ABSTRACTS

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Encore Presentations: Abstracts marked with an "E" are Encore Presentations. Encore Presentations undergo the same peer review process as do Original Presentations, but may have been presented elsewhere or published in abstract form only prior to the 2004 Annual Meeting. For Encore Presentations, the abstract title, authors, and original citation (if provided) are published in Pharmacotherapy. The full abstract will be published in the meeting program book.

ORIGINAL RESEARCH

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

ADR/Drug Interactions

1. Evaluation of a pharmacokinetic interaction between eszopiclone and digoxin. *Andrea J. Anderson, Pharm.D.*, Susan M. Skolly, Pharm.D., Gary Maier, Ph.D.; Sepracor Inc., Marlborough, MA.

PURPOSE: To study the effect of a single dose of eszopiclone on the pharmacokinetics of digoxin at steady state.
METHODS: In this single-center, inpatient, open-label, daytime dosing study in healthy adults, a loading dose of digoxin on Day 1 (0.5 mg BID, doses separated by 12 hours), was followed by once daily dosing of digoxin 0.25 mg on Days 2–7. A single dose of eszopiclone 3 mg was administered with digoxin on Day 7. To evaluate digoxin pharmacokinetics, blood was drawn predose on Days 4–7 and at 1, 2, 4, 6, 8, 12 hours on Days 6 and 7, and 24 hours postdose, on day 8. Primary endpoints were comparisons of $AUC_{(0-t)}$, and C_{max} of steady state digoxin administered alone (Day 6) to the combined treatment with eszopiclone (Day 7).
RESULTS: Twelve subjects (7 male) aged 24–64 years (mean 40.7) completed the study. Steady state digoxin levels were achieved by Day 4. On Day 6, with digoxin (alone), mean C_{max} was 2.3 ng/mL, median t_{max} was 1.0 hr, and mean $AUC_{(0-t)}$ was 21.2 ng•hr/mL. On Day 7 (concomitant eszopiclone administration), the digoxin mean C_{max} was 2.1 ng/mL, median t_{max} was 1.0 hr, and mean $AUC_{(0-t)}$ was 21.0 ng•hr/mL (90% CI for C_{max} and $AUC_{(0-t)}$ within reference range). There were no serious adverse events and none that led to discontinuation.
CONCLUSIONS: In this study, a single dose of eszopiclone 3 mg did not affect the steady state pharmacokinetics of digoxin in healthy volunteers. Eszopiclone in combination with digoxin was well tolerated.

2. Hepatic panel abnormalities associated with medications in the medical intensive care unit. *Anastasia M. Rivkin, Pharm.D., BCPS*, Ellina Dan, Pharm.D.; Long Island University, Arnold and Marie Schwartz College of Pharmacy and Health Sciences, Brooklyn, NY.

PURPOSE: This study documented hepatic panel changes in 107 intensive care unit admissions over three months in order evaluate incidence of medication-related hepatic panel abnormalities during the admission, and characterize common medications implicated.
METHODS: This prospective observational 12 week study conducted in a medical intensive care unit from January through April 2004 included 107 men and women aged 16–96 years. Patient's charts were reviewed to identify reasons for hepatic panel abnormalities. Available imaging studies, viral hepatitis serologies, prior medications and medications during hospitalization were documented. Medication profile was evaluated with order start and stop dates recorded.
RESULTS: Out of 107 cases analyzed, 73 patients had abnormal hepatic panel (68%). Out of those 73, 57 patients were admitted with already abnormal hepatic panel. We identified 6 cases of medications used prior to admission as possible cause for hepatic panel abnormalities. We also identified 16 patients with initially normal hepatic panel which converted to abnormal over the course of ICU stay. Out of those 16, ten were identified as possibly medication-related (10/107, 9.4%). Implicated medications included ceftriaxone (4), enoxaparin (1), heparin (1), phenytoin (1), rifampin (1), simvastatin (1), valproic acid (1).
CONCLUSIONS: Most medications cause idiosyncratic liver injury relatively infrequently. It is not known how interaction between patient factors, disease states, number of medications administered, and drug-drug interactions affect the incidence of abnormalities in hepatic panel in the patients admitted to the intensive care unit. This study shows 9.4% incidence of hepatic panel abnormalities possibly related to medication administration.

3. Characteristics of sulfa allergy and use of potentially cross-reactive medications amongst adult inpatients. *Brian A. Hemstreet, Pharm.D., BCPS*, Robert L. Page III, Pharm.D., BCPS; University of Colorado School of Pharmacy, Denver, CO.

PURPOSE: This descriptive study documented characteristics of sulfa allergies reported by adult inpatients. Use of arylamine and non-arylamine sulfa containing drugs was assessed.
METHODS: Consecutive adult inpatients identified by computer generated allergy reports were interviewed regarding their medical and allergy histories. Patients were followed during their hospital admission to document usage and safety of arylamine and non-arylamine sulfa containing medications. Analysis consisted of descriptive statistics and qualitative analysis.
RESULTS: Ninety-four patients with reported sulfa allergy were assessed. Trimethoprim/sulfamethoxazole allergy was reported by 45% of patients, while 45% didn't recall the medication they were allergic to. Sixty-three percent reported rash, 14% anaphylaxis, and 2% Stevens- Johnson's. Median time since last reported allergic reaction to a sulfa-containing agent was 20 years. Forty three percent of patients were taking a non-arylamine agent as an outpatient for an average of 6.2 years. Forty percent of this subset reported an allergy to trimethoprim/sulfamethoxazole, while furosemide use was reported by 60%. Ten percent with no prior use received a non-arylamine as an inpatient. Furosemide was most commonly prescribed. One patient received topical silver sulfadiazine. No adverse effects were observed during inpatient stay (2–23 days).
CONCLUSIONS: Trimethoprim/sulfamethoxazole allergy was most commonly reported. Many reactions occurred in the remote past. Numerous patients were unable to give an accurate allergy history. Inpatient and outpatient use of potentially cross-reactive medications was observed in a large number of patients. No adverse effects were reported or documented with outpatient or inpatient non-arylamine use, even amongst patients with serious or life-threatening reactions.

4. Efficacy, safety, and appropriateness of intravenous phosphate replacement in adult inpatients. *Brian A. Hemstreet, Pharm.D., BCPS*, Marianne McCollum, R.Ph., Ph.D., BCPS; University of Colorado School of Pharmacy, Denver, CO.

PURPOSE: This retrospective descriptive study assessed phosphate repletion in adult inpatients. Efficacy, safety, appropriateness of prescribing, and eligibility for oral therapy or use of alternate intravenous replacement was evaluated.
METHODS: Adult inpatient medication profiles were randomly screened for use of phosphate replacement products. Information regarding past medical history and laboratory aspects of each episode of phosphate repletion was documented utilizing electronic laboratory and medical records. Eligibility for oral therapy was defined by the presence of at least one scheduled oral medication on the drug profile. Analysis using descriptive statistics was performed.
RESULTS: Thirty-six episodes of phosphate replacement in 27 patients were assessed. Mean admission and discharge phosphorus concentrations were 3.1 mg/dl and 3.4 mg/dl. Seventy-five percent of replacement episodes involved single doses of intravenous potassium phosphate (mean 13.1 mmol). Forty-one percent of intravenous use was for mild cases of hypophosphatemia (2.1–2.4 mg/dl), and 44% for moderate (1–2 mg/dl). Normalization of phosphorus upon initial repeat lab assessment was 61%. Thirty-three percent of mild cases receiving intravenous replacement were eligible for oral therapy, and 85% were eligible for alternate use of sodium phosphate based on average potassium and sodium values of 4.1 mEq/L and 139 mmol/L. No hyperphosphatemia was documented.
CONCLUSIONS: Intravenous potassium phosphate use predominated despite numerous cases of mild hypophosphatemia with normokalemia. Many patients were eligible for oral therapy or intravenous sodium phosphate. Identification of patients eligible for these alternate therapies may lead to reductions in medication errors, adverse effects, and medication administration time by avoiding intravenous potassium-containing products.

5. Characterization and economic impact of drug-related hospital admissions to a general medicine service in Singapore. *Grant E. Sklar, Pharm.D.*[1], Josephine Y. Lee, B.Sc.(Pharm)[1], Vernon M.S. Oh, M.D.[2]; (1)Department of Pharmacy, National University of Singapore, Singapore, Singapore; (2)National University Hospital, Singapore, Singapore.

PURPOSE: This study reviewed drug-related hospital admissions to a general medicine service in a tertiary-care hospital in order to 1) characterize the drug-related hospital admissions, and 2) determine the economic impact of such admissions.
METHODS: Medical records of 397 admissions to the general medicine service from 4 randomly selected months in 2001–02 were reviewed.

Attempted suicide, drug overdose, and transfers from other hospitals were excluded (n=21). Admissions with a drug-related problem (DRP) as the main contributing factor were classified as: improper drug selection; sub-therapeutic dosage; failure to receive drug; overdosage; adverse drug reaction; or drug-drug interaction. The DRP prevalence, type, outcome and economic impact were analyzed.
RESULTS: DRP's were identified in 14% (53/376) of the admissions. Failure to receive drug, adverse drug reaction and sub-therapeutic dosage were the most common DRP's leading to admission (32%, 24% and 23%, respectively). Overdosage and improper drug selection accounted for the remaining admissions. Antidiabetic and anticonvulsant drugs were the two most common causative agents (45% and 26%, respectively). Most patients (48/53) resolved their DRP's without complication or permanent disability, and 98% were discharged. DRP-related hospital admissions resulted in an average length of stay of 4.9 ± 3.5 days. The average cost per DRP-related admission was S$2,096; ranging from S$500 to S$7,169. This translates to approximately S$333,000 annually.
CONCLUSIONS: DRP's are a significant cause of hospital admissions to the general medicine service in our institution, with failure to receive drug the most common problem. A substantial amount of resources is used to treat these potentially preventable admissions.

6. Adverse effects associated with extra doses of bupropion. *Greene Shepherd, Pharm.D.*; University of Georgia, College of Pharmacy, Augusta, GA.

PURPOSE: Bupropion is a widely used drug with a risk of adverse effects at therapeutic doses, including seizures in 0.4% of patients. Unintentional extra doses were studied to describe frequency of adverse effects and examine possible dose response relationships.
METHODS: A retrospective review was conducted to describe cases of dosing errors with bupropion reported to the American Association of Poison Control Centers (AAPCC) between 2000–2003. Acute-on-chronic exposures to bupropion due to unintentional extra doses were included. AAPCC coding for dose, treatment site, symptoms and clinical outcome was evaluated.
RESULTS: During a 4-year period 476 cases were reported meeting our inclusion and exclusion criteria. Women (n=354, 74.4%) were more commonly involved than men. Doses ranged between 75 mg and 1500 mg with a median and mode of 300 mg. Most cases (n=349, 82.7%) were managed outside of hospitals. Seizures were reported in 4 cases (8.4%) and one case developed status epilepticus. Other prominent effects included agitation (8.2%), dizziness (7.4%), drowsiness (6.1%), nausea/vomiting (6.6%), hallucination (0.4%), tremor (7.1%) and tachycardia (5.5%). Clinical outcomes were: no effect n=293(61.6%), minor effect n=132(27.7%), moderate effect n=49(10.3%) and major effect n=2(0.4%). Doses were higher (p=0.045) in cases with adverse effects vs. no effect. Doses were slightly higher in moderate and major outcomes but not significantly (p=0.083).
CONCLUSIONS: In this series, significant adverse effects were present in >10% of patients following extra doses of bupropion. Seizures were present twice as often as expected with usual dosing. Extra doses of bupropion appear to increase risk of adverse effect.

7. Drug interactions of nateglinide, a new glucose-lowering agent. *Hyesun Gwak, Pharm.D., Ph.D.*, Junghyun Oh, B.S., Hyunsun Chou, B.S.; College of Pharmacy, Chosun University, Gwangju, South Korea.

PURPOSE: To investigate the drug interactions of nateglinide with various agents including calcium channel blockers and lipid lowering agents.
METHODS: A dose of 30 mg/kg of nateglinide was administered alone orally to each of rabbits or 30 min after the administration of diltiazem (10 mg/kg), verapamil (20 mg/kg), nifedipine (5 mg/kg), gemfibrozil (150 mg/kg), lovastatin (3 mg/kg) or fluvastatin (3 mg/kg). Serum samples (0.15 ml) were collected from the femoral artery cannula at predetermined time intervals and analyzed by HPLC.
RESULTS: With co-administration with nifedipine, $AUC_{0-\infty}$ and AUC_{0-8} were 201.8% (P<0.05) and 180.7% (P<0.05) of the respective control value. The C_{max} and half-life of nateglinide increased from 21.7 to 39.4 μg/ml (P<0.01) and 3.1 to 7.1 hr (P<0.05) by nifedipine, respectively. Diltiazem also increased C_{max} and AUC_{0-8} of nateglinide from 21.7 to 39.0 μg/ml (P<0.05) and 68.7 to 91.8 μg•hr/ml (P<0.05), respectively. Among lipid-lowering agents, gemfibrozil decreased the $AUC_{0-\infty}$, AUC_{0-8} and C_{max} of nateglinide from 96.2 to 43.1 μg•hr/ml (P<0.05), 68.7 to 30.8 μg•hr/ml (P<0.005) and 21.7 to 10.3 μg/ml (P<0.0001), respectively.
CONCLUSIONS: Concomitant use of nifedipine or diltiazem with nateglinide may increase the risk of hypoglycemia while co-administration of gemfibrozil with nateglinide may reduce the blood glucose-lowering effect of nateglinide.

8. Pharmacokinetic and pharmacodynamic interaction of eszopiclone and lorazepam in healthy subjects. *John Niewoehner, Pharm.D.*, Andrea J. Anderson, Pharm.D., Gary Maier, Ph.D.; Sepracor Inc., Marlborough, MA.

PURPOSE: To study pharmacokinetic and pharmacodynamic interactions of single oral doses of eszopiclone 3 mg and lorazepam 2 mg.
METHODS: Single-center, randomized, four-arm, parallel, daytime administration, inpatient, single-dose, single-blind study in 36 healthy volunteers (15 male), 20–64 years old who received eszopiclone 3 mg alone, lorazepam 2 mg alone, eszopiclone 3 mg and lorazepam co-administered, or placebo. Blood drawn at 8 a.m. was analyzed at various time points up to 24 hours postdose. Digit Symbol Substitution Test (DSST) was conducted to evaluate pharmacodynamic effects.
RESULTS: Coadministration of eszopiclone with lorazepam decreased the eszopiclone mean C_{max} by 22.69% and the lorazepam mean C_{max} by 21.1%. After combined treatment, the eszopiclone mean $AUC_{(0-last)}$ decreased by 7% and the lorazepam mean $AUC_{(0-last)}$ decreased by 9.5%. Analysis of the interactive effects on DSST for the combination treatment showed no decremental effect on Emax (p=0.8322) or AUC_{DSST} (p=0.3651). There was no clinically relevant difference in the number of subjects who reported adverse events or in severity or discontinuation rates between those administered the combination of eszopiclone and lorazepam and those administered each drug alone.
CONCLUSIONS: In this study of healthy volunteers, combined treatment with eszopiclone and lorazepam reveal a minor (21–23%) mutual reduction in C_{max} but little change (7–9.5%) in $AUC_{(0-last)}$. The pharmacodynamic evaluation of the combination of eszopiclone and lorazepam showed no effect on DSST by Emax and AUC_{DSST}.

9E. Safety and tolerability of double-dose esomeprazole (40 mg twice daily). Joel Richter, M.D.[1], Michael Vaezi, M.D., Ph.D.[1], C. Richard Stasney, M.D.[2], Reza Shaker, M.D.[3], Clara Hwang, MApStat[4], *David R. Rutledge, Pharm.D., FCCP*[5], Mark Sostek, M.D.[4]; (1)Cleveland Clinic, Cleveland, OH; (2)Texas Voice Center, Houston, TX; (3)Medical College of Wisconsin, Milwaukee, WI; (4)AstraZeneca LP, Wilmington, DE; (5)AstraZeneca LP, Naperville, IL.

Presented at the Society of Gastroenterology Nurses and Associates Annual Course, Dallas, TX, May 14–19, 2004.

10. Pattern of medications usage and potentially inappropriate medication usage among Korean ambulatory elderly patients based on explicit criteria. *Jin Sun Nam, M.S.*, Jung Mi Oh, Pharm.D.; Graduate School of Clinical Pharmacy, Sookmyung Women's University, Seoul, South Korea.

PURPOSE: To determine the extent and rate of prescription drug therapy, especially polypharmacy and the prevalence of potentially inappropriate medication use in Korean elderly ambulatory patients based on explicit criteria.
METHODS: Performed a retrospective study of 65 years or older ambulatory patients visiting a university hospital based clinic from January 2002 to April 2004. Study determined the patterns of drug prescription using the Anatomical Therapeutic Chemical Classification and the potentially inappropriate medication usage based on explicit Beer's criteria.
RESULTS: Of the 4042 elderly patients the mean number of prescription was 2.2±2.0, which was similar between genders and all age groups within the elderly. 10.7% of patients were prescribed with more than 5 medications concurrently. The most frequently prescribed medication was the drugs used for treating nervous system diseases (44.3%), followed by alimentary tract/metabolism disorders (27.6%), cardiovascular disease (10.7%), blood/blood forming disorders (4.3%), respiratory disorders (6.5%), and musculoskeletal diseases (3.2%). A total of 511 elderly (13%) was prescribed with medication that met the criteria for ∞√1 potentially inappropriate drugs for the elderly. This proportion was similar between genders and all age groups within the elderly. Among these 511 elderly patients the mean number of potentially inappropriate drugs prescribed were 5.1±3.3 drugs. Potentially inappropriately prescribed drugs were amitriptyline (76case), diazepam (69case), ketorolac (57case), short acting nifedipine (44case), triazolam (38case), and hydroxyzine (38case).
CONCLUSIONS: Potentially inappropriate drug prescribing in Korean ambulatory elderly patients are common. Education programs and interventions aimed at optimizing the prescribing and dispensing of the most appropriate drugs are needed.

11. Is occurrence of an antiepileptic drug related adverse drug reaction related to an active or prior history of neoplasm? Sunita Dergalust, Pharm.D., BCPS, Eliot Licht, M.D., *Ma. Cristina Ferrer, Pharm.D.*, Adam R Baumhefner, None, Wayman T Lee, Pharm.D., Jeffrey F Sayers, Pharm.D.; VA Greater Los Angeles Healthcare System, Los Angeles, CA.

PURPOSE: In the last decade the number of available anti-epileptic drugs (AEDs) and their usage has grown. Increased recognition of AED related adverse drug reactions (ADRs) has followed. Commonly reported AED-related ADRs include cutaneous reactions, hepatic dysfunction, and hematological abnormalities. This study examined how patient and disease specific characteristics may impact potential for AED related ADRs. Clarification of this relationship will improve quality of care and patient outcome.
METHODS: Patients were identified through direct patient interaction by the pharmacy service and through the Pharmacy database of ADRs. Key characteristics used included a recent or past history of neoplasm and exposure to an AED.
RESULTS: 100 patient records were identified. Patients ranged in age from 38 to 82 years (average: 62 years). Seventy-four (74%) met inclusion criteria. Of

the 74 patients, 15 (20%) were found to have key criteria of a selected AED related ADR with an underlying neoplasm. Of these 15 patients, 4 (27%) had a history of radiotherapy (XRT) and 11 (73%) had no history of XRT. The most commonly reported ADR was rash in 10/15 patients (67%). The most commonly noted "offending" AED was phenytoin: 9/15 patients (60%).
CONCLUSIONS: XRT therapy has been reported to be an important risk factor for the development of AED-related ADRs. In our sample a majority of patients with an AED-related ADR did not receive XRT. Our findings suggest that neoplasm itself (active or by history) may be an underappreciated risk factor for an ADR. Further studies are underway.

12. Pharmacokinetic and pharmacodynamic interaction of eszopiclone and paroxetine in healthy subjects. *Susan M. Skolly, Pharm.D.*, John Niewoehner, Pharm.D., Gary Maier, Ph.D.; Sepracor Inc., Marlborough, MA.

PURPOSE: To study pharmacokinetic and pharmacodynamic interactions of single oral doses of eszopiclone 3 mg and paroxetine 20 mg.
METHODS: Single-center, four-arm, parallel, daytime administration, inpatient, single-dose, single-blind study in 40 healthy volunteers (27 male), 21–55 years, randomized to receive one of four oral treatments: eszopiclone 3 mg alone, paroxetine 20 mg alone, coadministered eszopiclone 3 mg and paroxetine 20 mg, or placebo. Blood was drawn predose and at various time points up to 24 hours postdose. Digit Symbol Substitution Test (DSST) was conducted to evaluate pharmacodynamic effects.
RESULTS: When given in combination, little mean change in paroxetine C_{max} (1.5% increase), and $AUC_{(0–last)}$ (3.5% decrease) was seen. The eszopiclone mean C_{max} increased by 12%, and $AUC_{(0–last)}$ increased by 9%. Analysis of the interactive effects on DSST for the combination treatment showed no decremental effect on Emax (p=0.1229), and no decrement in AUC_{DSST}. There were no clinically relevant differences or changes between the treatment groups for severity or number of AEs or laboratory values, vital signs, or ECG parameters.
CONCLUSIONS: The results of this study suggest that coadministration of eszopiclone 3 mg and paroxetine 20 mg had no clinically significant pharmacokinetic or pharmacodynamic interactions.

13. Assessment of intravenous immunoglobulin drug utilization and the incidence of acute renal failure. *Sachin R. Shah, Pharm.D., BCOP*, Marne Vervan, Pharm.D.; Texas Tech Universtiy HSC-School of Pharmacy/VA North Texas Health Care System, Dallas, TX.

PURPOSE: Intravenous immunoglobulin (IGIV) therapy has been utilized for various labeled and off labeled conditions, since 1981. The primary objective of the study was to perform a drug utilization evaluation of IGIV. The study also evaluated the incidence of ARF and thrombosis, and attempted to identify a subgroup of patients at higher risk for developing ARF.
METHODS: A retrospective chart review was performed on all patients who received IGIV therapy from May 1, 1998 to June 30, 2003. Patients were identified through a query performed on the VA computerized database system. Data was collected pertaining to patient demographics and co-morbidities, concomitant medications, and IGIV therapy. ARF was defined as an increase in SCr levels > 0.5 mg/dL.
RESULTS: The three main indications for IGIV were hypogammaglobulinemia, immune thrombocytopenic purpura, and chronic inflammatory demyelinating polyneuropathy. The incidence rate of ARF was found to be 13% (6/46 patients) and occurred with the first cycle of sucrose containing IGIV therapy. Age > 65, chronic renal insufficiency, diabetes mellitus, IGIV dose > 400 mg/kg/day showed a trend towards significant risk factor for ARF (p=0.078, 0.079, 0.079, and 0.074, respectively). The study did not find any new occurrence of thromboembolic event.
CONCLUSIONS: This is the first study evaluating the incidence of ARF in all patients with various indications receiving IGIV therapy. The study has given more support to the increasing documentation suggesting association between the sucrose content of the IGIV and the development of ARF.

