for pharmacy data entry and subsequent delivery to nursing staff, time the antibiotic was actually administrated by nursing staff, and time of the day and week the order was written (to find a correlation/discordance between pharmacy services operating under higher staff volumes during the day versus lower volumes during evening and weekend hours.
CONCLUSIONS: Physicians, pharmacists, and nursing staff all play a critical role in the early administration of antibiotics in the septic population. Pharmacy order entry times have a direct effect on nursing administration times and may improve patient outcomes.

180. The prevalence and mechanism of ceftazidime resistance in *Pseudomonas aeruginosa*. *Amy N. Schilling, B.S.*[1], Kevin W. Garey, Pharm.D.[1], Mark T. LaRocco, Ph.D.[2], Vincent H. Tam, Pharm.D.[1]; (1)University of Houston College of Pharmacy, Houston, TX; (2)St. Luke's Episcopal Hospital, Houston, TX.

PURPOSE: *Pseudomonas aeruginosa* (*PA*) is a common cause of nosocomial infections, and ceftazidime (CAZ) is often used to treat these infections. *PA* resistance to CAZ is an increasing problem, which could be due to multiple mechanisms of resistance. The purpose of our study was to determine the predominate mechanism of CAZ resistance in our institution.
METHODS: Bloodstream *PA* isolates from 2003 were obtained from St. Luke's Episcopal Hospital. The susceptibility to CAZ +/- clauvulanic acid (CLA) was determined using Etests, to assess the presence of plasmid mediated extended spectrum , β-lactamase (ESBL). A spectrophotometric assay was performed using nitrocefin as the substrate to confirm , β-lactamase overproduction in the CAZ resistant isolates. The pI of the cell lysate was assessed using isoelectric focusing +/- cloxacillin (CLX) inhibition. Point mutations in ampC and ampR (negative regulatory gene for AmpC production) genes of the CAZ resistant isolates were screened using polymerase chain reaction.
RESULTS: Of the 76 *PA* isolates collected, 14 were found to be resistant to CAZ, and the susceptibility was not reversed in the presence of CLA. The spectrophotometric assay established a greater than 20-fold increase in enzymatic activity compared with a microbiological wild-type standard (ATCC 27853) which was most likely AmpC (pI=8.7, inhibited by CLX). Point mutations in ampC and ampR genes were detected in 12 and 9 out of the 14 CAZ-resistant isolates, respectively.
CONCLUSION: The prevalence of CAZ resistance in *PA* isolates was found to be 18%. The predominant mechanism of CAZ resistance was due to an overproduction of AmpC.

181. Cost of providing medications via prescription assistance programs to medically indigent patients. Patrick G. Clay, Pharm.D., *Eric Vaught, BS*, Alan Glaros, Ph.D.; Kansas City University of Medicine and Biosciences - College of Medicine, Kansas City, MO.

BACKGROUND: Providing free or low-cost prescription drugs improves medication compliance, decreases secondary co-morbidities, and reduces emergency room visits. Most pharmaceutical companies (PhRMA) have addressed this issue by offering Prescription Assistance Programs (PAP). This study measured costs associated with accessing, completing, and submitting PAP forms.
METHODS: Each PAP is the same for all medicines from an individual PhRMA. A representative drug was selected from each PhRMA. A standardized protocol for acquiring PAP medicines was determined. Analysis of personnel time and costs associated with completion and transmission of PAP applications were conducted using 10 iterations of fictitious patient data. Personnel time and materials data were also collected post-receipt of medicines using actual PAP acquisitions. Refill requirements were used to determine cost of providing the service for one year.
RESULTS: 32 pharmaceutical companies met inclusion criteria. Average total cost to complete one PAP is $25.69 (+/- $18.42). One application (n= 15) over the course of a year, cost was $10.42 (+/- $1.36), whereas 4 applications (n=12) per year cost an average of $47.65(+/- $8.58). Personnel time (47:23 min +/- 37:19 min) and costs ($12.82 +/- $10.10) accounted for 48%–50% of total costs associated with providing this service annually or quarterly, respectively. When the completed application was submitted by mail (n=27) vs. electronic transmission (fax (n=4) or on-line (n=1)), average total costs were $28.63 (+/- 18.57), $10.13 (+/- 4.55), and $8.47, respectively.
CONCLUSION: Pharmaceutical companies that require one application per year and allow the completed application to be faxed or electronically

submitted substantially decreased the amount of time and costs absorbed by the medical clinic. By limiting the cost associated with providing this program, there is a greater chance that medical clinics will include this service in their care to the medically indigent population.