14. Thiazolidinedione use, weight gain, edema, and congestive heart failure. *Sabrina W. Cole, Pharm.D.*, Courtney L. Bickford, Pharm.D., Sarah J. Schwiesow, Pharm.D., Andrea M. Wessell, Pharm.D., BCPS, CDE, Nannett M. Berensen, Pharm.D., BCPS; Medical University of South Carolina, Charleston, SC.

PURPOSE: To evaluate weight gain, edema, and congestive heart failure (CHF) in patients receiving thiazolidinediones (TZD).
METHODS: Patients were identified by reviewing daily appointment schedules from November 2003 through February 2004, in a family medicine clinic. In addition to patient demographics and TZD regimens, the following data were obtained pre- and post-TZD initiation: weight, A1C, CHF diagnosis, loop diuretic regimen, and other antidiabetic agents. If patients gained at least 10 pounds, had a loop diuretic started or dose increased, or received a diagnosis of CHF; then recommendations for additional monitoring or TZD discontinuation were made.
RESULTS: Ninety-one patients were assessed. Eighty-one patients had pre- and post-TZD weights documented. Of these, 32 (40%) patients had a greater than 10-pound weight gain. Of the 73 patients who had pre- and post-TZD A1Cs, the average reduction was 1%. Six patients (7%) received a new diagnosis of CHF. Twenty-eight (31%) patients required treatment with a loop diuretic after TZD initiation and 12 (13%) patients required an increased diuretic dosage. Seventy-nine patients (87%) were receiving other antidiabetic agents. Recommendations for additional monitoring were made for 17 (18%) patients. A recommendation to discontinue TZD treatment was made for 12 (13%) patients. Recommendations to discontinue TZD therapy were accepted in 5 patients, not accepted in 4 patients, and unknown in 3 patients.
CONCLUSIONS: These results underscore the importance of increasing awareness of and adherence to the suggested monitoring parameters for patients receiving TZD therapy set forth by the American Heart Association and American Diabetes Association.

Analgesia

15E. Testosterone patch therapy increases sex hormone levels with associated improvements in sexual function, mood and hematocrit in men with opioid induced androgen deficiency (OPIAD). *Harry W. Daniell, M.D., FACP*[1], Robin Lentz, CCRA[2], Norman A. Mazer, M.D., Ph.D.[3]; (1)University of California Davis Medical School, Redding, CA; (2)Mercy Medical Center, Redding, CA; (3)Watson Laboratories, Inc., Salt Lake City, UT.

Presented at the 86th Annual Meeting of the Endocrine Society, New Orleans, LA, June 16–19, 2004.

16. Low-dose botulinum toxin type A in the treatment of piriformis syndrome unresponsive to the conventional therapy. *Jin Ho, B.S.*[1], Se Jin Yoon, M.D.[2], Ho Yong Kang, M.D.[3], Sang Ho Lee, M.D., Ph.D.[4], Jung Mi Oh, Pharm.D.[5]; (1)Department of Pharmacy, Wooridul Spine Hospital, Seoul, South Korea; (2)Department of Rehabilitation Medicine, Wooridul Spine Hospital, Seoul, South Korea; (3)Department of Radiology, Wooridul Spine Hospital, Seoul, South Korea; (4)Department of Neurosurgery, Wooridul Spine Hospital, Seoul, South Korea; (5)Graduate School of Clinical Pharmacy, Sookmyung Women's University, Seoul, South Korea.

PURPOSE: Investigated the effectiveness of single, low dose of botulinum toxin type A (BTX-A) in improving the pain and quality of life (QOL) for patients with conventional therapy resistant piriformis syndrome (PS).
METHODS: Total of 30 patients with chronic PS were enrolled in an open label, prospective and single center trial from April 2003 to February 2004. 150 units of BTX-A (Dysport¢Á) were injected into the affected unilateral piriformis muscle under the CT guidance. Patients' pain ratings using visual analog scale (VAS) or numeric rating scale (NRS) were obtained at baseline, 4, 8 and 12 weeks of treatment. Health-related QOL was assessed using Medical Outcome Study 36-item Short Form Health Survey (SF-36) at baseline and 4 weeks of treatment on visit to clinic. SF-36 was also collected from 82 healthy normal Korean volunteers.
RESULTS: The pain intensity scores at 4, 8 and 12 weeks of post BTX-A treatment measured by VAS or NRS were all significantly lower (p<0.0001) than baseline. The baseline score of SF-36 subscales in patients with PS was significantly lower than the score of the age and sex matched 82 healthy normal subjects. After 4 weeks of BTX-A treatment, patients significantly improved in physical functioning (p=0.003), role physical (p=0.021), bodily pain (p=0.016), general health (p=0.013), vitality (p=0.031) and social functioning (p=0.035). However, no significant improvement was seen with role emotional (p=0.151) and mental health (p=0.170) scales.
CONCLUSIONS: Relatively low dose of BTX-A has significant impact on improving the pain and the QOL in patients with refractory piriformis syndrome.

17. Duloxetine in treatment of diabetic neuropathic pain (DNP). Joachim Wernicke, M.D., Yili Lu, Ph.D., Deborah D'Souza, Ph.D., *Megan Jones, Pharm.D.*, Amy Waninger, B.S., Pierre Tran, M.D.; Eli Lilly and Company, Indianapolis, IN.

PURPOSE: Serotonin (5-HT) and norepinephrine (NE) are involved in pain modulation via descending inhibitory pathways in the brain and spinal cord. This study assessed the efficacy of duloxetine, a potent and balanced inhibitor of 5-HT and NE reuptake, on the reduction of pain severity in patients with DNP.
METHODS: Patients with DNP (without comorbid depression) were randomized to treatment with duloxetine 60 mg QD, 60 mg BID, or placebo for 12 weeks. The primary outcome measure was the weekly mean score of 24-hour average pain severity on the 11-point Likert scale. Secondary measures included night and 24-hour worst pain severity, Brief Pain Inventory (BPI), Clinical Global Impression of Severity (CGI-Severity), Patient Global Impression of Improvement (PGI-Improvement), Short-form McGill Pain Questionnaire, Dynamic Allodynia, and Average Daily Intake of Acetaminophen.
RESULTS: Duloxetine 60 mg QD and 60 mg BID demonstrated significant improvement in the treatment of DNP with rapid onset of action and separation from placebo at Week one on the 24-hour average pain severity score. For all secondary measures for pain (except allodynia), mean changes showed superiority of duloxetine over placebo, with no significant difference between 60 mg QD and 60 mg BID. CGI and PGI evaluation also demonstrated greater improvement on duloxetine- versus placebo-treated

patients. Duloxetine showed no notable interference on diabetic control and both doses were safely administered and well tolerated.
CONCLUSIONS: This study confirms previous findings that duloxetine at 60 mg QD and 60 mg BID is safe and effective in treating DNP.

18E. Opioid induced androgen deficiency in men (OPIAD): An estimate of the potential patient population in the U.S. and Canada. *Norman A. Mazer, M.D., Ph.D.*[1], C. Richard Chapman, Ph.D.[2], Harry W. Daniell, M.D., FACP[3], Ernest Volinn, Ph.D.[2]; (1)Watson Laboratories Inc., Salt Lake City, UT; (2)Pain Research Center, University of Utah School of Medicine, Salt Lake City, UT; (3)University of California Davis Medical School, Redding, CA.

American and Canadian Pain Societies, Vancouver, BC, May 6–9, 2004

19E. Naloxone utilization in determining appropriate opioid use, avoiding adverse effects, and minimizing medication errors. *Rob W. Hutchison, Pharm.D.*, Omar Gonzalez, Pharm.D.; Presbyterian Hospital Dallas, Dallas, TX.

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Cardiovascular

20. Use of venous thromboembolism prophylaxis on medical at-risk patients. *Hongjun Yin, M.S.*[1], Leo Lichtig, Ph.D.[2], Paul J. O'Connor, RPh, M.B.A[2], F. Randy Vogenberg, RPh, Ph.D.[2]; (1)University of Illinois at Chicago, Chicago, IL; (2)Aon Consulting Life Sciences Practice, Wellesley, MA.

PURPOSE: Patients having prolonged immobility are at high risk of developing venous thromboembolism (VTE). Use of thromboprophylaxis (TP) for preventing VTE was recommended by the 2001 American College of Chest Physicians guidelines. Consequently, patients with inpatient stays longer than 5 days should be given TP. TP utilization, however, varies widely across hospitals. This study focused on heart failure and shock patients to show utilization rate of TP and factors associated with its use.
METHODS: An administrative database from 15 hospitals across the United States was used to identify and analyze the cohort. Descriptive statistical analysis was done to identify TP utilization rates. Logistic regression was performed to identify factors associated with TP as well as the relationship between length of stay (LOS) and VTE risk. VTEs identified within 90 days after the index admission were assumed to be associated with that admission. The analysis included 31co-morbidities, using Charlson's and Elixhauser's co-morbidity measures.
RESULTS: For patients with LOS ≥ 5 days, only 61.1% received TP. TP utilization ranged from 32.2% to 87.5% across the hospitals. Patients with longer LOS, history of thrombosis, myocardial infarction, cardiac arrhythmias, valvular disease, obesity or greater number of co-morbidities were more likely to receive TP. Patients with mild liver disease, anemia, or older patients are less likely to receive TP.
CONCLUSIONS: Rate of TP use should be increased to achieve desired improved clinical and economic outcomes. Further study is needed on the factors influencing use of TP and specific role(s) for pharmacists.

21. Assessment of physician satisfaction with services provided by a clinical pharmacist managed cardiac risk reduction service. *James D. Nash, Pharm.D.*, Kari L. Olson, Pharm.D., Angela Hardy, Pharm.D., Kara Uram, Pharm.D.; Kaiser Permanente Colorado Region, Aurora, CO.

PURPOSE: The Clinical Pharmacy Cardiac Risk Service (CPCRS) of Kaiser Permanente of Colorado (KPCO) collaborates with primary care physicians and cardiologists in co-managing cardiac risk factors in approximately 10,000 patients with cardiovascular disease. Since its inception in 1998, no evaluation of physician satisfaction has been conducted. The purpose of this study was to determine physician satisfaction with services provided by CPCRS.
METHODS: Eligible physicians from internal medicine, family practice, preventive medicine and cardiology, who had one or more patients enrolled in CPCRS for at least one year were mailed a 21-question survey. The survey was reviewed for content and face validity by experts prior to mailing. Surveys were mailed, collected, and tabulated by an external independent research firm to maintain confidentiality. The questions pertained to overall satisfaction and to individual components of the service using a Likert-type scale for the majority of questions. Analysis of results was primarily descriptive.
RESULTS: Of 183 surveys mailed, 84 (46%) were returned. The majority of physicians (91%) were aware of the services provided by CPCRS. Most (88%) were satisfied with services provided by CPCRS. Most (88%) were satisfied with the extent of follow-up their patients received. The majority (81%) felt that cholesterol control in their patients had improved since enrollment.
CONCLUSIONS: Overall, physicians indicated a high level of satisfaction with the services provided by clinical pharmacy specialists at CPCRS and to a lesser degree with various components of the service.

22. Atherosclerotic risk factor control in peripheral arterial disease is better managed in patients with a concomitant diagnosis of coronary artery disease. *Ryan S. Stolcpart, Pharm.D.*, Thomas F. Rehring, M.D., Brian G. Sandhoff, Pharm.D., Harris W. Hollis, M.D., John A. Merenich, M.D.; Kaiser Permanente Colorado Region, Aurora, CO.

PURPOSE: Peripheral arterial disease (PAD) is a common diagnosis in elderly patients and is considered a coronary artery disease (CAD) risk equivalent. Current guidelines suggest identical risk factor reduction strategies in these patient populations. The purpose of this study was to determine the quality of atherosclerotic risk factor control in patients with isolated PAD compared to patients with a diagnosis of CAD in addition to PAD.
METHODS: We administratively identified patients with a diagnosis of PAD at two regional clinics serving 92,939 individuals. This cohort was stratified into two groups, those with isolated PAD (PAD) and those with both PAD and CAD (PAD + CAD). Full physical examination, pharmacy and laboratory data were available for all patients. Care for the PAD group was provided by the primary care provider. The PAD + CAD group was managed by a clinical pharmacist administered risk factor reduction service.
RESULTS: We identified 2,418 patients with PAD.

Risk Factor	PAD (n=1733)	PAD + CAD (n=685)
Average Age (yrs)	67.4 (± 13.7)	72.6 (± 8.6)
Percent Male	43% (742/1733)	63% (431/685)
*Annual Cholesterol Screen	54% (931/1733)	96% (656/685)
*LDL-c <100 mg/dL	44% (413/931)	82% (536/656)
*Statin Therapy	31% (543/1733)	79% (542/685)
*ACEi/ARB Therapy	32% (562/1733)	58% (399/685)
Aspirin therapy	Unable to validate	86% (588/685)

*(P<0.001)

CONCLUSIONS: Atherosclerotic risk factors are more aggressively treated in PAD patients that have a concurrent diagnosis of CAD. We submit that implementation of a pharmacist managed risk factor control service targeting all PAD patients might ameliorate this discrepancy.

23. Demographic and environmental influences of warfarin response in African Americans. *Kathryn M. Momary, Pharm.D.*, Lucy A. Fashingbauer, B.S., Nancy L. Shapiro, Pharm.D., Edith A. Nutescu, Pharm.D., Cathy M. Helgason, M.D., Dillip K. Pandey, M.D., Ph.D., Larisa H. Cavallari, Pharm.D.; University of Illinois at Chicago, Chicago, IL.

PURPOSE: Warfarin response studies have been conducted primarily in Caucasians. The objective of this study was to identify demographic and environmental factors contributing to warfarin dose requirements in African Americans.
METHODS: Sixty African Americans on a stable dose of warfarin, defined as the same dose for 3 consecutive clinic visits, were enrolled and asked to complete a questionnaire assessing dietary vitamin K intake and warfarin adherence. Information on demographics, laboratory values, and concomitant medications was also collected. Vitamin K intake was assessed in terms of units based on published content of vitamin K in specified foods. Data were compared between patients on low (<5mg/day) and traditional (≥5mg/day) warfarin doses using the Wilcoxon Rank-Sum or Pearson's χ^2 test as appropriate.
RESULTS: Sex, warfarin adherence, hepatic function, and INR were similar between the low (n=22) and traditional (n=38) warfarin dose groups. Advanced age, lower body mass index (BMI), and lower vitamin K intake were associated with lower warfarin dose requirements. Median (range) values in the low and traditional dose groups, respectively, were as follows: age = 70 (49–87) and 59 (23–80) years (p=0.006), BMI = 29 (22–53) and 34 (24–80) kg/m^2 (p=0.02), and vitamin K intake = 1.1 (0–17.1) and 6.3 (0–41.6) units (p=0.007).
CONCLUSIONS: Demographic and dietary factors are strongly associated with warfarin dose requirements in African Americans. Our data suggest that warfarin doses <5 mg/day should be started in African Americans of advanced age, of lower body weight, or with minimal intake of vitamin K-containing foods.

24. Racial differences in spironolactone response. *Larisa H. Cavallari, Pharm.D.*[1], Lucy A. Fashingbauer, B.S.[1], Vicki L. Groo, Pharm.D.[1], Mary R. Southworth, Pharm.D.[1], Deidre Fontana, R.N., BA[1], Randall E. Williams, M.D.[2], Paul Vaitkus, M.D.[1]; (1)University of Illinois at Chicago, Chicago, IL; (2)Northwestern University, Northfield, IL.

PURPOSE: The benefits of spironolactone in heart failure have largely been demonstrated in Caucasians. The objective of this prospective study was to determine whether there are racial differences in spironolactone response by comparing the effects of spironolactone on potassium concentrations between Caucasians and African Americans with heart failure.
METHODS: Spironolactone-naive heart failure patients of African American (n=22) or Caucasian (n=10) race were enrolled and started on spironolactone 12.5 mg/day, titrated to 25 mg/day if tolerated. Serum potassium and creatinine concentrations were determined at baseline and one week after spironolactone dose titration. Serum aldosterone was measured before and 3 months after spironolactone initiation in a subset of patients.
RESULTS: Heart failure severity, medications, and laboratory values were

similar between racial groups at baseline. Spironolactone was titrated to a mean±SD dose of 21±7 mg/day in African Americans and 17.5±6 mg/day in Caucasians, p=NS. Neither concomitant medications nor creatinine concentrations changed significantly in either group during the data collection period. With spironolactone, mean±SD potassium increased significantly from baseline in Caucasians (4.3±0.5 to 5.2±0.4 mEq/L, p<0.01) but not African Americans (4.3±0.5 to 4.5±0.5 mEq/L). Caucasians also tended to have greater increases in aldosterone with spironolactone; median (range) increase in aldosterone was 165 (-43 to 1712) pmol/L in Caucasians (n=5) versus 60 (-103 to 772) pmol/L in African Americans (n=10).
CONCLUSIONS: Heart failure treatment with spironolactone was associated with greater serum potassium elevation in Caucasians compared to African Americans. Our data suggest that African Americans may be less responsive to the renal effects of spironolactone.

25. Phosphodiesterase-type 5 inhibition increases microcirculatory vasodilation. *John M. Dopp, Pharm.D.*[1], Alexei V. Agapitov, M.D.[2], Christine A. Sinkey, R.N.[2], William G. Haynes, M.D.[2], Bradley G. Phillips, Pharm.D.[2]; (1)University of Wisconsin-Madison, Madison, WI; (2)University of Iowa, Iowa City, IA.

PURPOSE: Phosphodiesterase type-5 (PDE-5) inhibitors have important effects on vascular function and performance. Skin microcirculation contributes importantly to systemic vascular resistance and regulation of blood pressure. The effects of PDE-5 inhibition on microvascular circulation have not been investigated. The purpose of this study was to evaluate the role of PDE-5 inhibition on skin vascular reactivity.
METHODS: We studied 17 healthy males (44±2 years) who were randomized in a double-blind, crossover fashion to receive sildenafil 100 mg or placebo on separate study visits. Blood pressure and forearm skin blood flow (SBF) were determined at rest before and 45 minutes after study drug administration. Mechanistic studies were then completed (n=8) by infusing intra-brachial (IB) drugs to evaluate the contribution of alpha-receptors (IB norepinephrine), cyclic-AMP (IB isoproterenol), and sympathetic vascular tone (IB phentolamine) on skin blood flow following sildenafil and placebo. SBF was measured at the end of each IB infused drug and skin vascular resistance (SVR) was calculated by dividing mean arterial pressure by SBF.
RESULTS: PDE-5 inhibition reduced resting SVR from 59±7 at baseline to 42±4 (p=0.04) following sildenafil: SVR was unchanged after placebo (p=0.01 sildenafil versus placebo). Following sildenafil, SVR changes mediated by alpha-receptors, cyclic AMP, and sympathetic vascular tone were not different than placebo (p=NS for all).
CONCLUSIONS: PDE-5 inhibition significantly increased resting microcirculatory vasodilation in healthy, middle-aged men. These responses were not explained by differences in alpha-receptor sensitivity, cyclic AMP mediated dilation or sympathetic vascular tone. Microcirculatory changes may contribute to the hemodynamic changes associated with PDE-5 inhibition.

26. Evaluating the risk of Torsades de pointes with fluoroquinolones: an analysis of QT-interval and QT-dispersion. *Michael J. Peeters, Pharm.D.*, James P. Tsikouris, Pharm.D., Craig D. Cox, Pharm.D., Gary E. Meyerrose, M.D., Charles F. Seifert, Pharm.D.; Texas Tech University Health Sciences Center, Lubbock, TX.

PURPOSE: Fluoroquinolone antimicrobial medications (FQs) have been speculated to influence the risk of Torsades de pointes (Tdp). Methods of evaluating this risk are varied and not systematic. QTc-interval prolongation, while the most commonly used marker of Tdp, has questionable utility. QTc-dispersion may be a more selective marker of Tdp risk. No assessment of QTc-dispersion for FQs has been reported. The main objective of our investigation was to evaluate the effects of three commonly prescribed FQs by comprehensive QTc-analysis.
METHODS: In an open-label, crossover study, 13 healthy participants received 3 treatments in random order: ciprofloxacin 500mg BID, levofloxacin 500mg QD, moxifloxacin 400mg QD. Each treatment was given for 7 days with 1-week washout period between. Twelve-lead electrocardiographic measurements were performed immediately prior to the first dose, 2 hours after, and following a 7-day medication course. QTc-interval prolongation was determined by measurement of lead II, and QTc-dispersion represents the difference between maximum and minimum QTc-intervals among the 12 leads. Data was analyzed by repeated-measures ANOVA and Friedman's test with Bonferroni adjustment, with p<0.05 significance.
RESULTS: No difference was seen in baseline QTc-interval (p=0.665) or baseline QTc-dispersion (p=0.907). Moxifloxacin prolonged the QTc-interval by 12 msec after 7 days (2 hour = 408 msec, p=0.0134). Ciprofloxacin and levofloxacin had no effect on QTc-interval, and no FQ changed the QTc-dispersion.
CONCLUSIONS: Within our study population, ciprofloxacin and levofloxacin did not display an increased risk for Tdp. Moxifloxacin, while showing QTc-interval prolongation, did not affect QTc-dispersion, and an increased risk of Tdp is questionable.

27. Development of an updated risk model to predict post-cardiac surgery atrial fibrillation in patients receiving amiodarone prophylaxis. *Brian J. Barnes, Pharm.D.*, Patricia A. Howard, Pharm.D., FCCP, BCPS (AQ CV), Dennis W. Grauer, M.S., Ph.D., Erin A. Oswald, Pharm.D., Brian C. O'Neal, M.S., Pharm.D., Gregory F. Muehlebach, M.D., Jeffrey B. Kramer, M.D., Michael E. Gorton, M.D.; The University of Kansas Medical Center, Kansas City, KS.

PURPOSE: Prophylactic amiodarone has been shown to reduce postoperative atrial fibrillation (POAF) which occurs in 32.3% of cardiac surgery patients. This study evaluated the predictive accuracy of a validated risk index (VRI) for POAF (JAMA 2004;291:1720) and updated the model in a contemporary population receiving amiodarone prophylaxis (AMP).
METHODS: We conducted a retrospective analysis of institution-specific data (06/2002-12/2003) obtained from the Society of Thoracic Surgeons and the University HealthSystem Consortium. The effect of AMP on POAF was evaluated among 3 risk groups generated by the VRI (chi square analyses). Logistic regression was used to determine the predictive accuracy of the VRI in our patients and to develop and validate a new model to predict POAF in patients receiving AMP.
RESULTS: When applied to 713 patients the VRI classified 62.7% at low risk, 33.9% at medium risk, and 3.4% at high risk for developing POAF. AMP was used in 47% (334/713) of patients and decreased POAF by 32% (37% vs. 5%, p<0.001), 22% (28% vs. 6%, p<0.001), and 40% (40% vs. 0%, p=0.052) in these respective groups. The 11 variable VRI model yielded a predictive accuracy of 79.7% in our patients. Our newly developed model based on two variables (age and AMP), achieved similar accuracy in our derivation (80.8%) and validation (79.5%) cohorts.
CONCLUSIONS: The use of AMP significantly decreases the risk of POAF in cardiac surgery patients. We developed a simplified model, based on the contemporary use of AMP, which achieved similar predictive accuracy compared to the more complex VRI.

28. Evaluation of nesiritide in postoperative coronary artery bypass patients. *Corrie A. Martin, Pharm.D.*[1], Kerry Pickworth, Pharm.D.[1], Benjamin S. Sun, M.D.[2]; (1)The Ohio State University Medical Center, Department of Pharmacy, Columbus, OH; (2)The Ohio State University Medical Center, Division of Cardiothoracic Surgery, Columbus, OH.

PURPOSE: Nesiritide may offer a therapeutic benefit in patients with left ventricular dysfunction (LVD) undergoing coronary artery bypass grafting (CABG), however, this has not been investigated. The objective of this study is to evaluate nesiritide plus standard care for improving hemodynamics and medical stabilization after CABG, among patients with LVD.
METHODS: A retrospective analysis was conducted of adult patients with LVD, who underwent CABG, and received nesiritide plus standard of care postoperatively. Patients with ventricular assist devices were excluded. Primary endpoints were change in mean pulmonary artery pressure (MPAP), pulmonary artery diastolic pressure (PAD), and dose / duration of intravenous inotropes. Hemodynamic data and laboratory values were collected during 48 hours following nesiritide initiation. Duration of intravenous vasoactive medications and adverse effects were recorded.
RESULTS: Twenty-four patients received nesiritide after open-heart surgery from 03/2002 through 03/2004, and thirteen met inclusion criteria. After nesiritide initiation, MPAP and PAD did not change from baseline. Six of eight patients, receiving concomitant inotropes, were down titrated or discontinued at 48 hours. Four patients, not on an inotrope at baseline, required addition of an inotrope after nesiritide initiation. The incidence of hypotension was 20%.

	MPAP (mean)	PAD (mean)	p-value (compared to baseline)
Baseline	29	20	
8h	33	22	NS
16h	30	22	NS
24h	31	23	NS
48h	33	24	NS

NS= non significant for MPAP and PAD compared to baseline

CONCLUSIONS: Nesiritide did not offer any therapeutic benefit over standard care after CABG. Further studies are needed to elucidate nesiritide's role after CABG.

29. Survey of prophylaxis against venous thromboembolism in acutely ill medical patients. *Carla M. Peterman, Pharm.D.*[1], Daniel Kolansky, M.D.[2], Sarah Spinler, Pharm.D.[3]; (1)Philadelphia College of Pharmacy, Philadelphia, PA; (2)University of Pennsylvania, Philadelphia, PA; (3)Philadelphia College of Pharmacy, University of the Sciences in Philadelphia, Philadelphia, PA.

PURPOSE: To assess the frequency and type of VTE prophylaxis modalities utilized in acutely ill medical patients.
METHODS: An investigator concurrently reviewed charts of consecutive patients with a primary admission to 3 general medical units lasting ≥ 3 days. Patients excluded from the study were those transferred from another floor to the medicine units, and those that were discharged before 3 days.
RESULTS: 179 were enrolled (72 males) with an average age of 59 years and an average length of hospital stay of 7.2 days. Concurrent review of patient medical records revealed that 138 (77.1%) patients received one or more forms of prophylaxis during their hospital stay and 41 (22.9%) patients received no prophylaxis. Of those that received prophylaxis, 6.6% received

non-pharmacologic prophylaxis, 36.9% received therapeutic doses of anticoagulants for indications other than VTE prophylaxis, 70.3% received low-dose anticoagulants for VTE prophylaxis and 25.4% received more than one form of prophylaxis at some time during hospital admission. Of the 41 patients who received no prophylaxis, 22 (54%) had a documented contra-indication to anticoagulation and 19 (46%) did not. Adverse events (either VTE, bleeding or thrombocytopenia) developed in 2.9% of patients receiving anticoagulants.
CONCLUSIONS: At our institution, the rate of VTE prophylaxis appears to be higher than previously published experience, perhaps because large proportions (27.9%) of our patients are receiving therapeutic anticoagulation. The rate of adverse outcomes in patients receiving anticoagulants was low. Additional efforts are needed to enhance utilization of non-pharmacologic methods.

30E. Renal dysfunction is common in patients with heart failure and preserved systolic function: retrospective analysis of the Digitalis Investigation Group (DIG) trial. *Craig R. Lee, Pharm.D.*[1], J. Herbert Patterson, Pharm.D.[1], Wendy A. Gattis, Pharm.D.[2], Jalal Ghali, M.D.[3], Pinal J. Shah, Pharm.D.[1], Todd A. Schwartz, M.S.[1], Mihai Gheorghiade, M.D.[4], Kirkwood F. Adams, M.D.[1]; (1)UNC-Chapel Hill, Chapel Hill, NC; (2)Duke University, Durham, NC; (3)Cardiac Centers of Louisiana, Shreveport, LA; (4)Northwestern University, Chicago, IL.

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31. Evaluation of serum digoxin concentrations in patients treated for heart failure. *Douglas N. Carroll, Pharm.D.*, Timothy M. Murray, Pharm.D.; University of Oklahoma College of Pharmacy, Tulsa, OK.

PURPOSE: A recent post-hoc analysis of the Digitalis Investigation Group trial provides evidence that serum digoxin concentrations between 0.5 and 0.8 ng/ml may be optimal in the management of heart failure. In addition, serum concentrations greater than 1.1 ng/ml may be associated with increased mortality in men.
METHODS: We evaluated serum digoxin concentrations and any subsequent changes in digoxin dosing for hospitalized patients diagnosed with heart failure. Concentrations between 0.5 and 0.8 ng/ml were considered optimal.
RESULTS: We evaluated 119 patient admissions that accounted for 192 serum digoxin measurements. Of these, 118 (61.5%) met both inclusion criteria of post-distributional and steady state concentrations. Thirty-five (29.7%) concentrations were within the optimal range for heart failure. Of these, 8 (22.9%) received subsequent dose adjustments. Of the 83 concentrations considered to be inappropriate for heart failure, only 18 (21.7%) received subsequent dose adjustments. In addition, 49 (59%) of these concentrations were observed to be greater than 1.1 ng/ml.
CONCLUSIONS: This evaluation reveals that digoxin concentrations frequently lie outside of the optimal range for the management of heart failure. These values are commonly managed inappropriately indicating that there may be a gap in applying recent evidence into clinical practice. An additional source of confusion comes from the "normal" values of digoxin reported by most laboratories (0.8–2.0 ng/ml). In conclusion, we feel there is a need for education about the use of digoxin in heart failure and adjustment in the "normal" range of digoxin concentrations reported by laboratories.

32. Oral ritonavir increases expression of myocardial P-glycoprotein. *J. Jason Sims, Pharm.D.*[1], Jennifer M. Loeb, B.S.[2], Nicholas A. Wiegert, B.S.[3], Robert M. Tweig, B.S.[3], Brien L. Neudeck, Pharm.D.[4]; (1)Medtronic, Minneapolis, MN; (2)Pierce Biotechnology, Rockford, IL; (3)University of Wisconsin School of Pharmacy, Madison, WI; (4)University of Tennessee College of Pharmacy, Memphis, TN.

PURPOSE: P-glycoprotein(Pgp) is a multi-drug efflux protein. Although the exact physiologic role of Pgp is not known, it appears that Pgp is involved in cellular protection against potentially toxic compounds. Moreover, it is known that many oral drugs alter expression of Pgp in the intestine and liver. However, it is not clear if oral drugs affect Pgp expression in the heart. It may be that oral drugs alter myocardial Pgp resulting in impaired or enhanced Pgp activity. Thus, the objective of this study was to determine the effects of an oral Pgp inducer on myocardial Pgp expression.
METHODS: 30 mice were gavaged with ritonavir 350mg/kg/day (n=15) or vehicle(43% ethanol)(n=15) for 14 days. Mice were sacrificed day 15, with hearts and livers excised for Real-time PCR and Western blot protein analysis.
RESULTS: PCR revealed that ritonavir increased myocardial mdr3 mRNA (0.85±0.12 vs. 0.31±0.07 arbitrary units, p<0.001). This coincided with increased Pgp protein. As expected, ritonavir increased liver mdr3 mRNA (1.89±0.42 vs. 0.15±0.04 arbitrary units, p<0.001) with an associated increase in Pgp protein. Myocardial mdr1a mRNA increased (0.58±0.08 vs. 0.39±0.09 arbitrary units, p=0.12), but did not reach statistical significance.
CONCLUSIONS: Oral ritonavir increased myocardial Pgp expression and protein. Thus, oral drugs known to induce or inhibit Pgp may affect myocardial Pgp activity. Alteration in Pgp activity may change the normal cellular protection mechanisms of the heart. Moreover, it may alter the activity of cardiac drugs that are Pgp substrates. This study is limited by not assessing the functionality of increased myocardial Pgp.

33. Nesiritide in the outpatient setting in a small community hospital. *John Noviasky, Pharm.D.*[1], Rick Simpson, R.N.[2], Shirley Smith, R.N.[2], Kathy Lee, Rph[2]; (1)St Elizabeth Medical Center, Utica, NY; (2)Rome Memorial Hospital, Rome, NY.

PURPOSE: The use of nesiritide in the outpatient setting is currently being trialed in many locations. This study provides observational information about one community hospital's experience.
METHODS: The demographic data collected include patient age, sex, weight, and diuretics. Outcome measures were collected before and after entry into program include hospital stay, quality of life (QOL) assessment, and Beta-Natriuretic Peptide (BNP) levels.
RESULTS: Thirteen patients entered into the program, with average age of 74.1(± 11) years, weight of 81(± 21.6)Kg, and furosemide dose of 109(± 74)mg. Mean BNP went from 1615.2(± 1221) to 812.3(± 891.6),p=0.09, after program entry. Hospital days per patient went from 6.7(± 4.6)days in the 6 months prior to program to 0.3(± 0.9)days,p<0.05, for diagnosis of heart failure (average time in program 3.38 months). Admission for diagnoses other than heart failure went from 5.1(± 6.6) days to 0 days,p<0.05, for the same time period. The Average Score on the Modified Kansas City Cardiomyopathy QOL Questionnaire (1=worst, 6=best) went from 3.1(± 0.6) to 3.9(± 0.7) (P<0.05). Four patients have been discharged from program, 2 patients have expired, and the rest continue to get nesiritide on routine basis.
CONCLUSIONS: Preliminary results of this program are encouraging for decreased days in hospital, decreased BNP levels, and increased QOL measure. Further studies on pharmacoeconomics of this type of program are warranted.

34. Impact of prophylactic amiodarone on length-of-stay and stroke after cardiothoracic surgery. *Kristen A. Perkerson, Pharm.D.*[1], Effie L. Gillespie, Pharm.D.[2], C. Michael White, Pharm.D.[1], Jeffrey Kluger, M.D.[2], Hiroyoshi Takata, M.D.[2], Agron Ismaili, BSPharm[1], Michael Kardas, BSPharm[1], Craig I. Coleman, Pharm.D.[1]; (1)University of Connecticut, Hartford, CT; (2)Hartford Hospital, Hartford, CT.

PURPOSE: The Atrial Fibrillation Suppression Trials (AFIST) showed that prophylactic amiodarone reduces the incidence of postoperative atrial fibrillation (POAF). However, these previous studies were not powered to evaluate length-of-stay (LOS) and showed inconsistent effect on stroke.
METHODS: A large, retrospective cohort study was conducted in patients undergoing cardiothoracic surgery (CTS) at our institution between February 1998 and October 2003 to evaluate the impact of prophylactic amiodarone on LOS, stroke and POAF. Patients receiving any of the prophylactic amiodarone regimens utilized in the AFIST trials (e.g., 6g over 6 days or 7g over 10 days of oral amiodarone beginning on postoperative day 1 and 5, respectively, or a hybrid intravenous/oral loading regimen delivering 7g over 5 postoperative days) were propensity score matched (1:10 matching) with patients not receiving prophylaxis for age, valvular surgery, history of atrial fibrillation, gender, beta-blocker intolerance and preoperative digoxin use.
RESULTS: A total of 2,046 patients (n=186 amiodarone, n=1,860 control; 68.9±9.8 years, 75% male, 21% valvular surgery) were evaluated. Patients receiving prophylactic amiodarone had a decreased LOS (8.6±6.0 vs. 11.6±14.0, p=0.003) and a reduction in POAF (23.1% vs. 29.9%, p=0.05). The incidence of stroke was not significantly impacted (2.0% vs. 2.7%, p=0.61 and 2.7% vs. 5.8%, p=0.09, respectively).
CONCLUSIONS: Using the prophylactic amiodarone regimens from the AFIST trials reduces LOS by 3.0 days and the incidence of POAF by 22.7%.

35. Assessment of lipid management in high-risk individuals in an ambulatory setting. *Kari A. Stonely, Pharm.D.*[1], Kelly A. Kelsey, Pharm.D.[1], Richard H. Ensign II, Pharm.D.[2]; (1)University of Utah Hospitals and Clinics, Salt Lake City, UT; (2)Pfizer Inc., Kaysville, UT.

PURPOSE: This study determined baseline control of hyperlipidemia in high-risk patients as classified by National Cholesterol Education Program Adult Treatment Panel III Guidelines. We sought to determine need for intense lipid management through a pharmacist-managed hyperlipidemia clinic at the University of Utah Hospitals and Clinics (UUHC).
METHODS: We identified patients with diagnoses of diabetes and/or coronary heart disease in the electronic medical record. We collected retrospective data including lipid profiles, liver function tests (LFTs) and lipid medications. The primary outcome was percent meeting LDL goal and secondary outcomes included percent meeting non-HDL goal, percent with lipid panels, prescribing of lipid lowering medications and percent with LFT monitoring.
RESULTS: Of 2916 patients, LDL analysis showed 38% not at goal, 33% at or below goal and 29% without data. Calculated non-HDL levels were 46% not at goal, 29% at or below goal and 25% without data. Forty eight percent had previously been prescribed lipid-lowering medications. Of 1375 patients on lipid-lowering medications for which LFT monitoring was recommended, 75% had LFT data within the previous year and 97% had LFT data within three years.
CONCLUSIONS: The percentage of patients at UUHC that are high-risk for cardiovascular events and yet do not meet recommended cholesterol goals leaves room for improvement. This analysis supports aggressive lipid management through a pharmacist-run hyperlipidemia clinic at UUHC.

36. Cost-effectiveness analysis of antithrombotic therapy in non-urgent percutaneous coronary intervention. *Kelly M. Summers, Pharm.D.*, David A. Holdford, Ph.D., Michael A. Crouch, Pharm.D.; Virginia Commonwealth University Medical Center/VCU School of Pharmacy, MCV Campus, P.O. Box 980533, Richmond, VA.

PURPOSE: Periprocedural unfractionated heparin (UFH) and glycoprotein IIb/IIIa receptor inhibitors (GP inhibitors) are standard treatments during percutaneous coronary intervention (PCI). An alternative strategy consisting of bivalirudin with provisional GP inhibitor therapy was shown in the REPLACE-2 trial to be non-inferior, based on acute ischemic endpoints, to UFH plus planned GP inhibitor therapy. This trial also demonstrated lower hemorrhagic endpoints in the bivalirudin group. The current study describes a cost-effectiveness analysis (CEA) comparing three treatment approaches: 1) bivalirudin and provisional GP inhibitor therapy, 2) UFH and eptifibatide, and 3) UFH and abciximab.
METHODS: This CEA is a literature-based decision analysis model from an institutional perspective. We considered patient populations undergoing contemporary non-urgent PCI (EPISTENT, ESPRIT, TARGET, and REPLACE-2 served as reference studies) to identify probabilities of MI, urgent revascularization, thrombocytopenia, and TIMI-major or minor bleeding at 30 days. Costs were assigned to each of these outcomes incorporating DRG or CPT-assigned costs, institutional drug acquisition costs, and unit costs of platelets and blood.
RESULTS: In the base case analysis, the bivalirudin with provisional GP inhibitor therapy dominated the UFH/eptifibatide and UFH/abciximab approaches. The corresponding cost-effectiveness ratios were $985, $1067, and $1771, respectively. Sensitivity analyses incorporating a range of efficacy and cost estimates to assess the model's robustness will be presented.
CONCLUSIONS: Initial analysis from this literature-based, cross-trial comparison of antithrombotic treatment strategies in non-urgent PCI indicates bivalirudin with provisional GP inhibitor therapy is the most cost effective approach. Additional research is necessary to evaluate bivalirudin in urgent PCI.

37. Perioperative use of nesiritide in cardiac surgery patients. *Laura T. Ota, Pharm.D.*, Pat L. Masters, Pharm.D., BCPS, Carolyn A. Maroun-Monaco, RPh, M.S.; Caritas St. Elizabeth's Medical Center, Boston, MA.

PURPOSE: Brief reports have documented the potential additive benefits of nesiritide in the treatment of cardiac surgery patients with renal insufficiency and left ventricular dysfunction. The purpose of this case series was to evaluate the use of perioperative nesiritide in cardiac surgery patients.
METHODS: During August 2003–June 2004, 37 cardiac surgery patients received nesiritide perioperatively. Patient demographics, medical history, dose and duration of nesiritide, concomitant medication use, change in renal function, adverse effects, outcomes, and cost were documented.
RESULTS: Of 23 patients reviewed, the average baseline EF was 33.9% and the average baseline Scr and calculated CrCl was 1.9 mg/dl and 43.2 ml/min, respectively. The average duration of infusion was 38.2 hours. Postoperatively, the average urine output during the fist 24 hours was 2915.6 ml. The average peak Scr was 2.65 mg/dl (0.7–8.8 mg/dl), and 40.9% (9/22) of patients met the criteria for acute renal failure. Hypotension occurred in 26.1% of patients and 4 patients receiving doses greater than 0.01µg/kg/min required vasopressor initiation or titration to maintain blood pressure. The median length of stay in the ICU and duration of hospitalization was 2.96 days and 11 days, respectively. The average cost of nesiritide per patient was $816 ($408–$2040).
CONCLUSIONS: Patients that received nesiritide had improved hemodynamic parameters and urine output postoperatively. Acute renal failure occurred in 40.9% of patients and hypotension occurred more frequently in patients receiving doses greater than 0.01µg/kg/min. Formal randomized studies are needed to determine in which patients nesiritide will be most beneficial and cost effective.

38. Design, implementation, and impact of a pharmacist-managed hypertension intervention clinic: an 8-month evaluation. *Michelle E Gonzales, B.S., Pharm.D.*, Suzanne T Thompson, Pharm.D., Marie C. Vilme, Pharm.D., Celeste L. Oatman, Pharm.D., Deidree E. Edwards, Pharm.D., Patricia Fernandez-Quevedo, Pharm.D., BCPS, Ada B. Izquierdo-SanJuan, Pharm.D., Julia M. Ortega, Pharm.D.; Miami Veterans Affairs Medical Center, Miami, FL.

PURPOSE: Hypertension affects over 20% of Americans between the ages of 35 and 74 and accounts for more than 20,000 deaths per year. Pharmacist managed clinics aid in improving quality of care by providing education, ensuring treatment goals, and improving compliance. The Pharmacist Hypertension Intervention and Treatment (PHIT) Clinic was developed to assess patients on a bi-weekly basis and promptly adjust medications to achieve standard goals.
METHODS: A comprehensive protocol was developed and presented to the Pharmacy and Therapeutics committee for approval. Patient enrollment began in September 2003 with appointments scheduled at 2-week intervals. Patients are followed by the PHIT clinic until their blood pressure is at goal for 2 consecutive visits.
RESULTS: On average, 20 patients were enrolled each month and 158 patients have come to at least one visit. Majority of patients (64.5%) have no compelling indications and have a goal blood pressure of less than 140/90 mm Hg. Thirty-eight patients (22.7%) have diabetes or renal problems and 20 patients (13.4%) have proteinuria. The 162 interventions include increasing doses (50%), initiating new medications (32.7%), discontinuing medications (13%), and decreasing doses (4.3%). ACE inhibitors (30.9%) and hydrochlorathiazide (18.5%) are the medications most often modified. Thirty-eight patients (24.1%) have been referred back to their Primary Care providers at goal. Sixty-six patients are actively followed in PHIT clinic at present and 13 patients are scheduled for initial visits.
CONCLUSIONS: The PHIT clinic is making an impact on controlling hypertension with an average of four patients a month discharged at goal.

39. Amiodarone dose response for preventing atrial fibrillation following cardiac surgery: a meta-analysis. *Mitchell S. Buckley, Pharm.D.*[1], Paul E. Nolan Jr., Pharm.D.[1], Marion K. Slack, Ph.D.[1], James E. Tisdale, Pharm.D.[2], Daniel E. Hilleman, Pharm.D.[3], Jack G. Copeland, M.D.[1]; (1)University of Arizona, Tucson, AZ; (2)Purdue University, West Lafayette, IN; (3)Creighton University Medical Center, Omaha, NE.

PURPOSE: We previously reported that amiodarone (AM) significantly reduces post-cardiac surgery atrial fibrillation (PCSAF). The purpose of this study was (a) to examine a possible dose-response relationship between AM and reduction in PCSAF; and (b) to determine whether preoperative (PRE) or postoperative (POST) AM administration is superior in reducing PCSAF.
METHODS: Using MEDLINE database for English language reports published between January, 1966 and June, 2004, 14 prospective, randomized, placebo-controlled trials were identified as using AM to prevent PCSAF. 13 studies (n = 2666 total patients) were used in this analysis. For each study total AM dose was categorized as low (<3000 mg), medium (3000 mg to 5000 mg) or high (>5000 mg) and PRE or POST, and then aggregated using standard meta-analytic techniques.
RESULTS: Compared to placebo, patients administered AM had a lower incidence of PCSAF regardless of dose (low: OR=0.60, CI: 0.44–0.80, p=0.001; medium: OR=0.44, CI: 0.33–0.58, p<0.001; high: OR=0.45, CI: 0.30–0.69, p<0.001). A comparison of the mean risk reductions suggested a greater reduction in PCSAF with medium and high doses (56% and 55%) as compared to low dose (40%). Compared to placebo the reduction in PCSAF was similar between PRE AM and POST AM (OR=0.49; CI: 0.37–0.65, p<0.001; and OR=0.50; CI: 0.39–0.63; p<0.001, respectively), corresponding to mean risk reductions of 51% and 50%, respectively.
CONCLUSIONS: Total doses of AM >3000mg appear optimal for reducing PCSAF. Similar outcome benefits should be expected whether this dose is administered preoperatively or postoperatively.