182. Changes in lipid lowering and heart failure medications associated with thiazolidinedione (TZD) use in a Medicaid population. *Stacia Topham, Pharm.D., Candidate*, Christopher T. Owens, Pharm.D., Rex W. Force, Pharm.D., BCPS; Idaho State University College of Pharmacy, Pocatello, ID.

PURPOSE: Available evidence suggests equivalent glycemic control and propensity to induce fluid retention with both pioglitazone and rosiglitazone. However, recent data suggest differences in lipid effects. The purpose of this study was to evaluate changes in drug therapy reflecting potential adverse effects of TZDs on fluid retention and lipids.
METHODS: Retrospective review of Medicaid claims was performed identifying Type 2 diabetics, aged greater than or equal to 50, who received greater than or equal to 10 of 12 months of therapy with pioglitazone or rosiglitazone from 5/1999-11/2004. TZD patients were matched to diabetic controls not receiving a TZD. An index date (ID) was defined as the start date of TZD. CHF and lipid medication dosages were assessed for 12 months following ID by calculating mean daily dose per member per month (PMPM) for each medication (furosemide, ACE inhibitors, statins, fibrates). Mean percent of patients receiving these drugs was also analyzed.
RESULTS: Four hundred seventy-two pioglitazone and 531 rosiglitazone patients were matched with 419 control patients. The mean change in percent of patients on furosemide over 12 months was +4.6%, +3.7%, and -1.3% for pioglitazone, rosiglitazone, and control, respectively. The mean change in furosemide dose over 12 months was +3.20 mg, +2.25 mg, and -1.21 mg PMPM for pioglitazone, rosiglitazone, and control, respectively. Statistical analysis and results for lipid-lowering and ACE inhibitor therapy will be available at the time of poster presentation.
CONCLUSIONS: Preliminary analysis of this research in progress indicates that the chronic use of either TZD is associated with increased diuretic utilization. Data on the usage of ACE inhibitors and lipid lowering agents will be made available at the time of poster presentation.

183. New diagnosis of CHF/edema and dyslipidemia associated with thiazolidinedione (TZD) use in a Medicaid population. *Stacia Topham, Pharm.D., Candidate*, Christopher T. Owens, Pharm.D., Rex W. Force, Pharm.D., BCPS; Idaho State University College of Pharmacy, Pocatello, ID.

PURPOSE: Available evidence suggests equivalent glycemic control and propensity to induce fluid retention with pioglitazone and rosiglitazone. However, recent data suggest differences in lipid effects. The purpose of this study was to evaluate the number of patients with new diagnoses of CHF, edema, and dyslipidemia after starting a TZD.
METHODS: Retrospective review of Medicaid claims was performed identifying Type 2 diabetics, aged 50 and older, who received greater than 10 of 12 months of therapy with pioglitazone or rosiglitazone from 5/1999-11/2004. Patients were matched to diabetic controls not receiving a TZD. An index date (ID) was defined as the start date of TZD. New diagnoses of CHF, edema, and dyslipidemia were analyzed for 12 months following ID. Relative risks (with 95% CI) versus control and between TZDs were calculated.
RESULTS: Four hundred seventy-two pioglitazone and 531 rosiglitazone patients were matched with 419 control patients. At baseline, CHF and edema were more common in controls than TZD patients ($p<0.05$); dyslipidemia was less common in controls ($p<0.05$). There were no baseline differences between the TZDs. New CHF was identified for 5.72%, 4.90%, and 7.64%, of the pioglitazone, rosiglitazone, and control groups, respectively ($p>0.05$). New edema was identified for 4.45% (RR=1.33, 95% CI 0.99–1.80 vs. control), 6.97% (RR=1.47, 95% CI 1.18–1.84 vs. control), and 2.15% of the pioglitazone, rosiglitazone, and control groups, respectively. New dyslipidemia was identified for 11.23% (RR=1.40, 95% CI 1.15–1.70 vs. control), 12.05% (RR 1.39, 95% CI 1.17–1.66 vs. control), and 6.92% of the pioglitazone, rosiglitazone, and control groups, respectively. There were no statistically significant differences between pioglitazone and rosiglitazone with regard to the development of any diagnoses.
CONCLUSIONS: Compared with controls, TZD use was associated with an increased risk of developing edema and dyslipidemia. However, the risk of development of CHF was not increased in patients receiving a TZD.

2006 ACCP Spring Practice and Research Forum Abstracts

Index of Corresponding Authors