40. Prophylactic amiodarone decreases atrial fibrillation and hospital length of stay following cardiac surgery: a meta-analysis. *Mitchell S. Buckley, Pharm.D.*[1], Paul E. Nolan Jr., Pharm.D.[1], Marion K. Slack, Ph.D.[1], James E. Tisdale, Pharm.D.[2], Daniel E. Hilleman, Pharm.D.[3], Jack G. Copeland, M.D.[1]; (1)University of Arizona, Tucson, AZ; (2)Purdue University, West Lafayette, IN; (3)Creighton University Medical Center, Omaha, NE.

PURPOSE: The purpose of this study was to evaluate the effectiveness of prophylactically administered amiodarone (AM) with respect to reducing atrial fibrillation (AF) and hospital length of stay (LOS) following cardiac surgery (CS).
METHODS: Using MEDLINE database for English language reports published between January, 1966 and June, 2004, 16 prospective, randomized, controlled trials (RCTs) and 2 nonrandomized studies were identified as using AM to prevent post-CS AF. For each study the number of patients, incidence of post-CS AF, LOS and a number of other clinical variables were recorded for both AM and control groups and then aggregated using standard meta-analytic techniques.
RESULTS: Using all 18 studies (n=6096 patients), AM decreased post-CS AF by 43% (OR=0.57; CI 0.51, 0.64; p<0.001). Subanalysis using only RCT data (n=3198 patients) showed AM lowered post-CS AF by 48% (OR=0.52; CI 0.43, 0.62, p<0.001). AM also reduced LOS by a mean of 1.04 days (p<0.001).
CONCLUSIONS: In patients undergoing CS AM significantly decreases both the incidence of AF and LOS.

41. Adherence to recommendations for low-density lipoprotein lowering in patients with type 2 diabetes mellitus. *Nabila Ahmed, Pharm.D.*, Stephanie L Evans, Pharm.D., Julie A Brousil, Pharm.D.; St. Louis College of Pharmacy/ Family Medicine of St. Louis, St. Louis, MO.

PURPOSE: The purpose of this study was to determine the impact of pharmacy initiated recommendations to 1) improve compliance with the recommended LDL monitoring schedule for patients with type 2 Diabetes Mellitus (DM) and 2) increase the percentage of patients that meet goal LDL cholesterol levels in a family medicine residency clinic.
METHODS: The study was a retrospective chart review of 217 patients with type 2 DM seen between June 2002 and July 2003. Data was collected to determine if a fasting lipid profile (FLP) had been performed within the previous year and whether or not the patient had achieved the recommended

LDL goal. An intervention form with recommendations for physicians was placed in the medical record if the FLP had not been checked within the previous year or if the LDL was not at goal. Medical records were reviewed four months following the placement of the intervention form.
RESULTS: The average patient age was 50.5 (+ 11.7) years, the average BMI was 34.2 (+7.71) kg/m2, and 59% were female. At baseline, 26.7% of the patients had a Hemoglobin A1c value of <7% and 36.5% of the patients had reached their goal LDL. Following the intervention period the percentage of patients with documented LDL values increased from 60.1% to 79.7% (p=NS). The LDL goal attainment rate also increased from 36.5% to 43.2% post-intervention (p=0.023).
CONCLUSIONS: Overall, the rate of adherence to the recommended LDL monitoring schedule improved. The percentage of patients that met goal LDL cholesterol levels increased significantly post-intervention.

42E. Healthcare and drug utilzation patterns in patients receiving long-term thienopyridine therapy. *Patrick L. McCollam, Pharm.D.*[1], Maureen J. Lage, Ph.D.[2], Lee Bowman, Ph.D.[1]; (1)Lilly Research Laboratories, Indianapolis, IN; (2)HealthMetrics Outcomes Research, LLC, Groton, CT.

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43E. Total cost of acute coronary syndromes patients in a managed care population during the one-year following initial presentation. *Patrick L. McCollam, Pharm.D.*[1], Lida Etemad, Pharm.D., M.S.[2]; (1)Lilly Research Laboratories, Indianapolis, IN; (2)Ingenix, Eden Prairie, MN.

Published in Journal of Managed Care Pharmacy 2004;10:202.

44E. Altered aldosterone disposition in P-glycoprotein knockout mice. *Robert B. Parker, Pharm.D.*[1], C. Ryan Yates, Pharm.D., Ph.D.[2], S. Casey Laizure, Pharm.D.[1]; (1)University of Tennessee Dept of Pharmacy, Memphis, TN; (2)University of Tennessee Dept of Pharmaceutical Sciences, Memphis, TN.

Presented at the American College of Cardiology Scientific Sessions, Chicago, IL, April 2003.

45E. Management of acute coronary syndrome within a veteran population: A six-month review. *Suzanne T. Thompson, Pharm.D.*, Judy H. Tseng, Pharm.D., Deidree E. Edwards, Pharm.D.; Veterans Affairs Medical Center, Miami, FL.

Presented at the 35th Annual Southeastern Residency Conference of the American Society of Health-System Pharmacists, Athens, GA, May 6–7, 2004.

46. Adjunctive sedation during shock delivery with an implanted atrial defibrillator (IAD): pharmacokinetic and pharmacological responses to triazolam. *Tanya J. Fabian, Pharm.D., Ph.D.*[1], Michael R. Ujhelyi, Pharm.D.[2], David S. Schwartzman, M.D.[1], Sharon E. Corey, Ph.D.[1], Kristin L. Bigos, B.S.[1], Bruce G. Pollock, M.D., Ph.D.[1], Patricia D. Kroboth, Ph.D.[1]; (1)University of Pittsburgh, Pittsburgh, PA; (2)Medtronic, Inc, Minneapolis, MN.

PURPOSE: Significant anxiety and discomfort have been associated with patient-activated atrial shock delivery. The purpose of this study was to determine whether adjunctive oral triazolam produced the desired therapeutic effects of sedation and anterograde amnesia without interfering with the patient's ability to administer the atrial shock.
METHODS: In this double-blind, placebo-controlled trial, 15 men and women (39 to 77 years; 59 Ñb 9.6 years) were randomly assigned to receive triazolam 0.375 mg or placebo 75 minutes prior to shock delivery. Serial blood samples were obtained for measuring plasma concentrations of triazolam. Assessments of sedation and memory were collected throughout the study.
RESULTS: Nearly a four-fold difference in triazolam concentration was observed at the peak (1.20 ng/ml to 4.46 ng/ml) and at the time of shock (0.75 ng/ml to 2.86 ng/ml). Despite the dose administered, patients were not overtly sedated, and all were able to self-activate their IAD device. Maximum decrement in memory impairment (33%) and psychomotor performance (28% to 34%) were relatively low. There were no correlations between triazolam exposure and response.
CONCLUSIONS: This is the first placebo-controlled clinical evaluation of an oral sedative administered prior to shock delivery in patients with IADs. These data suggest that triazolam 0.375 mg produced the desired therapeutic effects of sedation and memory impairment for the purpose to mitigating atrial shock discomfort in this group of patients. The absence of a concentration effect relationship suggests that other factors may influence triazolam sensitivity in this population including varying levels of shock-related anxiety.

47. Th1- and Th2-related cytokine and chemokine balance in blood pressure responders and non-responders to metoprolol monotherapy. *Issam Zineh, Pharm.D.*[1], Xiaoping Luo, M.D.[2], Taimour Y. Langaee, Ph.D.[1], Julie A. Johnson, Pharm.D.[1], Nasser Chegini, Ph.D.[2]; (1)Department of Pharmacy Practice, University of Florida, Gainesville, FL; (2)Department of Obstetrics and Gynecology, University of Florida College of Medicine, Gainesville, FL.

PURPOSE: Inflammation mediates many diseases including hypertension. Additionally, some cardiovascular drugs exhibit immunomodulatory effects. We investigated T-helper (Th)1- (pro-inflammatory) and Th2-related (anti-inflammatory) cytokine/chemokine balance in blood pressure (BP) "responders" and "non-responders" to metoprolol.
METHODS: The following were measured by 22-plex detection (Upstate, Charlottesville): IL-1α , IL-1β , IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-10, IL-12 (p40), IL-12 (p70), IL-13, IL-15, GM-CSF, IFNγ , TNFα , eotaxin, MCP-1, RANTES, MIP-1α , and IP-10. Median concentrations were calculated for five patients that achieved goal BP and five that did not in response to a minimum four weeks of metoprolol at maximum tolerated doses.
RESULTS: There were no differences in demographics between groups (not shown). IL-1 isotypes, IL-3, and IP-10 were 1.5–7 times higher in non-responders ($p<0.05$, Table). GM-CSF, IL-12p40, and IL-4 trended to being higher in non-responders ($p<0.1$).
Table. Cytokine/chemokine profiles for metoprolol responders and non-responders

Phenotype	Eotaxin	GM-CSF	IFNg	IL-10	IL-12 p40	IL-12 p70
Resp	414	3.2	17.6	0.51	20.9	3.0
Non-resp	456	21.7	143	5.2	38.5	9.8
	IL-3	IL-4	IL-5	IL-6	IL-7	IL-8
Resp	9.1	0.55	0.23	23.2	105	2.4
Non-Resp	38.8	0.97	0.34	19.1	34.6	1.71

(table continued)

Phenotype	IL-13	IL-15	IL-1a	IL-1b	IL-2
Resp	1.8	7.5	14.7	0.58	—
Non-resp	1.8	18.5	33.4	4.0	—
	IP-10	MCP1	MIP1a	RANTES	TNFa
Resp	1652	45.1	10.2	979	0.49
Non-Resp	2449	50.8	20	1527	1.85

CONCLUSIONS: Multiplexing allowed us to immunologically profile hypertensive subjects with variable BP response to metoprolol. These hypothesis-generating data suggests a Th1 (pro-inflammatory) bias in patients who do not achieve adequate BP control compared with those who reach target.

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48. Propofol associated hypertriglyceridemia and pancreatitis: an incidence and risk factor analysis. *John W. Devlin, Pharm.D., BCPS, FCCM*[1], Adah Lau, Pharm.D.[2], Maged Tanios, M.D., M.P.H., FCCP[3]; (1)Northeastern University School of Pharmacy, Boston, MA; (2)Tufts-New England Medical Center, Boston, MA; (3)Long Beach Memorial Medical Center, Long Beach, CA.

PURPOSE: Propofol is routinely used for sedation at our institution but has been anecdotally associated with hypertriglyceridemia (HTG) and HTG-related pancreatitis. We sought to characterize the incidence, severity, and risk factors associated with propofol-related HTG and pancreatitis.
METHODS: Consecutive ICU patients administered propofol for ≥ 24 hours during 2003 were reviewed to identify incidence of HTG [serum triglyceride (STG) ≥ 400 mg/dL] and pancreatitis [(amylase ≥ 125 IU/L and lipase ≥ 60 IU/L) and abdominal CT or exam consistent with pancreatitis]. Patients with baseline STG ≥ 250 mg/dL, receiving another lipid product, or with baseline pancreatitis were excluded.
RESULTS: Of 512 patients reviewed, only 159 patients (31%) had ≥ 1 STG drawn. Of these, 29/159 (18%) developed HTG with 6/29 (21%) having a STG ≥ 1000 mg/dL. At initial HTG detection, the average maximum STG was 696 mg/dL (403 to 1737) [median (range)], propofol infusion rate 50 µg/kg/min (5 to 275) and duration of propofol therapy 54 (14 to 319) hours. Propofol therapy was discontinued within 24 hours of HTG detection 64% of the time. Independent risk factors associated with HTG include patient age (p=0.029), ICU length of stay (p=0.009), and duration of propofol therapy (p=0.001). Three of the 29 (10%) HTG patients developed pancreatitis.
CONCLUSIONS: HTG and HTG-associated pancreatitis are commonly seen in ICU patients receiving propofol at our institution. Serum TG concentrations should be routinely monitored for patients receiving propofol therapy and the dose decreased or held when HTG is detected.

49. Glycemic control in critically ill patients via implementation of an "insulin drip" protocol. *Jessica Bollinger, Pharmacy, Intern*, Harrison Weed, M.D., Samuel Cataland, M.D., Anthony Gerlach, Pharm.D., BCPS; The Ohio State University Medical Center, Columbus, OH.

PURPOSE: Strict control of hyperglycemia with continuous insulin infusion has been shown to decrease morbidity and mortality in ICU patients, but tight glucose control carries the risk of hypoglycemia. As a safety initiative, we implemented an insulin infusion protocol in our ICUs. We studied the impact of this initiative on the incidence of hypoglycemia and the time to glycemic control.
METHODS: Subjects were ICU patients receiving continuous insulin infusion. We collected data by retrospective chart review. We defined hypoglycemia as blood sugar below 64 mg/dL and controlled glucose as blood

sugar below 150 mg/dL. We used χ^2 to analyze categorical data and Student's *t*-test to analyze continuous data.
RESULTS: As a baseline we studied 49 patients in the ICU from 6/16/03 to 7/30/03. After implementation of the protocol we studied 47 patients in the ICU from 9/24/03 to 11/14/03.

	Baseline N=49	Post-Implementation N=47	p-value
Male:Female	33:16	27:20	0.32
Mean Age (Years)	59.3 (± 10.5)	63.3 (±10.4)	0.06
History Diabetes	61.2%	66.0%	0.63
Mean duration ay (Days)	3.8 (± 3.0)	4.87 (± 6.6)	0.32
Hypoglycemic Events	17	3	0.0006
Mean highest glucose before start of infusion (mg/dL)	331 ± 105	279 ± 62	0.0054
Mean time to glycemic control	9.8 hours	7.9 hours	0.137

CONCLUSIONS: Our implementation of a continuous insulin infusion protocol resulted in significantly less hypoglycemia without effecting glycemic control.

50. Utility of a QTc monitoring algorithm in the adult intensive care unit. *Megan A McCartan, Pharm.D.*[1], Katie M Speidel, Pharm.D.[2], Melissa A Miller, Pharm.D.[2], Keith M Olsen, Pharm.D.[2], Tien M Ng, Pharm.D.[3]; (1)The Nebraska Medical Center, Omaha, NE; (2)University of Nebraska Medical Center, Omaha, NE; (3)University of Southern California, 1985 Zonal Ave, Los Angeles, CA.

PURPOSE: QTc prolonging medications are commonly initiated in intensive care unit (ICU) patients without consideration for monitoring, alternatives, or adjustment of doses. No guidelines exist to help in determining which medications require more vigilant electrophysiologic monitoring. The purpose of this pilot study was to assess the utility of a pharmacist QTc monitoring algorithm for adult ICU patients.
METHODS: A step-wise algorithm (including daily assessments of QTc duration, electrolytes, renal/hepatic function, concomitant medications, comorbid illnesses, and monitoring orders) was developed for monitoring pre-specified QTc prolonging medications. In a prospective, observational study, consecutive adult ICU patients prescribed QTc prolonging medications were followed. The primary endpoint was the mean number of interventions per patient. Secondary endpoints included total number of interventions based on the specific type, frequency of patients with specific types of interventions, and frequency of patients with possible interventions.
RESULTS: In 3 months, 267 patients (64±18 years, 50.2% female, 72.3% Caucasian, baseline QTc 398±147 ms) were identified. The algorithm generated a total of 1126 interventions (mean 4.2±3.9 interventions per patient). The most common types of interventions were: correct electrolytes (68.9%), order follow-up laboratory measures (47.2%), and discontinue QTc drug or consider alternative (40.8%). Only 15 (5.6%) patients did not have a possible intervention.
CONCLUSIONS: This pilot study demonstrates that numerous opportunities exist for pharmacists to provide therapeutic recommendations pertaining to the use of QTc prolonging medications in ICU patients. These interventions can be derived from a standardized monitoring algorithm. Validation of this algorithm in a prospective, randomized trial is planned.

51. Cardiac critical care post-operative blood glucose control: A revised intensive intravenous insulin protocol. *Marybeth Boudreau, Pharm.D.*, Cynthia Downs, R.N., MSN, Renee M. Ford, Pharm.D., Jamie L. Cronin, Pharm.D., Dan Moellentin, Pharm.D., Shewan M Aziz, Ph.D., BCOP; Eastern Maine Medical Center, Bangor, ME.

PURPOSE: To examine and compare blood glucose control in a post-operative coronary artery by-pass graft (CABG) population following the implementation of an intensive intravenous (IV) insulin protocol.
METHODS: Two separate retrospective blood glucose evaluations were performed before and after the revision of an intensive IV insulin protocol. Eighty post-operative CABG patients were randomly selected for each evaluation and separated into four classes: insulin dependent diabetic (IDD), non-insulin dependent diabetic (NIDD), GIK and non-GIK non-diabetic (NGND). Mean glucose levels, hourly insulin requirements and number of hyper and hypoglycemic episodes were collected. Statistical analysis was performed using the Student's *t*-test and significance was considered at a p value less than or equal to 0.05.
RESULTS:

	Protocol 2002 (goal 100–200)		Protocol 2003 (goal 90–130)		
Groups	Mean 48hr Glucose	S. deviation	Mean 48 hr Glucose	S. deviation	P value
IDD	195	26.2	141	54.3	<0.05
NIDD	180	28.5	130	36.4	<0.05
GIK	180	34	154	82	NS
NGND	171	31	138	37.2	<0.05

CONCLUSIONS: One year following the revision of an intensive intravenous insulin protocol, post-operative glucose control for most patient populations was significantly improved.

52. Use of the Multiple Disease Risk Assessment Database© to identify patients at risk for fungal infections in a surgical intensive care unit. *Neil E. Ernst, Pharm.D.*[1], Steven E. Pass, Pharm.D., BCPS[1], Lisa B. Greenstein, Pharm.D.[2]; (1)University Hospital, Cincinnati, OH; (2)Pfizer Inc, Union, KY.

PURPOSE: The use of antifungal prophylaxis for surgical patients is a controversial but well accepted practice. However, there is little evidence to identify which patients are at high risk for developing invasive fungal infections. Establishment of definitive risk factors may help identify patients that may benefit from routine use of antifungal prophylaxis in the SICU.
METHODS: Medical records of all patients 18 years of age or greater admitted to the SICU for more than 48 hours between 9/1/03 and 2/29/04 were reviewed. Clinical and demographic data on all patients enrolled in the study were collected. All identifiable risk factors, microbiologic results, treatment regimens, and patient outcomes were entered into the MDRA© (Pfizer, Inc) database. Risk factors were analyzed for significance of correlation by univariate analysis using Fisher's exact test.
RESULTS: 159 patients met criteria for study enrollment. 13/159 (8.2%) had positive fungal cultures. The most frequent Candida species encountered were C. albicans and C. glabrata. One patient was determined to have a clinically significant bloodstream infection. The overall rate of candidemia was extrapolated to 6.29 per 1000 SICU patient admissions. Factors associated with an increased risk for fungal infections by univariate analysis included diabetes (RR 1.2) and duration of antibiotic use of 7 days or greater (RR 1.4).
CONCLUSIONS: C. albicans was the primary fungal pathogen in this patient population and should be the focus of empiric treatment and/or prophylaxis. Future studies should be designed to determine the efficacy and safety of antifungal prophylaxis in high-risk patients.

53. Cost-effectiveness of rHuEPO for reducing RBC transfusions in critically ill patients. *Robert MacLaren, Pharm.D.*, Patrick W. Sullivan, Ph.D.; University of Colorado School of Pharmacy, Denver, CO

PURPOSE: To examine the cost-effectiveness of using rHuEPO to reduce RBC transfusions in ICU patients.
METHODS: Decision analysis examining costs and effectiveness of using rHuEPO vs. not using rHuEPO in a simulated adult mixed ICU. Two independent cost-effectiveness models were created based on the results of two multicenter studies that investigated the use of rHuEPO. Base case assumptions and estimates of effectiveness were obtained from these two studies. The models accounted for feasibility (the deferral rate for allogeneic RBC transfusions), rHuEPO efficacy (the reduction in allogeneic RBC use), and adverse effects of rHuEPO and allogeneic RBC transfusions. Model estimates were obtained from published sources. Costs were expressed in $US (2002) using 3% as the discount rate. Effectiveness was measured using discounted quality-adjusted life years (QALYs). Probabilistic sensitivity analysis was conducted using second-order Monte Carlo simulation.
RESULTS: Incremental cost of using rHuEPO to reduce RBC transfusions amounted to $1918 and $1439; incremental effectiveness was 0.0563 and 0.0305; and the cost-effectiveness ratio was $34,088 and $47,149 per QALY for studies one and two, respectively. The results of the model were most sensitive to the attributable risk of nosocomial bacterial infections per RBC unit. rHuEPO was cost-effective in 52.0% of the Monte Carlo simulations for a willingness to pay of $50,000/QALY. Incorporating a restrictive transfusion strategy into the model resulted in a cost-effectiveness ratio of $145,455 per QALY.
CONCLUSIONS: rHuEPO may be cost-effective for reducing RBC transfusions in mixed ICU populations, assuming RBC transfusions increase the risk of nosocomial bacterial infections.

54. Evaluation of direct thrombin inhibitor use in patients with proven or suspected heparin induced thrombocytopenia (HIT). *Tyree H. Kiser IV, Pharm.D.*, Doug N. Fish, Pharm.D., Rose Jung, Pharm.D., Rob MacLaren, Pharm.D.; University of Colorado Health Sciences Center, Denver, CO.

PURPOSE: Evaluate argatroban and lepirudin use in patients with proven or suspected HIT.
METHODS: Patients diagnosed with HIT and treated with lepirudin or argatroban between January 2000 and December 2003 at the University of Colorado Hospital were retrospectively evaluated. Patients were assessed for dose and duration of lepirudin or argatroban therapy, HIT diagnostic tests, and clinically significant adverse effects.
RESULTS: Seventy-six patients were identified: 32 patients received argatroban, 39 received lepirudin, and 5 received both argatroban and lepirudin at different times during the admission. Mean doses were argatroban 1.6 ± 1.84 µg/kg/min and lepirudin 0.09 ± 0.12 mg/kg/hr, both 25% to 50% lower than recommended doses. Mean duration of therapy was 11.5 ± 20.5 days. Clinically significant bleeding occurred in 6.25% of argatroban patients and 2.7% receiving lepirudin (p=0.18); all patients had an aPTT >100. No patient achieved a definitive diagnosis of HIT due to equivocal or

contradictory platelet aggregation tests in 30% of patients, negative ELISA assay in 78%, and performance of serotonin release assays in only three patients. Although commonly ordered (72% of patients), platelet aggregation tests were seldom useful in diagnosing HIT. Drug acquisition costs were approximately $450,000 in these patients.
CONCLUSIONS: Critically ill patients may require lower doses of lepirudin and argatroban than usually recommended. These drugs should be started at lower doses and titrated to achieve targeted aPTT and avoid increased risk of bleeding. Appropriate diagnostic methods should be used to avoid unnecessary drug use. Platelet aggregation tests should not be used in evaluating HIT.

55. Low dose recomdinant factor VIIa in trauma or coagulopathy. *William Dager, Pharm.D.*, Ronald Regalia, Pharm.D., Dean Williamson, Pharm.D., Robert Gosselin, CLS, John Owings, M.D., Jeffery King, Pharm.D.; University of California, Davis Medical Center, Sacramento, CA.

PURPOSE: Coagulopathies associated with trauma related massive hemorrhage, extensive organ damage or liver impairment causing impaired thrombin generation and thrombocytopenia resulting in continued bleeding, declining hematocrit and/or elevated INR/aPTT despite aggressive blood product transfusions can be challenging to manage. An alternative strategy for achieving hemostasis in these patients includes recombinant activated factor VIIa (rFVIIa; NOVOSEVEN). rFVIIa becomes a prohemostatic agent once bound to tissue factor released from damaged endothelium. The dose response of rVIIa in non-hemophiliac patients with continued bleeding; declining hematocrit or elevated INR/aPTT despite aggressive blood product transfusions including fresh frozen plasma (FFP) is unclear.
METHODS: An ongoing consecutive series of non-hemophiliac patients receiving low dose rVIIa (< 90µg/kg) were evaluated. rVIIa was not dispensed until pre-administration assessment determined that adequate blood product transfusions (including FFP) or other adjunct therapies to reverse the symptomatic coagulopathy were not sufficient. Laboratory values and bleeding observations pre and post-rVIIa were recorded.
RESULTS: After administration of < 90µg/kg rVIIa (n=9; ~30–45 µg/kg in most cases), small vessel (field) bleeding in the traumatic injury patients rapidly reversed (within 10–15 minutes) and correction of laboratory measurements of coagulation (mean initial INR=2.5; post rVIIa INR=1.1) was noted. Additionally, a very small dose (1.2mg rVIIa with FFP) corrected life-threatening bleeding with concurrent warfarin (INR 5.08 to 0.95).
CONCLUSIONS: Low dose rVIIa can rapidly reverse traumatic small vessel "field" bleeding or a coagulopathy in rare occasions where traditional management using FFP or other blood products is insufficient to achieve desirable hemostasis.

56. Use of drotrecogin alfa activated in septic AIDS patients. *Annette M Rowden, Pharm.D.*; The Johns Hopkins Hospital, Baltimore, M.D.

PURPOSE: Drotrecogin alfa (DA) was FDA approved for the treatment of severe sepsis in patients at high risk of death. Few patients with known HIV were included in the PROWESS trial. Advanced HIV patients (CD4 < 50/mm^3) were excluded due to presumed high risk of death within the 28 day study period from preexisting non-sepsis related disease. AIDS patients are not excluded from The Johns Hopkins Hospital (JHH) DA guidelines. Purpose is to review outcomes of such patients at JHH.
METHODS: Retrospective data collection for each AIDS patient receiving DA during the period December 2001–May 2004 was conducted. The following data elements were collected: last CD4; infection; organ failure(s) at therapy initiation; APACHE II score; infusion duration; complications; 28 day survival.
RESULTS: Seven AIDS patients received DA. Two patients survived. Both surviving patients had single organ failure.

CD4/mm^3	Infection	Organ Failures*	APACHE II	Infusion (hrs)	Complications	Survived?
133	Bacteremia, pneumonia	CRA	31	72	bleeding	No
33	pyomyositis	C	26	96	none	Yes
324	pneumonia	CKA	NR	93	none	No
1	"sepsis"	CKHA	44	95	subarrachnoid hemorrhage	No
93	"sepsis"	CRHA	30	34	none; stopped for thrombocytopenia	No
115	Pneumonia; urosepsis	RA	22	94	none	No
81	"sepsis"; c. diff colitis	R	23	94	none	Yes

*cardiovascular(C); kidney (K); respiratory (R); hematologic (H); acidosis (A)

CONCLUSIONS: Twenty eight day survival in our patients with multiorgan failure was zero. Future studies should attempt to discern the relationship between multiorgan failure and survival benefit from DA in this population.

57E. Prompt administration of drotrecogin alfa (activated) is associated with improved survivial. Arthur Wheeler, M.D.[1], Jay Steingrub, M.D.[2], Becky Bates, M.S.[3], Walter Linde-Zwirble, M.S.[4], *Jill Shwed McCollam, Pharm.D.*[3], Michael Zeckel, M.D.[3]; (1)Vanderbilt Medical Center, Nashville, TN; (2)Baystate Medical Center, Springfield, MA; (3)Eli Lilly and Company, Indianapolis, IN; (4)Health Process Management (HPM), Doylestown, PA.

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58. Clinical significance of Candida sp. isolated from bronchoalveolar lavage in critically ill trauma patients. *G. Christopher Wood, Pharm.D.*[1], Eric W. Mueller, Pharm.D.[1], Martin A. Croce, M.D.[2], Bradley A. Boucher, Pharm.D.[1], Timothy C. Fabian, M.D.[2]; (1)University of Tennessee College of Pharmacy, Memphis, TN; (2)University of Tennessee College of Medicine, Memphis, TN.

PURPOSE: Determine the clinical significance of *Candida* sp. isolated from bronchoalveolar lavage (BAL) in critically ill trauma patients. This is the first such study in this population. Two previous studies in immunocompetent medical ICU patients suggested that *Candida* sp. in BAL does not require antifungal therapy.
METHODS: A retrospective study of all BALs performed for diagnosing ventilator-associated pneumonia (VAP) in critically ill patients at a level 1 trauma center over a three-year period (1998–2001). Demographics and outcomes of patients with *Candida* sp. isolated from BAL were analyzed.
RESULTS: A total of 1077 BAL cultures were performed in 555 patients. *Candida* sp. was isolated from 85 BAL cultures in 62 patients (mean age 47 ± 19 years, mean injury severity score 28 ± 10). No isolates exceeded the threshold for VAP used at the study center (≥ 10^5 colony forming units (cfu)/mL). Seven isolates grew ≥ 10^4 cfu/mL and 78 grew ≤10^4 cfu/mL. Two patients received antifungal therapy for possible *Candida* sp. VAP. Neither grew *Candida* sp. on follow-up BAL. No patients developed systemic Candidal infections. Three other patients were concomitantly treated for preexisting *Candida* sp. bacteremia (2) or Candiduria (1). Overall mortality (17%) was no different than a patient cohort from the study center with similar injury severity (18%; *Ann Surg* 1998;227:743–755).
CONCLUSIONS: Critically ill trauma patients with quantities of *Candida* sp. from BAL below the diagnostic threshold for VAP do not require antifungal therapy. It is unknown if colony counts ≥ 10^5 cfu/mL require therapy.

Drug Information

59. Increased availability of information resources and the effects on the complexity of drug information requests asked to an academic center. *Erin M. Timpe, Pharm.D., BCPS*, Susannah E. Motl, Pharm.D.; University of Tennessee Drug Information Center, Memphis, TN.

PURPOSE: With the increased availability of information on the Internet, we hypothesized that the number of requests asked to our Drug Information Center has decreased, while becoming more complex. Secondarily, the classification of requests has also changed, since questions about general drug information are easily accessible on the Internet.
METHODS: Drug information requests from 1995–2003 were reviewed. Descriptive statistics assessing the difficulty of requests were evaluated for each year; specifically focusing on the total number of requests, time spent answering each request, the type and number of resources used to answer each request, and question classification.
RESULTS: Over a 9-year time span, requests asked to our center decreased by 33%. Time spent on requests increased from an average of 28 minutes to 55 minutes (p=0.027). Additionally, requests requiring primary literature searches and content evaluation increased from 11% of the total requests to 37% (p<0.0001). The time spent on the requests requiring a literature search also increased from an average of 70 minutes to 104 minutes, however this increase was not statistically significant (P=0.064). The classifications of the questions changed very little during this time period, with a decrease in reference and monograph requests (10%), product identifications (5%), and product availability (2%).
CONCLUSIONS: The increased availability of information may be aiding healthcare professionals in answering basic drug information requests. Although a correlation analysis was not conducted, requests requiring a primary literature search and the time spent on requests significantly increased over time while the total number of requests decreased.

60. Preparation of sphingosomal vincristine is a reliable procedure at clinical pharmacies. *Georgeta Puscalau, M.Sc.*, Paul Johnson, Ph.D., Thomas P Weber, Ph.D.; Inex Pharmaceuticals Corp., Burnaby, BC, Canada.

PURPOSE: Sphingosomal vincristine is supplied as a 3-vial kit. Prior to administration, the contents must be constituted to load vincristine into the sphingosomes. A Laboratory Study and a Field Test were conducted to assess the effect of minor variations in constitution conditions on final product quality and if the product can be reliably constituted in clinical pharmacies.
METHODS: The Laboratory Study determined the effects of deliberately varying the constitution conditions, including such key parameters as incubation time and incubation temperature. In the Field Test, 20 pharmacists unfamiliar with sphingosomal vincristine constituted the product using the written instructions as sole guidance. All samples in both studies were evaluated by measuring key product characteristics including free (unencapsulated) vincristine, total vincristine, vincristine degradation products, and in vitro release rate. Vincristine loading into sphingosomes was considered acceptable if the free vincristine was 10% or less.

RESULTS: In the Laboratory Study, samples that were incubated at 60–75∞C for 5–60 minutes met all the acceptance criteria. However, acceptable loading was not achieved for samples that were incubated at 55∞C for 10 minutes or less. In the Field Test, all the pharmacist-prepared samples passed all acceptance criteria, with the results for free vincristine demonstrating a high degree of statistical confidence in the reliability of the loading procedure.
CONCLUSIONS: Constitution of sphingosomal vincristine from the 3-vial kit is robust with respect to minor variations in the time and temperature of incubation. The reliability of the constitution procedure in clinical pharmacies was demonstrated with a high degree of confidence.

61. Evaluation of the accuracy of health studies presented in the written media. *Susannah E. Motl, Pharm.D.*, Erin M. Timpe, Pharm.D., BCPS, Samantha F. Eichner, Pharm.D.; University of Tennessee, Memphis, TN.

PURPOSE: The public is flooded daily with media releases on new medical findings. This excessive amount of information has the potential to be miscommunicated in the media due to the volume and speed of release. The Consolidated Standards of Reporting Trials (CONSORT) guidelines direct reporting of randomized controlled trials, but there are no criteria guiding communication of this information in the media. The purpose of this project was to evaluate communication of clinical research in the media for content and accuracy.
METHODS: All media reports discussing RCTs published in two national newspapers, two news magazines, and two online news sources over three months were retrieved. The corresponding RCTs were identified and evaluated. A modified, validated form of the CONSORT guidelines was used to compare the content of the media report to the original research. Ten content areas were identified in the RCT and, if present, were evaluated in the media report. Each report was evaluated and scored by three reviewers. An average was calculated, and media reports were classified as poor, fair, or excellent.
RESULTS: From 10/11/02–12/20/02, there were 60 media reports discussing results of 26 RCTs. On average, reports were categorized as fair. However, numerous content areas received poor rankings, specifically, adverse effect and outcome data reporting. No content area was rated excellent.
CONCLUSIONS: This pilot project identified areas in media reports of RCTs that are often incomplete. Future goals include helping major journalism associations develop quality assurance measures for media releases on RCTs.

Education/Training

62. Validation of an experiential teaching peer assessment tool. *Craig D Cox, Pharm.D., BCPS*[1], Brad L Stanford, Pharm.D., BCOP[1], Sara Brouse, Pharm.D., BCPS[2], Krystal K Haase, Pharm.D., BCPS[3], Ronda L Akins, Pharm.D.[3], Venita L Bowie, Pharm.D.[3], James P Tsikouris, Pharm.D.[1], Anthony J Busti, Pharm.D., BCPS[2], Sachin Shah, Pharm.D., BCOP[2], Ronald Hall, Pharm.D., BCPS[2], Brian Burleson, Pharm.D., BCPS[3], Charles F Seifert, Pharm.D., FCCP, BCPS[1]; (1)Texas Tech University Health Sciences Center, Lubbock, TX; (2)Texas Tech University Health Sciences Center, VA Medical Center, 4500 South Lancaster Rd, Dallas, TX; (3)Texas Tech University Health Sciences Center, Amarillo, TX.

PURPOSE: Documentation of excellence in teaching plays a pivotal role in the promotion process of pharmacy practice faculty. Peer evaluation of didactic teaching is commonplace for schools of pharmacy. However, a validated peer teaching assessment tool for experiential teaching is not available. Previously we developed a peer assessment tool for evaluating experiential teaching (Cox CD et al. Pharmacotherapy 2003;23:1336). Herein, we describe the prospective validation of this tool for internal medicine experiential rotations.
METHODS: The assessment tool was implemented for faculty peer evaluation of clerkship rotations during the 2003–04 academic year. For validation of the tool, responses to eleven questions that appeared identically on the student and peer evaluation forms of the preceptor (n=6) and practice site (n=5) were directly compared.
RESULTS: Eight internal medicine pharmacy practice faculty utilized this evaluation form for experiential peer review. Twenty students completed evaluations of the faculty during the same rotations as the peer review. No statistically significant differences were observed between student and peer evaluations for any of the eleven questions assessed. In addition, no differences between preceptor and site questions were found.
CONCLUSIONS: The validity of the form was demonstrated between student and peer evaluations of internal medicine experiential rotations at our institution. Future plans involve expansion of its use to the entire pharmacy practice faculty to verify its applicability across multiple practice settings.

63. Assessing the effectiveness of a student-driven course design as a teaching method. *Denise D. Hopkins, Pharm.D.*; University of Arkansas for Medical Sciences College of Pharmacy, Little Rock, AR.

PURPOSE: The purpose of this project was to determine if a student-driven elective course on women's health is an effective method of teaching.
METHODS: An elective course titled "Topics in Women's Health" was developed for 3rd year Pharm.D. candidates. Enrolled students selected topics to be studied (15 of 22 topics) in addition to those provided by guest lecturers (7 of 22 topics). Each student was responsible for leading the discussion of their topic one week after providing class participants with a current review article. The student facilitating the discussion also provided 10 objectives that promoted class participation as well as providing potential exam material. Three exams were generated from these objectives in addition to guest lecturer material. At the end of the semester, students completed a course evaluation that consisted of 14 questions.
RESULTS: Exam scores ranged from 86% to 100% with class averages of 97(exam 1), 98(exam 2), and 94(exam 3). Thirteen of the fifteen enrolled students completed course evaluations and indicated that the class was intellectually stimulating (mean of 4.92 on a scale of 1 to 5) and enhanced their learning (mean of 5 on a scale of 1 to 5).
CONCLUSIONS: The class was effective in introducing the students to a variety of issues relating to women's health. It also provided an excellent opportunity for self-directed learning. A student-driven elective course on women's health is an effective method of teaching.

64. Teaching students to diagnose drug-induced etiology where formal consult requested by prescriber. *Dan Moellentin, Pharm.D.*, Marybeth Boudreau, Pharm.D.; Eastern Maine Medical Center, Bangor, ME.

PURPOSE: Evaluate student performance of symptom-based, physician-ordered pharmacology consults.
METHODS: Students from 4 Colleges of Pharmacy trained in methods to evaluate in-patients referred to clinical pharmacists by physicians. Over 2 year period, 9 students attended medical rounds with medical residents, medical staff, and a clinical pharmacist. Pharmacoepidemiology, drug-disease, drug-drug interaction databases involving pgp, UGT, CYP450, reviewed in context of symptoms. Categories requested: dermal, motor weakness, syncope, neuropathy, changes in hearing or smell, gastrointestinal, behavioral, CNS changes, pain, strokes, fevers, bladder control,and memory-loss. Outcomes measured as probability of reduction in length of stay, laboratory tests, imaging, etc., and corrected for EMMC DRG average.
RESULTS: Medication side effects are sometimes missed by physicians because interactions are un-published, rare, or newly discovered. Pharmacy students trained in school to perform rule-out drug assessments, but need added skills. All 9 students taught to assess drug-induced symptoms and provide written consults in charts with suggestions for alleviating or attenuating symptoms. All students able to discover missed drug-induced symptoms/etiology without assistance by week 4. Average LOS decreased 0.7 days in student-reviewed cases. Average cost-reduction $235.00 per patient. Each student averaged 7 self-initiated interventions over 4 week period. Students had other functions.
CONCLUSIONS: Where pharmacy students are utilized to review specific patients referred to a clinical pharmacist for consult by a physician having ruled out most likely medical causes, outcomes can be postive for medical center, patient, and student. Using students can produce a reduction in patient LOS or hospitalization costs where drug-related etiologies are found.

65. Adherence to HMG coenzyme-A reductase inhibitor therapy in a north Dallas suburban area. *Deeatra Seaborn, Pharm.D*[1], Trina Ballard, Pharm.D[2]; (1)Texas Tech University Health Sciences Center, Dallas, TX; (2)Pfizer, Inc, Frisco, TX.

PURPOSE: Medication adherence remains the cornerstone of good clinical outcomes. Lowering cholesterol is critical in reducing morbidity and mortality from coronary heart disease (CHD). Persistence to pharmacological treatment for hyperlipidemia is paramount for positive therapeutic responses where treatment with medication is warranted. To evaluate a pharmacy claims database as a measure of patient adherence to statin therapy. To define and identify adherence performance measures including: average days of therapy, persistence, medication possession ratio and median gap days. To design and discuss interventions to improve adherence with a patient's primary care physician.
METHODS: This was a retrospective review of 12 month pharmacy claims data for patients getting statin prescriptions filled at Community Pharmacy. All dates and patient identifiers were de-identified to assure patient confidentiality. Blinded pharmacy claims were converted to a Microsoft Access® 2000 database and imported into the Standardized Therapy Adherence Research Tool (START)® developed by Pfizer, Inc. This software was utilized to calculate all adherence performance measures.
RESULTS: The average days of therapy for all statins was less than 6 months. Terminal persistence at month 12 was 32 % regardless of product. Statin medication possession ratio was 0.84 based on average days of therapy and average median gap calculation was 10.07 days.
CONCLUSIONS: The database demonstrates the quick and massive decline of patients having statin prescriptions refilled. Results of this data identify a significant opportunity to improve medication adherence among patrons of Community Pharmacy and ultimately improve patient outcomes.

66E. Using multiple-choice test questions as a means of assessing the influence of the pharmaceutical industry on the selection of medications by medical residents. *Fei Wang, M.Sc, Pharm.D., BCPS*, Cunegundo M. Vergara,

M.D., FACP, Michael Lindberg, M.D., FACP, Cynthia Gruman, Ph.D.; Hartford Hospital Department of Medicine, Hartford, CT.

Presented at the New England Regional Meeting of the Society of General Internal Medicine, Boston, MA, March 5, 2004.

67. Evaluating preceptors' perceptions of student preparedness for clinical rotations: a pilot study. *Lisa Murphey, Pharm.D., BCPS*, Shirley Hogan, Pharm.D., Holly Moore, Pharm.D., BCPS, Carter Haines, Pharm.D., Billy Brown, Pharm.D.; University of MS School of Pharmacy, Jackson, MS.

PURPOSE: The purpose of this pilot study was to evaluate preceptors' assessment of students' preparedness for rotations after completing the University of Mississippi School of Pharmacy's problem based learning (PBL) curriculum during the third professional year. This information serves as baseline data for future surveys and continuous curricula development.
METHODS: Survey questions were developed utilizing the group performance evaluation tool. Participants were to rate the adequacy of students' preparedness in knowledge acquisition, self-directed learning, and clinical reasoning on a 1–5 scale with 1 = very well and 5 = very poorly. The survey was administered to all preceptors in attendance at the annual Preceptors Conference held in March 2004.
RESULTS: Seventy-one of 141 current preceptors (50%) attended the conference and participated. Preceptors reported students perform very well or well researching reputable and pertinent primary literature (90%) and incorporating primary literature into patient care decision making (77%), efficiently retrieving current medical information (88%), and evaluating drug regimen appropriateness (76%). Thirty percent or more of preceptors reported only average or poor performance in identifying and utilizing drug assistance programs (51%), identifying significant drug interactions (43%), evaluating regimen appropriateness based on characteristics of agents within a class (33%), and accurately performing calculations (31%).
CONCLUSIONS: A majority of preceptors report PBL effectively prepares students to research and utilize current medical literature and tailor drug therapy regimens while incorporating information from a variety of disciplines. However, areas in need of further evaluation have been identified and will be addressed in future research initiatives.

68. Evaluation of the employment dynamics affecting Internal Medicine Residency trained pharmacists. *Lori Proeschel, Pharm.D.*, Anne Spencer, Pharm.D.; Medical University of South Carolina, Charleston, SC.

PURPOSE: To assess the supply and demand for Internal Medicine Residency trained clinical pharmacists.
METHODS: The number of IM residency positions was determined by identifying those accredited by ASHP or listed in the ACCP Directory of Residencies and Fellowships. Through the Personal Placement Service (PPS) database in December 2003, employers were identified who advertised a position that was Internal Medicine (IM) in nature. Employers were categorized as 1. IM prerequisite (requirement or preference for an IM residency), or 2. General (IM residency not mentioned). An 8 question online survey was e-mailed to the identified employers. Between May 1 and June 15, 2004, data was collected describing the available IM position(s), and the qualifications of the individual(s) hired for the position.
RESULTS: There are 20 active IM residency programs, providing 31 funded positions. Through the PPS database, 110 employers were identified, and 48% responded to the survey. Fifty-three percent of employers intended to hire for two or more IM positions. A total of 95 IM positions were available at the respondent institutions. For the IM prerequisite group, 58% of the individuals hired had completed an IM residency. For the general group, 13% of the new hires had completed an IM residency. Six months after advertisement in the PPS, 56% of the positions had been filled.
CONCLUSIONS: The current supply of pharmacists with IM residency training does not meet the current market demand. More Internal Medicine Residency trained pharmacists need to be produced in order to meet the workforce demands for their expertise.

69. An educational intervention to increase cardiovascular disease awareness in young women. *Michael J. Gonyeau, B.S., Pharm.D., BCPS*, Lori Arena, Pharm.D.; Northeastern University School of Pharmacy, Boston, MA.

PURPOSE: To assess the knowledge of young women regarding cardiovascular disease (CVD) before and after an educational intervention.
METHODS: A survey was distributed to female students 18 and older at Northeastern University. Data collected included age, race, and responses to questions evaluating current knowledge of CVD risk factors and preventative measures. After completing the initial survey, an informational pamphlet describing women and CVD was distributed. A similar survey was administered to the same population 2–4 weeks later to reassess knowledge of CVD.
RESULTS: Three hundred forty-eight college-aged women (mean age: 20) completed survey I, with 146 (42%) completing survey II. Half of the respondents (n=173) were health science majors. Participants citing CVD as the leading cause of death in women increased (56% survey I to 85% survey II ($p<0.001$). This was coupled with a decrease in breast cancer responses (32% to 12% respectively $p<0.001$). Non-health science majors were more likely to respond breast cancer (37% vs. 27% $p=0.05$). Diabetes (DM) and age>65 were less likely to be associated with CVD in survey I, but identification increased after the educational intervention (DM: 74% to 94% $p<0.0001$, age>65: 76% to 92% $p=0.0002$). Seventy-five percent indicated that the informational pamphlet increased their awareness of CVD in women.
CONCLUSIONS: Despite the high prevalence and morbidity and mortality associated with cardiovascular disease, many young women do not know common risks and preventative measures. This study highlights the need for increased education, and illustrates that such education can increase awareness in this patient population.

70. Clinical pharmacy impact on appropriate renal dosing in an urban academic medical center. *Michael J. Gonyeau, B.S., Pharm.D., BCPS*, Jane Lee, Pharm.D., Danielle Dalton, Pharm.D.; Northeastern University School of Pharmacy, Boston, MA.

PURPOSE: To evaluate patients with renal insufficiency and assess medications requiring renal dose adjustment, assess impact and acceptance of pharmacy interventions on appropriate dosing, and calculate cost avoidance of potential adverse drug events.
METHODS: A 6 week prospective interventional study was performed. Computer generated reports of 19 pre-specified medications requiring renal adjustment identified patients. Demographic and lab data were obtained, and average values for serum creatinine and creatinine clearance (Clcr) calculated. Based upon pharmacy evaluation, verbal interventions were attempted in patients requiring dosage adjustment. Three attempts were made to contact clinicians. If no response occurred, the intervention was considered rejected. Three days of additional follow-up was conducted to assess recommendation response.
RESULTS: We evaluated 292 patients, resulting in 104 renal dosing interventions. Intervention patients were older (79 vs. 66 ($p<0.0001$)) and more likely female (64% vs. 44% $p=0.003$). Interventions for antibiotics were most common (63%), followed by metformin (12%) and famotidine (12%). Intervention resulted in a 15% increase in appropriate renal drug dosing (66.5% to 81.2% $p<0.0001$), with 38% of interventions accepted. The major reason for rejection was failure to renally adjust within 72 hours (58%). Other reasons included: clinician did not find adjustment necessary (25%) and lack of response (17%). An estimated 5 adverse drug reactions and 3 medication errors were prevented through intervention, accounting for savings of $29,166.
CONCLUSIONS: Pharmacy intervention increases appropriate renal dosing of medications. Education efforts to further improve renal dosing compliance to established references with a focus on follow-up is warranted.

71. An assessment of promotion committees and criteria for promotion within departments of pharmacy practice. *Mark L. Glover, Pharm.D.*, Graciela M. Armayor, Pharm.D.; Nova Southeastern University, West Palm Beach, FL.

PURPOSE: To determine the composition of promotion committees and the criteria evaluated for the promotion from assistant to associate professor of faculty within the department of pharmacy practice.
METHODS: A survey identifying the composition of promotion committees and criteria for promotion was mailed to the respective dean of 89 United States Schools of Pharmacy. Responses to each of the survey questions were assessed and where appropriate, compared between tenure and non-tenure faculty.
RESULTS: A total of 61 (69%) surveys were returned. The mean number of committee members was 6.3 with the majority (80%) consisting of members from multiple departments of which pharmacy practice and pharmaceutical sciences were the most common constituents (57.5%). Professors and Associate Professors were the most frequently reported committee members at 88.5 and 84.6%, respectively. A mean number of 4.4 external reviewers were used by the committees. Of the criteria assessed for promotion, scholarly activities were most commonly cited with publications, poster presentations, funded grants, and editorial responsibilities being considered by all committees. Service, both to the pharmacy profession and to one's clinical site, was the least considered activity. No significant differences were observed between tenure and non-tenure faculty with respect to criteria for promotion.
CONCLUSIONS: Promotion committees consist predominantly of senior faculty with representation from multiple departments. Excelling in scholarly activities appears to be the major determinant in being awarded promotion from assistant to associate professor.

72E. The use of an audience response system to introduce an anticoagulation guide to physicians, pharmacists and pharmacy students. Philip J. Trapskin, Pharm.D., Kelly M. Smith, Pharm.D., John A. Armitstead, M.S., FASHP, *George A. Davis, Pharm.D.*; University of Kentucky Chandler Medical Center, Lexington, KY.

Presented at the Annual Meeting of the American Association of Colleges of Pharmacy, Salt Lake City, UT, July 10–14, 2004.

73. An investigation into pharmacy resident attrition and termination. *Peter S. Golenia, Pharm.D.*[1], Katherine P. Smith, Pharm.D., BCPS[2]; (1)University Medical Center of Southern Nevada, Las Vegas, NV; (2)University of Southern Nevada College of Pharmacy, Henderson, NV.

PURPOSE: This survey was designed to approximate pharmacy resident attrition and termination rates. In addition, we sought to determine the most common circumstances behind each cause for resident loss.
METHODS: Survey recipients were primarily identified using online residency directories. Surveys were distributed to residency contact email addresses by an email-marketing firm. The survey questionnaire addressed residency demographics, rates of attrition and termination, and specific circumstances behind each resident loss reported.
RESULTS: A total of 679 email surveys were successfully delivered of which 239 email surveys were completed (35% response rate). Residency sites completing the survey reported that a total of 2,426 residents completed their residency programs between July 1999 and June 2004. During that time span, 68 residents were reported as having resigned (2.70%) and 25 residents were terminated (0.99%). The most common reasons for attrition as reported by those who withdrew were: personal or family health (23.8%), change in career paths (14.3%), and lack of competency (12.7%). In 22.2% of the withdrawals, the cause was unknown or related to other issues. Terminations commonly occurred for the following reasons: lack of competency (32%), failure to obtain licensure (32%), and unprofessional behavior (12%).
CONCLUSIONS: The low pharmacy residency attrition rate of 2.7% over the last five years is encouraging. Most attrition-related losses were related to issues beyond the control of the residency program. Although the overall termination rate was low, they were most commonly related to competency issues; thus pharmacy education may not be adequately preparing students for residency training.

74. Evaluation of the accuracy of multiple-choice questions in testing students' understanding of complex concepts. *Reza Taheri, Pharm.D.*; Loma Linda University, 11262 Campus Street, Loma Linda, CA.

PURPOSE: To evaluate the success of multiple choice questions in assessing students' ability to analyze and apply knowledge.
METHODS: Students in the second year of a Pharm.D. Curriculum completed a case based, multiple-choice (MC) examination. Immediately following the written exam, an oral interview was conducted during which students were to provide rationale for their responses to three pre-selected higher-level questions requiring analysis and evaluation of data. The oral interview responses were compared with the response in the written exam using a Wilcoxon Signed Ranks Test.
RESULTS: The entire class, 92 students, completed the study. The individuals who had chosen the correct response in the written exam but could not justify a plausible rationale in the oral exam amounted to 26 on question #1 ($p<0.001$), 29 on question #2 ($p<0.001$), 62 on question #3 ($p<0.001$).
CONCLUSIONS: The lack of correlation between multiple-choice responses and their justification in an oral defense, demonstrates the inadequacy of multiple-choice questions in assessing students' ability to apply, analyze and synthesize knowledge in a complex question. The results suggest that multiple-choice questions may over-estimate students understanding of complex concepts.

Table 1: Analysis of Question #1

	Follow-up Oral Questioning		
Correct Justification	Incorrect Justification		
Written Exam	Correct Answer	49	26
Incorrect Answer		4	13

Table2: Analysis of Question #2

	Follow-up Oral Questioning		
Correct Justification	Incorrect Justification		
Written Exam	Correct Answer	46	29
Incorrect Answer		2	15

Table 3: Analysis of Question #3

	Follow-up Oral Questioning		
Correct Justification	Incorrect Justification		
Written Exam	Correct Answer	26	62
Incorrect Answer		0	4

75. Assessment of pharmacists' perceptions of psychiatric medications and illnesses. *Shelly J Enders, Pharm.D., BCPS*[1], J. Michael McGuire, Pharm.D., BCPP[2], Leigh Anne Nelson, Pharm.D., BCPP[3]; (1)St. Louis College of Pharmacy, St. Louis, MO; (2)Bristol-Myers Squibb Company, St. Louis, MO; (3)Bristol-Myers Squibb Company, Kansas City, MO.

PURPOSE: This study evaluated pharmacists' knowledge of psychiatric medications and comfort level with psychiatric drug therapy counseling. Associations with training in psychiatric therapeutics were examined.
METHODS: A survey assessed pharmacists' self-reported knowledge of medications (psychiatric versus non-psychiatric) and comfort level with drug therapy counseling (psychiatric versus non-psychiatric illnesses). Subjects rated their knowledge of 16 medications from 1 to 5 (1=excellent; 5=needs improvement). Comfort level of counseling for 10 illnesses was rated from 1 to 3 (1=very comfortable; 3=uncomfortable). Academic preparation in psychiatric therapeutics was also reported. This anonymous survey was mailed to 1000 randomly selected community and hospital pharmacists.
RESULTS: Pharmacists (N = 182) rated their knowledge of non-psychiatric medications higher than their knowledge of standard psychiatric medications. They also rated their knowledge of non-psychiatric and standard psychiatric medications higher than their knowledge of newer psychiatric medications. With regard to drug therapy counseling, pharmacists rated their comfort level higher for non-psychiatric illnesses than psychiatric illnesses. Continuing education (CE) hours on psychiatric topics in the previous 12 months moderated these effects: pharmacists with more than 4 CE hours indicated greater knowledge/comfort regarding psychiatric medications/illnesses than pharmacists with < 4 CE hours. No interactions or main effects were found for time devoted to psychiatric therapeutics in pharmacy school, post-graduate training, gender, age, or years since graduation.
CONCLUSIONS: Pharmacists rated knowledge of psychiatric medications as less adequate compared to non-psychiatric medications. Pharmacists were less comfortable counseling on drug therapy for psychiatric illnesses than non-psychiatric illnesses. CE hours on psychiatric topics reduced these differences.

76. Evaluating preparedness for clinical rotations: a pilot study of senior pharmacy students. *Shirley M. Hogan, Pharm.D.*, Holly Moore, Pharm.D., BCPS, Lisa Murphey, Pharm.D., BCPS, Carter Haines, Pharm.D., Billy Brown, Pharm.D.; University of MS School of Pharmacy-Department of Pharmacy Practice, Jackson, MS.

PURPOSE: The purpose of this study was to evaluate students' assessment of their preparedness for rotations after completing the University of Mississippi School of Pharmacy's problem based learning (PBL) curriculum during the third professional year. This information serves as baseline data for future surveys and in continuous program improvement.
METHODS: Survey questions were developed utilizing the group performance evaluation tool. Participants were to rate the adequacy of the their preparedness in knowledge acquisition, self-directed learning, and clinical reasoning on a 1–5 scale with 1 = very well and 5 = very poorly. The survey was administered to graduating pharmacy students in May 2004.
RESULTS: Sixty-nine of 79 students (87%) completed a survey. Greater than 50% reported PBL prepared them to perform very well or well in retrieving medical information (75%), discussing disease states and drug therapies at the basic science level (64%), evaluating regimen appropriateness based on patient problems (56%), and identifying drug interactions (53%) and therapeutic monitoring parameters (53%). Fifty percent or more reported only somewhat or poor preparation in accurately performing calculations (68%), incorporating knowledge from various disciplines (59%), and evaluating regimen appropriateness based on characteristics of agents within a class (50%). Students reported very poor preparedness to identify and utilize drug assistance programs (35%) and process a prescription/hospital order to dispense medications (38%).
CONCLUSIONS: Graduating students report PBL effectively prepares them for rotations in a variety of areas. However, areas in need of further evaluation have been identified and will be addressed in future research initiatives.

77. Impact of a diabetes educational program on state health plan members knowledge of diabetes self-management. *Sharm Steadman, Pharm.D., BCPS, CDE*[1], Tim Mullenix, Pharm.D., M.S.[2]; (1)USC Department of Family and Preventive Medicine, Columbia, SC; (2)Pfizer Inc, Irmo, SC.

PURPOSE: To determine whether an interactive pharmacist directed patient education program on diabetes results in improved knowledge of diabetes self-management for members of a State Health Plan.
METHODS: This prospective study consists of the following two components: 1) an interactive patient education program targeted at plan members with diabetes; and 2) a comparison of participant knowledge of diabetes self-management practices prior to and one month following the above educational program. The participants' diabetes knowledge was measured utilizing "The Diabetes Knowledge Test" from the Michigan Diabetes Research and Training Center.
RESULTS: There were 40 participants in the study group who attended the educational intervention and completed the initial baseline survey. After the intervention, participants were mailed a follow-up test to complete and 15 tests were returned representing a 38% response rate. The average age for the baseline and follow-up respondents were 60 (22 to 82) and 61 (45 to 72), respectively. 75% of the baseline respondents were female and 25% male versus 87% females and 13% males in the follow-up respondents. The baseline average percent correct was 61.4% and ranged from 8.7% to 91.3%. The reevaluation average percent correct 70.4% and ranged from 39.1% to 91.3%. The difference between the percent correct baseline evaluation and the post test evaluation was significantly different using a 2-sample *t*-test with $p=0.04$ (CI -17.7, -0.3).
CONCLUSIONS: Baseline diabetes knowledge scores for state health plan members with diabetes were generally low. Members knowledge measured one month following an pharmacist directed educational intervention resulted in significantly improved scores.

78. Assessment of third year pharmacy students' attitudes and abilities in evidence-based medicine (EBM). Timothy E Welty, Pharm.D., Paula A Thompson, Pharm.D., M.S., Michael G Kendrach, Pharm.D., *Jennifer W Beall,*

Pharm.D., Sunni J Yocom, Pharm.D., Renee M DeHart, Pharm.D., Robert P Henderson, Pharm.D., Roger D Lander, Pharm.D., Mary A Worthington, Pharm.D., D'Andrea F Skipwith, Pharm.D., Charles D Sands, Pharm.D.; McWhorter School of Pharmacy, Birmingham, AL.

PURPOSE: To introduce third-year students to EBM and assess the impact of student-focused learning compared to a formal drug literature evaluation course.
METHODS: A brief, two-day course on literature retrieval was provided at the beginning of Therapeutics. Throughout the first semester, students received 8 EBM cases. Small groups developed treatment plans based on the best available evidence. During the second semester, students completed a drug literature evaluation course, covering EBM principles. Attitudes toward and competencies in EBM were assessed using a standardized tool published in literature. Assessments were on the first day of Therapeutics, before the two-day lecture on drug information, at the end of the first semester, and at the end of the school year.
RESULTS: Competency in EBM terminology increased over the year. When comparing attitudes toward the value of EBM skills to future practice, perceived usefulness of developing a clinical question decreased from 65.5% to 54.6%. However, perceived value of EBM instruction to future practice increased from 56.8% to 65.7%. Other attitudinal responses decreased from September to December then increased from December to May. Students had fewer correct responses to objective questions related to EBM in May compared to September or December assessments.
CONCLUSIONS: The perceived value of EBM in students' future work increased over the year, as did understanding of terminology. The decrease in competency contradicts data from assessments in the drug literature evaluation course, and may be due to timing of the administration of the final assessment.

79. Cardiovascular risk factor assessment in pharmacy students. *Cynthia A. Sanoski, Pharm.D.*, Elena M. Umland, Pharm.D.; Philadelphia College of Pharmacy, University of the Sciences in Philadelphia, Philadelphia, PA.

PURPOSE: This study evaluated whether cardiovascular risk factor self-assessment and measurement of these risk factors would influence behavior among fifth-year Pharm.D. students.
METHODS: In Fall 2003, fifth-year Pharm.D. students reported their coronary heart disease (CHD) risk factors and perceptions of these risk factors via a questionnaire. Fasting lipid panel [total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides] and fasting blood glucose (FBG) were measured using the Cholestech LDX®; blood pressure (BP) was also measured. These findings and education regarding risk factor modification were provided to each student. These activities were repeated in Spring 2004.
RESULTS: Seventy-four students (mean age=23.7 years; 77% female; 49% Caucasian) had complete follow-up data. At baseline, 98.7% agreed that risk factor improvement and disease prevention should be the top priority of clinicians. More than 50% denied knowing their lipid panel or FBG. Mean body mass index (BMI) was 23.3 kg/m^2. The majority denied a family history of CHD or diabetes. Only 12% were current or past smokers. Mean BP was 109/71 mmHg (pre-hypertension observed in 24%). Mean TC, LDL-C, HDL-C, triglycerides, and FBG were 187.3 mg/dL, 99.0 mg/dL, 60.3 mg/dL, 139 mg/dL, and 92 mg/dL, respectively. Upon follow-up, the only significant differences observed were for BMI (23.65 kg/m^2; p=0.036 vs. baseline) and triglycerides (160.1 mg/dL; p=0.031 vs. baseline).
CONCLUSIONS: Although the majority of pharmacy students perceived risk-factor improvement and disease prevention as the top priority of clinicians, they were unaware of their own risk factors and failed to make significant lifestyle changes to improve them.

80. Teaching sixth year pharmacy students to provide feedback. *Carla A. Zeilmann, Pharm.D.*, Terry Seaton, Pharm.D., Russell Roberts, Pharm.D.; St. Louis College of Pharmacy, St. Louis, MO.

PURPOSE: The purpose of this project was to evaluate our ability to teach sixth year students to provide feedback on seminar presentations.
METHODS: Students in the Pharmacy Practice Seminar provided feedback for two sessions of pharmacy resident seminars using a written evaluation form. Between the sessions, the students were taught to improve the quality of their feedback by lecture and one-on-one sessions with the investigators. The lecture included a review of the criteria, their importance, and examples. The one-on-one sessions provided specific ways each student could improve their written feedback using their evaluation forms as an example. A tool was developed to evaluate feedback, including four criteria related to tone and eight criteria related to usefulness. The tool used a scale of "very poor", "poor", "average", "good", and "very good" for each criterion.
RESULTS: Tone and usefulness of feedback was evaluated on 45 students before and 39 students after intervention. Improvement was most notable in the criteria related to tone, where the median response rose from average to good for all four criteria. The change in usefulness of feedback was more varied, but demonstrated an improvement in all eight criteria.
CONCLUSIONS: Initial evaluation suggests that our approach to teaching feedback is effective at improving the tone and usefulness of feedback given by sixth year pharmacy students.

Endocrinology

81. Incidence and treatment of metabolic syndrome in adolescents enrolled in a type 2 diabetes clinic. *Brittany N. Harris, Pharm.D., candidate*, Donna S West, Ph.D., Lisa M Lubsch, Pharm.D.; University of Arkansas for Medical Sciences, Little Rock, AR.

PURPOSE: To investigate the incidence of metabolic syndrome in the patient population enrolled in a Children's Hospital Type 2 Diabetes Clinic and to describe medication treatment and adherence patterns.
METHODS: The study population consisted of 52 adolescent patients enrolled in the Type 2 Diabetes Clinic. The medical charts of all patients ages 12 to 20 years enrolled in the Clinic were reviewed. A data collection instrument was used to collect demographic data, laboratory values, medication lists, and documented adherence patterns. Data were entered into a database and analyzed using SPSS.
RESULTS: Data were collected for 52 patients with a mean age of 16.7 years. Of these patients, 40 (76.9%) had characteristics of metabolic syndrome, meeting three or more of the five criteria, although only 8 (15.4%) had a formal diagnosis. Among patients with characteristics of metabolic syndrome, 37 (92.5%) patients were on a glucose-lowering medication and 32 (86.5%) were on metformin. 15 (37.5%) were on a blood pressure lowering medication and 5 (12.5%) on a lipid-lowering medication. 41% of these patients were documented as being nonadherent with their prescribed medications, with nonadherent patients having a higher A1C (p<0.001).
CONCLUSIONS: Given these treatment and adherence patterns, management of metabolic syndrome in adolescent Type 2 diabetes patients may be suboptimal and may impact outcomes. It is important for pharmacists to be aware of the incidence of metabolic syndrome and ensure adolescent patients receive appropriate pharmacological treatment, medication adherence counseling, and lifestyle modification education.

82. Appropriate use of thiazolidinediones at Minneapolis Veterans Affairs Medical Center. *Elzie J. Jones, Pharm.D.*, Eric A. Geurking, Pharm.D., Kevin D. Burns, Pharm.D., Brian J. Neil, M.D.; Minneapolis Veterans Affairs Medical Center, Minneapolis, MN.

PURPOSE: There are conflicting views on safety and efficacy data suggesting thiazolidinediones (ëglitazones') may not be appropriately used in all patients. VAMC guidelines identified ineffective and potentially unsafe use of ëglitazones' in order to improve patient care while minimizing budget expenditures.
METHODS: Retrospective and concurrent review of patients with prescriptions for ëglitazones' (December 2002 thru October 2003). Patients were assessed for adverse reactions (CHF, edema, diuretics, LFT's) and effectiveness (baseline and 6-month A_{1c}). Pharmacy addressed providers of patients identified having inadequate response, adverse event, or contraindication with recommended alternative therapies via hard copy documentation.
RESULTS: A total of 333 retrospective patient records were reviewed. Of those, 44% (145) were determined to be outside treatment parameters (inadequate response, adverse event, or potential contraindication). Concurrent analysis identified 164 additional patients as falling outside the treatment parameters, however, due to resource allocation only 60 of those were acted upon. During the presentation we will show average ëglitazone' dose, average change in hemoglobin A_{1c}, age, weight, and other demographic and physical patient parameters for responders and non-responders.
CONCLUSIONS: Nearly half of the patients started on a ëglitazone' were identified as having an inadequate response, adverse event, or contraindication. This suggests that many patients lacked significant benefit from the medication and as a result were taking an unnecessary medication. VAMC associated ëglitazone' cost is conservatively $684/patient/year. Current VAMC guidelines for use have determined more appropriate and cost-effective use of ëglitazones' and are being used at initial approval process on requests to place patients on therapy.

83E. Effects on clinical outcomes of diabetic patients seen by a pharmacist working in collaboration with other primary care providers. *Jeffrey M. Brewer, Pharm.D.*[1], Nancy T Nkansah, Pharm.D.[1], Kenneth M Shermock, Pharm.D.[1], Robert L Connors, M.D.[2]; (1)The Johns Hopkins Hospital, Baltimore, M.D.; (2)Johns Hopkins Community Physicians, Baltimore, M.D.

Presented at the 2004 Summer Meeting of the American Society of Health-System Pharmacists, Las Vegas, NV, June 19–23, 2004.

84. Osteoporosis screening in men in a home-based primary care program. *Paula A. Thompson, Pharm.D., M.S., BCPS*[1], Gretchen L. Rinicker, Pharm.D.[1], Katherine C. Herndon, Pharm.D., BCPS[2]; (1)Samford University McWhorter School of Pharmacy, Birmingham, AL; (2)Pfizer Inc., Birmingham, AL.

PURPOSE: To evaluate the results of osteoporosis screening in men receiving care in the Home-Based Primary Care (HBPC) program at the Birmingham

Veterans Affairs Medical Center.
METHODS: Screening bone mineral density (BMD) measurements were obtained through quantitative ultrasound of the heel of the dominant foot during regular home visits by a member of HBPC team to identify patients with osteopenia (T score = -1– -2.5) or osteoporosis (T score < -2.5). Medical records were reviewed to assess disease states and medications associated with osteoporosis. A binary logistic regression model was used to identify significant risk factors for osteoporosis/osteopenia. Patients with a T score < -2 will be referred for dual energy x-ray absorptiometry (DXA) to confirm the diagnosis of osteoporosis.
RESULTS: BMD screening was completed in 74 patients (mean age = 75.2 years). The mean T score was -1.47 ± 1.28 (range = -3.9–1.2). Based on heel ultrasound results, 28 patients (37.8%) and 19 patients (25.7%) met the diagnostic criteria for osteopenia and osteoporosis, respectively. The mean number of medications (p=0.71) and disease states (p=0.86) associated with bone loss was similar in patients with and without osteopenia/osteoporosis. The presence of osteoporosis/osteopenia could not be predicted by a specific disease state or medication that has been associated with bone loss.
CONCLUSIONS: Osteopenia/osteoporosis was revealed in 63.5% of men in the HBPC program who underwent quantitative ultrasound screening for low BMD. BMD screening in elderly men resulted in a substantial number of referrals for DXA.

85. Barriers to medication adherence in poorly-controlled diabetes mellitus. *Peggy Odegard, Pharm.D., BCPS, CDE*, Shelly Gray, Pharm.D., M.S., BCPS; University of Washington, School of Pharmacy, Seattle, WA.

PURPOSE: Limited information is available about medication adherence barriers in Diabetes Mellitus (DM). The primary objectives were to 1) describe potential barriers to DM medication adherence, and 2) examine if adherence barriers are associated with A_{1c}.
METHODS: As part of a randomized, multi-clinic, controlled, intervention trial, 32 medication adherence factors and the influence of these factors on A_{1c} were assessed. Bivariate linear regression was used to correlate each adherence variable independently with baseline A1c. Multivariate regression for significant variables ($p<0.05$ in bivariate analysis) was used to examine the correlation with A_{1c}.
RESULTS: Seventy-seven subjects (mean 52 years old, 7 years DM, 1.9 DM medications, 6.5 total medications, 44% women, 80% high school education) enrolled with an A_{1c} >9% (mean 10.4). At baseline, 41% of subjects were on new DM medications, 38% had side effects, 30% were not monitoring home blood glucose, 24% were not taking DM medications as prescribed, 17% were taking >2 doses daily, and 6.5% did not believe adherence was important. Subjects reported difficulty with paying for medications (34%), remembering doses (32%), removing bottle cap (14%), swallowing pills (13%), and reading labels (12%). Difficulty reading the label (p=0.04) and taking >2 doses daily (p=0.02) correlated with poorer diabetes control at baseline (A_{1c} mean 0.8 higher).
CONCLUSIONS: Ability to read the prescription label and taking more than 2 doses of DM medications daily correlated with worse A_{1c}. Risk modification may facilitate A_{1c} improvement in those with poor control.

Gastroenterology

86. Safety and tolerability of the reformulated pantoprazole for injection compared with the original formulation in healthy adult subjects. *Brinda K Tammara, Ph.D*, Kathy Weisel, R.N., BSN, Gayle Orczyk, M.D., Ph.D, Meng Xu, Ph.D; Wyeth Research, Collegeville, PA.

PURPOSE: To evaluate the safety and tolerability of the new IV pantoprazole formulation, containing a small amount of EDTA, which eliminates the requirement of the in-line filter by the original formulation.
METHODS: This was a single-blind, randomized, parallel group study in 53 men and women aged 18 to 74 years. Subjects were randomly assigned to receive the new formulation or the original formulation, 80 mg every 8 hours for 7 days. Safety evaluations included measurement of serum anion gap, serum creatinine and serum cations calcium,magnesium, and zinc. Injection site reaction scales measuring phlebitis, infiltration, pain, and burning were used at scheduled times. Zinc urine excretion rates were examined against the normal range (150–1250 µg/day) and an estimated daily uptake (~ 3000 µg/day) based on RDA for zinc.
RESULTS: There were no appreciable differences in serum creatinine, calcium, magnesium, and zinc, or serum anion gap. Injection site reactions were similar for both treatments and mild in severity. The average daily urinary zinc excretion increased from baseline by 279 µg/day (to 796 µg/day) with EDTA formulation and by 44 µg/day (to 603 µg/day) with the original formulation. The increases were small, though statistically different ($p<0.05$). No adverse events indicative of trace metal deficiency were observed.
CONCLUSIONS: The new formulation of IV pantoprazole can be administered without an in-line filter as safely as the original formulation with an in-line filter.

87. Effect of a ginger extract on acute and chronic inflammation in Mongolian gerbils. *Gail B. Mahady, Ph.D.*[1], Susan L. Pendland, Pharm. D.[1], Dawn Israel, Ph.D.[2]; (1)University of Illinois at Chicago, Chicago, IL; (2)Vanderbilt University, Nashville, TN.

PURPOSE: This study determined the effect of a standardized ginger extract on acute and chronic inflammation induced by infection with Helicobacter pylori.
METHODS: A ginger extract was administered in a rodent model of H. pylori-induced disease, the Mongolian gerbil, to examine the effects of extract on both prevention and eradication of infection. The animals were administered 100 mg/kg body weight/day of the ginger extract in rations either 3 weeks prior to infection and treated for a further six weeks post-infection. Bacterial load and chronic and acute levels of inflammation were assessed four weeks after treatment.
RESULTS: As compared with controls, a significant reduction in bacterial load, as well as chronic and acute inflammation scores was observed in gerbils treated with the ginger extract (containing 6-, 8-, 10-gingerols and 6-shoagol, in a ratio of 7.5:1:13:2% w/w) and these changes were paralleled by reductions in the severity of epithelial cell degeneration and erosions. Importantly, the extract did not increase morbidity or mortality. Treatment with the standardized ginger extract reduced HP load as compared with controls and significantly ($P<0.05$) reduced both acute and chronic muscosal and submucosal inflammation, cryptitis, as well as epithelial cell degeneration and erosion induced by HP.
CONCLUSIONS: Ginger extracts reduce bacterial load, and reduced both acute and chronic inflammation in HP-infected Mongolian gerbils.

88. Intestinal and hepatic P-glycoprotein expression is preserved in mice receiving parenteral nutrition. *Gordon S. Sacks, Pharm.D., B.S.*, Brien L. Neudeck, Pharm.D., Jennifer M. Loeb, B.S.; The University of Wisconsin - Madison, Madison, WI.

PURPOSE: Parenteral nutrition (PN) administration has been associated with mucosal atrophy, bacterial overgrowth, and increased intestinal permeability. We hypothesized that PN in mice would alter intestinal and hepatic P-glycoprotein (P-gp)expression and influence drug transport and metabolism.
METHODS: Male ICR mice underwent cannulation with intravenous catheters with ad libitum access to chow and water for 48 hours. On postoperative day 3, animals were randomized to PN or chow for 5 days. After their respective diets, mice were sacrificed and P-gp amounts determined from intestinal scrapings and liver homogenates using Western immunoblotting and densitometry. Intestinal P-gp function was determined with in vitro transport of 20 nM 3H-digoxin across everted intestinal sacs (terminal ileum) over 20 minutes. Trace amounts of 14C-PEG4000 were added to the buffer to monitor segment permeability.
RESULTS: No differences in amount of intestinal or hepatic P-gp were detected between chow-fed and PN mice(Intestine: 381 ± 61 vs 391 ± 59 arbitrary units; Liver: 1110 ± 291 vs 1164 ± 287 arbitrary units, $p>0.05$). Likewise, there were no differences in the mucosal to serosal transport of 3H-digoxin in chow vs PN-fed mice (0.0445 ± 0.020 vs 0.0880 ± 0.045 percent/cm, $p>0.05$).
CONCLUSIONS: Many patients receiving PN continue taking oral medications that may be P-gp substrates and therefore knowledge concerning P-gp expression and function is important. Both intestinal and hepatic P-gp appear to be preserved in mice after 5 days of PN. Moreover, P-gp mediated transport of digoxin was unchanged compared to chow-fed mice.

89E. Comparative observed healing rates of gastric ulcers with esomeprazole versus ranitidine in patients taking either continuous COX-2-selective or nonselective NSAIDs. Jay L Goldstein, M.D.[1], John Johanson, M.D.[2], Lisa Suchower, MA[3], *David R. Rutledge, Pharm.D., FCCP*[4], Douglas S. Levine, M.D.[3]; (1)University of Illinois at Chicago, Chicago, IL; (2)Rockford Gastroenterology Association, Rockford, IL; (3)AstraZeneca LP, Wilmington, DE; (4)AstraZeneca LP, Naperville, IL.

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91. Re-bleeding in patients admitted for gastrointestinal bleeding from peptic ulcer. *JK Siepler, Pharm.D.*, C Miahora, Pharm.D., P Sellers, Pharm.D., J Lin, Pharm.D., M Rojany, M.D., JW Leung, M.D.; UC Davis Medical Center, Sacramento, CA.

PURPOSE: Recurrence of bleeding in patients admitted for peptic ulcer bleeding(PUB) is reduced by endoscopic intervention(EI) and intravenous proton pump inhibitors(PPIs). We surveyed rebleeding (RB) in patients admitted for PUB.
METHODS: Inpatients endoscoped for PUB from Jan 2001–Dec 2003 qualified. All received EI (heater probe, epinephrine injection, and/or clips). All lesions were oozing blood(OZ), had a visible blood vessel(VV), and/or an adherent clot (AC). After EI, patients were followed till discharge. Primary endpoint was RB. Secondary endpoints included mortality, and length of hospital stay. Acid suppressant treatment after endoscopy was recorded. Statistics were done using Minitab with significance being p=0.05.
RESULTS: Of 78 patients, 53 were males(68%) with a mean age of 59±18 years. Lesions included duodenal ulcer 53, gastric ulcer 34, and gastritis 12.

There were 28 AC, 38 VV, and 32 OZ. Several patients had >1 lesion and endoscopic findings. Therapy following endoscopy was IV H2RA 39 and oral PPI 39. No IV PPIs were used. There were 6 RBs(7.8%).Of those 4(12.8%) received IV H2RA, 2(5.1%)received ppi (p=0.34 Fisher exact). Length of stay was 8.1±10 days. 5 patients expired. Using logistic regression, AC was the only factor that predicted a more frequent re-bleeding rate (RR:12.8,95%CI:1.5–11.2,p=0.02).
CONCLUSIONS: We demonstrate a RB <10% for PUB following EI. The RB rate noted in the patients on IV H2RAs is lower than reported recent studies from Asia but similar to that reported in the ranitidine arm of the IV pantoprazole v. ranitidine European PUB trial(11.1%) (abstract:Barkun J,et al. Gastroenterol;4/04).

92. Antimicrobial therapy in patients with variceal hemorrhage. *Kerry Wilbur, BScPharm, Pharm.D.*[1], Kiran Sidhu, B.Sc.Pharm.[2]; (1)Vancouver General Hospital, Vancouver, BC, Canada; (2)Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC.

PURPOSE: Acute variceal hemorrhage is a serious complication of liver disease and hospital outcome is closely related to infection. Patients with cirrhosis are at greater risk of developing bacterial infection which is associated with failure to control bleeding and higher rates of hospital mortality. Many clinical practice guidelines endorse antimicrobial prophylaxis as standard of care for cirrhotic patients. This study was performed to characterize use of antimicrobial therapy for patients hospitalized with acute variceal hemorrhage.
METHODS: Medical records of 106 patients hospitalized with suspected variceal hemorrhage at a Canadian tertiary care hospital between January 2001 and September 2003 were retrospectively reviewed.
RESULTS: Only half of patients were prescribed antimicrobial therapy at any time during their hospital admission. Those who received antibiotics had more severe liver disease (MELD score 19.6 +/- 9.9 vs 12.8 +/- 7.8, p<0.05; Child-Pugh C score 78% vs 20%, p<0.05) and clinical or microbiological findings of infection. They also had worse in-hospital outcome (length of stay 20 vs 6.5 days, p<0.05; and mortality 30.5% vs 4.2%, p<0.05). Urinary tract infections (27%) and primary bacteremia (15%), caused by gram negative and gram positive organisms, respectively, were most prevalent. Fluoroquinolones were the most widely prescribed agents (47%), followed by cephalosporins (41%).
CONCLUSIONS: Patients with liver disease admitted with variceal hemorrhage were often not prescribed antimicrobial therapy to reduce risk of bacterial infection. Our results imply published practice guidelines are not being consistently observed and offer an opportunity for pharmacists to optimize antimicrobial drug therapy in this high risk population.

93. Pharmacotherapeutic prophylaxis for patients with variceal hemorrhage. *Kerry Wilbur, BScPharm, Pharm.D.*[1], Kiran Sidhu, BScPharm[2]; (1)Vancouver General Hospital, Vancouver, BC, Canada; (2)Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC.

PURPOSE: Variceal hemorrhage is a frequent and severe complication of portal hypertension due to liver disease. Up to a third of initial episodes are fatal and as many as 70% of survivors have recurrent bleeding within one year. Beta blocker therapy has been demonstrated to decrease risk of first bleed in patients with evidence of esophageal varices (primary prophylaxis) and recurrent bleeding and mortality in patients with history of prior variceal hemorrhage (secondary prophylaxis). This study was performed to characterize beta blocker therapy for the primary and secondary prevention of variceal hemorrhage.
METHODS: Medical records of 106 patients with liver disease hospitalized with suspected variceal hemorrhage at a Canadian tertiary care hospital between January 2001 and September 2003 were retrospectively reviewed.
RESULTS: Approximately half of patients had known varices, 44 (41.5%) of whom had experienced prior variceal hemorrhage. Only 21 (20%) were receiving beta blocker therapy at admission and 41 (48%) at discharge. Propranolol was the most widely prescribed. The majority of patients were not receiving beta blocker therapy for primary prophylaxis (94%). Specific characteristics associated with beta blocker use could not be identified, although more patients with history of greater than two variceal hemorrhages were receiving beta blocker therapy at admission (73% vs 41%, p=0.04).
CONCLUSIONS: Patients with liver disease and evidence of varices were often not receiving beta blocker therapy to reduce risk of first or subsequent variceal hemorrhage. Opportunity exists to optimize use of this proven prophylactic treatment and bridge an apparent gap in standard of care.

94. Paradoxical effect of berberine on listeria monocytogenes invasion in Caco-2 cells. *Brien L. Neudeck, Pharm., D.*[1], Jennifer M. Loeb, B.S.[2], Nancy G. Faith, B.S.[3], Charles J. Czuprynski, Ph., D.[3]; (1)University of Tennesse College of Pharmacy, Memphis, TN; (2)Pierce Biotechnology, Rockford, IL; (3)University of Wisconsin School of Veterinary Medicine, Madison, WI.

PURPOSE: To determine if prophylactic berberine could protect Caco-2 cells from invasion by the foodborne pathogen Listeria monocytogenes (LM) infection.
METHODS: Caco-2 cells were incubated with 10^5, 10^6, 10^7, or 10^8 of LM for 1 hour and intracellular bacteria quantified. One or four days prior to LM addition, cells were incubated with berberine 3.2 µM or media (n=6 per condition). LM attachment ELISAs were performed with 10^5 organisms (n=16 per condition). P-glycoprotein expression and function was measured using real-time PCR and 3H-digoxin uptake assays since berberine may be a P-glycoprotein substrate.
RESULTS: One day of berberine pre-treatment significantly decreased LM invasion whereas a 4d pre-incubation had no effect (control vs 1d vs 4d: 10^5: 1.53±0.23 vs 0.910±0.42 vs 1.50±0.35; 10^6: 2.40±0.2 vs 2.22 ±0.15 vs 2.60±0.20; 10^7: 3.57±0.22 vs 3.03±0.24 vs 3.76±0.15; 10^8: 4.68±0.17 vs 4.34±0.18 vs 4.60±0.12; p<0.05 for control vs 1d only). No difference in LM attachment was detected (control vs 1d vs 4d: 1.75±0.23 vs 1.82±1.92±0.14 O.D.). Moreover, 1 or 4d of berberine treatment had no effect on P-glycoprotein expression (0.639±0.02 vs 0.782±0.015 vs 0.741±0.02 AU) or function (digoxin uptake; control vs 1d vs 4d: 1468±116 vs 1446±85 vs 1536±108 CPM).
CONCLUSIONS: Acute berberine treatment results in a protective effect on LM invasion whereas a 4d incubation had no effect. Berberine did not modulate P-glycoprotein and therefore other mechanisms for protection must be explored.

95. Protective effect of the pluronic block copolymer P85 against listeria monocytogenes infections. *Brien L. Neudeck, Pharm., D.*[1], Nancy G. Faith, B.S.[2], Charles J. Czuprynski, Ph., D.[2]; (1)University of Tennesse College of Pharmacy, Memphis, TN; (2)University of Wisconsin School of Veterinary Medicine, Madison, WI.

PURPOSE: Listeria monocytogenes (LM) is a foodborne pathogen that causes considerable morbidity and mortality. Compounds that could protect individuals are a major research interest. This study evaluated P85 as a protective agent against LM.
METHODS: Caco-2 cells and FVB mice were employed. Caco-2 cells were treated with 0.1% P85 or media for 45 minutes prior to 10^7 LM addition (n=6 per condition). To test if differences were due to ATP depletion, ATP (50µM) was added to P85. As a control, cells were treated with (150µM) sodium azide/(50µM) 2-deoxy-D-glucose (SA2DG) to deplete ATP. After 1 hour, viable intracellular bacteria were quantified. Mice received P85 (150mg/kg) or water via oral gavage, 45 minutes prior to intragastric challenge of 10^7 LM (n=8 per group). Mice were euthanized 24 hours later and the liver and spleen harvested to determine LM load.
RESULTS: Pretreatment of Caco-2 cells with 0.1% P85 led to significantly decreased invasion compared to control (3.86 ± 0.06 vs 4.04 ± 0.09 CFU/ml lysate; p=0.002). Supplementation with ATP had no effect. However, SA2DG did protect cells versus controls (2.75 ± 0.37 vs 3.13 ± 0.16 CFU/ml lysate). Compared to controls, P85-treated mice had significantly fewer organisms in the spleen (0.95 ± 0.01 vs 3.60 ± 0.31 CFU/g tissue; p=0.029). No difference was detected in the liver (1.26 ± 0.61 vs 0.95 ± 0.01 CFU/g tissue; p>0.05).
CONCLUSIONS: Pretreatment of Caco-2 cells and mice with P85 led to significantly decreased invasion of LM compared to controls. Further study of P85 is therefore warranted.

Geriatrics

96. Fundamental reading process decline in community dwelling elders. *Cynthia Raehl, Pharm.D.*, CA Bond, Pharm.D., Tresa Woods, M.S., Roland Patry, D. P.H., Lynn Bickley, M.D.; Texas Tech University Health Sciences Center School of Pharmacy, Amarillo, TX.

PURPOSE: Evaluate the fundamental reading process skill in elders using a computerized infrared eye recording system and its association with a previously validated health literacy measure used to assess ability to comply with medication regimens.
METHODS: Subjects aged 65 or greater; eye movement recordings were generated by Visagraph II system.
RESULTS: Sixty-one volunteers mean age 73.92 years, 90% Caucasian, 67% females, 12.41 +/- 3.11 years schooling completed this study. Subjects were highly functioning (clock drawing 13.44 +/- 1.69). Most respondents managed their own medications (98%) and 64% lived alone. Overall, study participants were functionally health literate (S-TOFHLA 30.38 +/- 6.08). Oculomotor outcomes included: left eye fixations (no. of eye pauses per 100 words) 124.62 +/-56.72, right eye fixations 122.31 +/- 56.41, left eye regressions (no. reverse eye movements per 100 words) 19.46 +/- 14.32, and right eye regressions 22.41 +/- 16.24. When compared to norms for non-elders, fixations increased 30%, regressions increased 40% and reading rate (words/minute with comprehension 70%) declined 24%. Although more than half of the elders earned a high school diploma, computed reading grade level was only at a fifth grade level (5.30 +/- 1.71). Multiple regression analysis revealed that performance on the health literacy test (S-TOFHLA) and the computed reading level were the strongest predictors for reading comprehension.
CONCLUSIONS: The ability to read and comprehend medication regimen instructions may be limited by age related changes in the fundamental reading processes independent of cognitive status and other known confounders of measured health literacy.

97. Effect of antidepressants on cognition in Alzheimer's disease. *Joshua Caballero, Pharm.D.*[1], Michael Hitchcock, B.S.[1], Douglas Scharre, M.D.[2], David Beversdorf, M.D.[2], Milap C Nahata, Pharm.D.[1]; (1)The Ohio State University, College of Pharmacy, Columbus, OH; (2)The Ohio State University, Department of Neurology, Columbus, OH.

PURPOSE: Approximately 45% of the 4 million Americans with Alzheimer's disease (AD) may develop depression. It is unknown if cognition in depressed patients with AD declines faster than those not depressed. Antidepressants are used to treat depression in this population. Therefore, the objective of the study was to evaluate the efficacy of antidepressant therapy on cognition in patients with AD.
METHODS: Data for a minimum of nine months were retrospectively collected from patients with AD receiving cholinesterase (ChE) inhibitors. Demographic information included age, gender, medication regimens, and Mini Mental State Exam scores (MMSE). A minimum sample of 96 patients was calculated to provide sufficient power. Data were analyzed to compare patients with AD taking antidepressant therapy and those not receiving antidepressants using chi square and analysis of covariance (p-value <0.05).
RESULTS: One hundred patients (72% female) of 274 met our criteria. Fifty-one patients were prescribed an antidepressant. Sertraline (n=24) and citalopram (n=23) were the most commonly prescribed antidepressants at an average daily dose of 86 mg and 35 mg, respectively. The baseline mean MMSE score was 15.77 ±1.07 with an average annual rate of cognitive decline of 2.11 ±0.47 for patients receiving antidepressants compared to 16.59 ±0.90 (p=NS) and 2.44 ±0.41 (p=NS) for those not taking antidepressants.
CONCLUSIONS: The incidence of depression in our population was similar to previous studies. Depression is known to cause cognitive difficulties. Our data indicates the rate of cognitive decline was no different between either group, suggesting antidepressants are not contributing to cognitive decline.

98. Comparison of two methods to identify elderly patients at risk for medication related problems in a primary care setting. *Joanna L. Nohr, Pharm.D.*[1], Theresa R. Prosser, Pharm.D.[2]; (1)Pharmacy Care Associates, Cedar Rapids, IA; (2)St. Louis College of Pharmacy, St. Louis, MO.

PURPOSE: Pharmacists need to efficiently identify elderly patients who may benefit from pharmaceutical care services. In our primary care clinic for uninsured patients, we perform a medical record screen (MRS) to identify patients to receive pharmaceutical care services. We compared MRS to a validated patient administered questionnaire (Barenholtz-Levy Medication Use Questionnaire (BLQ)) for identifying elderly at risk for medication related problems (MRP).
METHODS: Medical records of all subjects over 65 were screened. Per BLQ protocol, subjects on < 2 medications or unable to complete the BLQ were prospectively excluded. "At risk" for MRP is defined as > 2 "yes" responses on the 10 item BLQ ("BLQ+"). Subjects with diabetes, asthma/COPD or specified cardiovascular diseases were classified as "MRS+". Risk status of each subject by the two methods was compared.
RESULTS: Of 96 records screened, 88 subjects were eligible and 74 BLQs were completed (7 could not complete and 7 declined). Sixty subjects were classified as "BLQ+" and 53 "MRS+". The results of the two methods concurred in 85% of subjects (51 subjects "at risk" and 12 subjects not "at risk"). The BLQ identified 9 additional "at risk" subjects.
CONCLUSIONS: The advantage of MRS in this setting is that all elderly could be screened for MRP. In contrast, not all elderly will complete the BLQ, but it may better identify risk for MRP. Use of the BLQ in elderly who are not MRS+ would likely identify more elderly at risk for MRP and who may benefit from pharmaceutical care services.

99E. Safety profile of oxandrolone in geriatric subjects. *Karin A. Greenberg, Pharm.D., BCPS*, Yih-Min W. Huang, Ph.D., Faith D. Ottery, M.D., Ph.D.; Savient Pharmaceuticals, Inc., East Brunswick, NJ.

Presented at the 2004 Summer Meeting American Society of Health-System Pharmacists, Las Vegas, NV, June 19–23, 2004.

100. Ethnicity and calcium absorption and vitamin D seasonal changes. *Mary Beth O'Connell, Pharm.D.*[1], Tiffany Czilli, Pharm.D., Candidate[1], Steve A. Abrams, M.D.[2], Michael Kleerekoper, M.D.[3]; (1)Wayne State University, College of Pharmacy and Health Sciences, Detroit, MI; (2)USDA/ARS Children's Nutrition Research Center and Baylor College of Medicine, Houston, TX; (3)Wayne State University, School of Medicine and Detroit Medical Center, Detroit, MI.

PURPOSE: To determine if ethnicity influenced calcium absorption and vitamin D seasonal changes in Black and White senior women.
METHODS: Senior women, with normal GI function and no interfering drugs or diseases, ingested at least 1200 mg calcium (OsCal, Tums, diet) and 650 units vitamin D supplements daily. After fasting, each woman received 1.2 mg ^{42}Ca (as $^{42}CaCl_2$) intravenously and 20 µg ^{46}Ca (as $^{46}CaCl_2$) in 8 oz calcium fortified orange juice with a Swanson's breakfast and 2 slices of buttered toast. Thermal ionization mass spectrometry was used for sample analysis. Fractional calcium absorption (CaF) was calculated as the relative enrichment of the ^{46}Ca vs. the ^{42}Ca in the 24-hour urine. SPSS was used for statistical analysis.
RESULTS: Thirteen Blacks and 14 Whites with similar demographics completed the study. Because of diet changes, the expected seasonal 25(OH)D drop was not seen. Primary outcomes [mean (± SD)] were (* = P≤0.05 within group):

	CaF Fall (%)	CaF Spring	Change CaF	25(OH)D Fall (ng/ml)	25(OH)D Spring	Change 25(OH)D
Blacks	13.8 ±6.4	20.1±12.3	-6.3±15.3	21.9±9.7	25.1±9.5	-3.2±5.6
Whites	13.2±4.9	24.6±15.1	-11.5±15.7	24±6.4	28.1±7.8*	-4.1±4.9

No difference for any primary outcome or demographic variable existed between ethnic groups. In Blacks, but not in Whites or the total sample, a relationship between vitamin D concentration and CaF existed ($y = -0.432 \times [25(OH)D] + 54.2$, $P = 0.017$, $r^2 = .4$)
CONCLUSIONS: Ethnicity wasn't found to influence responses to seasonal calcium absorption, however the sample was small and vitamin D did not drop throughout the winter.

101. Evaluation of usage patterns of cholinesterase inhibitor medications (CIM) in management of Alzheimer's dementia in a nursing home. *Shyam D Karki, Pharm.D.*; Monroe Community Hospital, Rochester, NY.

PURPOSE: This study looked in the usage patterns of CIM in nursing home residents with Alzheimer's dementia with special emphasis on indication, monitoring of Mini Mental Status Examination (MMSE) as efficacy parameter and tolerability of medications by the residents.
METHODS: Charts of residents on CIM were retrospectively reviewed. Demographic data such as age, sex, race and current medications were collected. MMSE results were used as a quantitative measure of disease progression. Clinician notes, nursing notes, and minimum data sheets (MDS) were also evaluated.
RESULTS: There were sixty two residents on CIM therapies. Ten (16.1%) residents had baseline and follow up MMSE done, twenty-four (38.7%) had baseline MMSE's only, and six (9.7%) had MMSE only after the initiation of therapy. Twenty-two residents (35.5%) had no record of ever having a MMSE done. Ten residents given pre and post treatment MMSE's were analyzed separately. Mean MMSE scores at pre and post treatment were 19.6 and 16.4 respectively. Paired *t*-test analysis ((t= 0.2218, SD = 4.94, p>0.005) indicated that the null hypothesis of no difference could not be rejected. Five residents had a MMSE score less than ten and CIM was discontinued in two of them. Most common side effects were nausea and vomiting (24.2%),diarrhea (17.7%), anorexia (14.5%), and dizziness (9.7%). CIM therapy was not discontinued in any resident due to side effects.
CONCLUSIONS: All patients on CIM were for appropriate indications. Evaluation of efficacy was difficult due to poor monitoring and documentation. Tolerability of CIM was good with only minor side effects.

Health Services Research

102. A randomized investigation of pharmacist versus physician management of warfarin in the inpatient setting. *Lindsay Arnold, Pharm.D.*[1], Sara Smith-Shull, Pharm.D., M.B.A.[2], Lindsay Nissen, Pharm.D.[2], Pam Coffman, Pharm.D.[2]; (1)Boston Medical Center, Boston, MA; (2)The Nebraska Medical Center, Omaha, NE.

PURPOSE: This study compares the effects of two strategies for managing warfarin therapy: standard of care (physician-management) versus pharmacist-management while adhering to a protocol. The primary outcome measure is time to goal International Normalized Ratio (INR). Secondary outcome measures include discharge INR status and length of stay (LOS).
METHODS: All patients initiating warfarin therapy for the first time during hospitalization from February 2003 through December 2003 were eligible. Following approval for participation by their primary physician, consenting patients were randomized through block stratification to management by either a physician or a pharmacist protocol. Fisher's exact test was used to evaluate categorical data; multivariate and logistic regressions were used to assess time to goal INR and LOS. All regression analyses were completed after controlling for significant drug interactions and goal INR.
RESULTS: The analysis included 39 patients (pharmacist-managed, n=19; physician-managed, n=20). The mean time to goal INR was 3.29 days (95%CI 2.62–3.97) and 4.61 days (95%CI 3.18–6.03) in the pharmacist-managed and the physician-managed group, respectively (p=NS). Incidence of therapeutic INR at discharge was 47.4% in the pharmacist-managed and 65% in the physician-managed group (p=0.69). Mean LOS was 9.79 days in the pharmacist-managed group and 9.80 days in the physician-managed group (p=0.50).
CONCLUSIONS: No significant difference was found in either the primary outcome or secondary outcomes when comparing physician to pharmacist-managed warfarin therapy in the inpatient setting. While this study is limited by the small sample size and restricted enrollment time, pharmacist management of warfarin therapy warrants further investigation.

103E. An evaluation of clinical pharmacy services in hematology/oncology out-patient setting. *Sachin R. Shah, Pharm.D., BCOP*[1], Jonathan Dowell,

M.D.[2], Pachal Wilson, M.D.[2], Randy Hughes, M.D.[2]; (1)Texas Tech Universtiy HSC-School of Pharmacy/VA North Texas Health Care System, Dallas, TX; (2)University of Texas-Southwestern Medical Center, Dallas, TX.

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104. Factors of patient trust related to the pharmaceutical industry: a qualitative analysis. *Yavonne Q. Evans-Martinez, Pharm.D.*[1], Michael L. Johnson, Ph.D.[2], Kimberly O'Malley, Ph.D.[3]; (1)Micheal E. DeBakey VA Medical Center and University of Texas-Houston School of Public Health, Houston, TX; (2)Michael E. DeBakey VA Medical Center, Houston Center for Quality of Care and Utilization Studies and Baylor College of Medicine, Houston, TX; (3)Pearson Educational Measurement, Austin, TX.

PURPOSE: This study examined factors of patients' trust related to the pharmaceutical industry and how these factors relate to trust in health care providers and the health care system.
METHODS: As a part of a larger study of patient trust, transcripts of 17 focus groups which had a total of 77 participants were reviewed. Of the seventeen participants who mentioned some aspect of the pharmaceutical industry, eight were contacted and interviewed by telephone. Participants' beliefs and values regarding pharmaceutical industries trustworthiness; influence on health systems, providers and government; and, relationship with health systems, facilities, providers, government and patients were explored using both a Likert scale and open-ended questions.
RESULTS: By re-weighting the scale to reflect 1= strongly disagree and 10 = strongly agree and calculating the group averages, the group believed that pharmaceutical industries had a relatively strong relationship with providers (9.1), mostly influenced the government (7.7) rather than the health care system (6.8), and were not honest (2.6). Common themes discovered by the open-ended questions were: pharmaceutical industries are primarily interested in their finances, their products are trustworthy, health care providers often prescribe the best drug for the patient, and the cost of drugs should be the same world-wide.
CONCLUSIONS: Pharmaceutical industries' products are trusted by patients; however, patients distrust their intentions and dislike high cost issues. Regardless of the perception of the pharmaceutical industries, patients maintained reasonable trust in the health care providers and health care system to provide the best drug therapy to them as individuals.

105. Population differences are significant prior to initiating therapy on atypical or conventional antipsychotics. Chris M. Kozma, Ph.D.[1], Luella M. Engelhart, M.S.[2], *Reshmi M. Siddique, Ph.D.*[2]; (1)Independent Outcome Research Consultant and Adjunct Professor, University of South Carolina, Columbia, SC; (2)Janssen Medical Affairs, LLC, Titusville, NJ.

PURPOSE: To describe the magnitude of population differences between patients with prescriptions for conventional and atypical antipsychotics, challenging the notion that treatment decisions are equivalent for the two groups.
METHODS: A retrospective comparison of "new" antipsychotic patients who had at least one claim for either an atypical or conventional antipsychotic between 2000 and 2001 in a large managed care database. The study describes patient characteristics in the year prior to antipsychotic use. Study variables included diagnoses, prescription costs by drug class, cost and frequency of hospitalization, office visits, home health care, emergency room, skilled nursing care, insurance status, and specialist care. Data were evaluated with *t*-tests, χ^2 tests and logistic regression.
RESULTS: There were 9,563 eligible patients(82.5% atypical antipsychotics;12.4% conventional antipsychotics). The atypical group was younger (45.1vs.51.1 years of age, p<0.0001) and had more females (61.4%vs.51.0%,p<0.0001). In the year prior to any antipsychotic use, the atypical group was more likely to have a mental health hospitalization (19.5%vs.6.4%,p<0.0001) and to have one or more mental health diagnoses (77.2%vs.47.1%,p<0.0001). Prior to antipsychotic use atypical patients also had higher non-antipsychotic mental health drug costs, lower laboratory costs and "other" claims, and greater mental health specialist use. Conventional patients were more likely to have non-mental health diagnoses. Predictors of atypical or conventional use were identified.
CONCLUSIONS: This study demonstrates that patient characteristics and service utilization in the year prior to atypical or conventional antipsychotic use are very different between these groups. This suggests that treatment decisions should be tailored to each group.

106. Health care utilization across the United States/Mexico border. *José O. Rivera, Pharm.D.*[1], Marvin Shepherd, Ph.D.[2], Kristin Richards, Ph.D.[2], Melchor Ortiz, Ph.D.[3]; (1)University of Texas at El Paso and University of Texas at Austin, El Paso, TX; (2)University of Texas at Austin, Austin, TX; (3)University of Texas at Houston, El Paso, TX.

PURPOSE: To determine the extent of healthcare utilization across the border between El Paso, Texas and Ciudad Juárez, Chihuahua, the largest US/México border population.
METHODS: Random selection of 500 households on each side of the border. Trained bi-lingual interviewers conducted semi-structured interviews with a bi-lingual questionnaire. The interviewers followed a strict procedure to select households and participants. Two study coordinators met with the interviewers on a weekly basis on each side of the border. A χ^2 test was used to compare utilization patterns.
RESULTS: El Paso residents (n=500) were older than Juarez residents (n=501) (44.3 vs. 31.6 years). An estimated 37% of El Paso residents received health care services in México. One-third of El Paso residents (33.0%) reported purchasing medications in México during the last year. Only 5.2% of Juarez residents reported purchasing medications in the US. Dental service was the second most common health care service in MÈxico reported by US citizens (7.2%), followed by physician visits (6.8%). When excluding medications, El Paso residents reported that the majority of the services they received in México were "effective" (76.0%). Only 11 Juarez residents (2.3%) reported receiving health care services in the US of which 63.6% were reported to be "effective."
CONCLUSIONS: A significant number of the El Paso population utilizes healthcare services in México. A much lower number of the Ciudad Ju·rez population utilizes healthcare services in the US. Purchasing medications in MÈxico is the most common healthcare service used by the El Paso population.

Hematology/Anticoagulation

107. Off-label use of recombinant factor VIIa in non-hemophilic patients. *Colleen M. Culley, Pharm.D., BCPS*, Richard M. Spiro, M.D., Margaret V. Ragni, M.D., Darrell J. Triulzi, M.D., Paige R. Gross, RPh, Susan Guttendorf, Pharm.D., Susan J. Skledar, RPh, M.P.H.; University of Pittsburgh, Pittsburgh, PA.

PURPOSE: Recombinant factor VIIa (rFVIIa) is FDA-approved for the treatment of bleeding episodes in hemophilia. Our institution restricts rFVIIa to Coagulation Service use for bleeding episodes in patients with hemophilia or factor VII deficiency. Utilization and clinical outcomes of off-label rFVIIa in non-hemophilic patients were evaluated.
METHODS: A retrospective review was conducted for rFVIIa-treated patients between October 2003 and March 2004. Patients with hemophilia or factor VII deficiency were excluded. Data were analyzed with paired Student's *t*-test.
RESULTS: Twenty-seven of 31 patients ordered rFVIIa were evaluated. Mean ± SD age was 63.3±17.8 years and mean ± SD weight was 80.3±20.6 kg. Mean ± SD total rFVIIa dose was 72.5±21.2 µg/kg (range 35 to 104 µg/kg) as a single dose. Seventy percent of rFVIIa doses were administered in the operating room. Ninety-three percent of doses were requested by Neurosurgery with 88% for intracranial hemorrhage. Mean ± SD INR decreased from 2.462±0.980 to 0.992±0.238 (p<.0001). Twenty-three of 25 patients were able to proceed to neurosurgical intervention, as the INR decreased to <2. Mortality was 22%. Adverse events included one suspected pulmonary embolism and one craniotomy for clot evacuation.
CONCLUSIONS: The off-label use of rFVIIa in non-hemophilic subjects requiring emergency surgery was effective in decreasing INR preoperatively and bleeding control. Safety concerns with rFVIIa are thrombotic events. Root cause analysis of the two adverse events was not performed. An off-label protocol addressing efficacy, safety and dosing of rFVIIa in non-hemophilics was developed at our institution.

108. Development and implementation of venous thromboembolism prophylaxis screening tool in hospitalized patients. *Dipti Patel, Pharm.D.*, Lih-Jen Wang, Pharm.D., BCPS, FASHP; COLUMBUS REGIONAL HEALTHCARE SYSTEM, COLUMBUS, GA.

PURPOSE: Venous thromboembolism (VTE) and pulmonary embolism (PE) are two of the most preventable causes of mortality in hospitalized patients. Appropriate pharmacotherapeutic intervention is warranted in those patients presenting with established risk factors to significantly reduce the prevalence of this pathology. The objective of the study was to develop and validate a screening tool that identifies patients at risk of developing VTE/PE and initiate appropriate prophylactic therapy.
METHODS: A retrospective chart review of 97 patients diagnosed with VTE or PE was conducted to obtain baseline data. The screening tool was then constructed based on the results, an extensive literature search and review of current clinical guidelines. Predefined criteria dictated the prophylactic therapy selected for study patients and subjects were followed for at least 90 days.
RESULTS: It was noted from the retrospective chart review that only 33% (n=32) of patients with risk factors for VTE/PE received preventive therapy. Implementation of the screening tool identified 185 patients with risk factors for VTE/PE. Prophylactic therapy was appropriately initiated in 92% (n=169) of patients. VTE was observed in five study patients that received prophylaxis therapy. Three additional patients also developed VTE but were not prescribed prophylactic intervention.
CONCLUSIONS: The implemented VTE screening protocol serves as a valuable tool in identifying patients at risk for developing VTE/PE. The success of this protocol reveals the need to further educate healthcare providers on this easily preventable disease state.

109. Evaluation of prophylactic anticoagulation use in orthopedic surgery patients. *Kamila A. Dell, Pharm.D., BCPS*, Michelle M. Wheeler, Pharm.D.; University of Utah Hospitals & Clinics, Salt Lake City, UT.

BACKGROUND: Thromboembolism is common after orthopedic surgery. Prophylactic agents with most data supporting their use include warfarin adjusted to an INR of 2.0–3.0 or low molecular weight heparin. Current practice at our hospital includes warfarin sliding scale, which aims to achieve an INR of 1.5–2.0, or enoxaparin 30 mg given subcutaneously twice daily post-operatively.
PURPOSE: Determine what drugs and regimens are being used for thromboembolic prophylaxis after total joint surgery, evaluate bleeding and thromboembolic event rates, and evaluate length of stay in patients with and without adverse events.
METHODS: The study was a retrospective chart review. Patients were excluded if they were under the age of 18, were pregnant, or had cancer.
RESULTS: We evaluated 305 patients who had total joint surgery. Warfarin sliding scale was used in 196 patients, of which 13 (6.6%) had thromboembolic events and 4 (2%) had bleeding events. Of the 93 patients who were given enoxaparin, 3 (3.3%) had thromboembolic events, none of which were considered to be within the time of risk or associated with surgery, and 5 (5.4%) had bleeding events. The other 16 patients were on warfarin prior to admission. The thromboembolic event rate is underestimated, as the patients were not necessarily followed at our hospital after the surgery.
CONCLUSIONS: The warfarin sliding scale is not adequate prophylaxis against thromboembolism in total joint surgery. Switching to enoxaparin or changing the INR goal should result in a decrease in the thromboembolic event rate. Another evaluation after change in practice will be necessary.

110. Differences in time within the target INR range between patients randomized to five fingerstick INR devices. *Kenneth M. Shermock, Pharm.D.*[1], Jason Connor, M.S.[2], Jodie M Fink, Pharm.D., BCPS[3], Lee Bragg, Pharm.D.[4]; (1)The Johns Hopkins Hospital, Baltimore, M.D.; (2)Carnegie Mellon University, Pittsburgh, PA; (3)The Cleveland Clinic Foundation, Cleveland, OH; (4)Kaiser Permanente, Cleveland, OH.

PURPOSE: Little is known about the effect of measurement errors over time when using fingerstick INR devices to manage warfarin therapy. Our goal was to determine differences in time spent within the target INR range among patients taking warfarin therapy who were randomized between five fingerstick INR devices.
METHODS: 287 patients were randomized to one of five FDA approved fingerstick INR devices (Coaguchek S, Coaguchek ProDM, Hemochron, ProTime, and Rapidpoint). Subjects were followed longitudinally at an anticoagulation clinic by pharmacy anticoagulation specialists. Warfarin dosing decisions were made during clinic visits based on the INR from the randomized fingerstick device. Subjects also provided simultaneous venous blood draws that were analyzed at the local reference laboratory. These laboratory measures served as the gold standard to determine the proportion of time each subject's INR was actually in the target range. Differences between devices were assessed using a Bayesian hierarchical model.
RESULTS: Subjects were followed for an average of 87 days. Two POC devices, Coaguchek S (58.5% of time in target INR range) and Coaguchek ProDM (55.5%) proved to be superior (posterior probability of being the best device 0.65 and 0.29, respectively), to Hemochron (50.5%), ProTime (48.5%), and Rapidpoint (43.2%). All devices were associated with low test-retest variability (range of median variance: 0.1–0.2 INR units).
CONCLUSIONS: Use of the Coaguchek S and Coaguchek ProDM devices to guide warfarin dosing decisions was associated with subjects' INR values being within the target range a greater proportion of time compared to other devices.

111. Differences between physician, dentist and pharmacist recommendations for anticoagulation management in patients undergoing dental procedures. Samuel L. Ellis, Pharm.D.[1], *Sunny A. Linnebur, Pharm.D.*[1], Jeffrey D. Astroth, DDS, MSPH[2], Robert J. Valuck, Ph.D.[1]; (1)University of Colorado Health Sciences Center, School of Pharmacy, Denver, CO; (2)University of Colorado Health Sciences Center, School of Dentistry, Denver, CO.

PURPOSE: This study assessed knowledge of anticoagulation management in health care professionals regarding anticoagulation management in patients undergoing dental procedures.
METHODS: A total of 1200 physicians, dentists and pharmacists in the state of Colorado were randomized to receive a survey about anticoagulation knowledge. The survey consisted of questions related to warfarin and heparin management in patients undergoing dental procedures. Descriptive statistics were used to characterize study subjects, χ^2 tests were used to identify differences across study groups, and multinomial logit models were used to determine where differences existed.
RESULTS: A total of 273 (23%) surveys were returned. The response rate was 16% for pharmacists, 21% for physicians and 32% for dentists. Dentists appropriately recommended continuing warfarin more often than physicians and pharmacists for routine dental procedures such as cleaning, restorative treatment and root canals ($p<0.001$). There were no differences between the groups regarding more invasive procedures. The majority of dentists were unsure about the role of heparin bridging in patients discontinuing warfarin therapy. Physicians and dentists were more likely to use colleagues to help guide clinical decisions, while pharmacists were likely to use medical literature. Physicians were identified as the provider who should take responsibility for managing warfarin therapy by 86% of dentists, 67% of physicians and 51% of pharmacists.
CONCLUSIONS: Dentists were more likely to recommend appropriate management of warfarin therapy for routine dental procedures. However, dentists were unsure about the role of peri-procedural heparin bridging, indicating a need for education in this area.

112. Recombinant human thrombin does not contain detectable Factor V impurities. *Shirley Rene, B.S.*, Michael R Stamm, B.S., Karlien Greeff, B.S., Kathleen M Walker, B.S., Fenella C Raymond, B.S., Robert R West, Ph.D.; ZymoGenetics Inc., Seattle, WA.

PURPOSE: Profuse bleeding can be a serious complication of many surgeries, and thrombin is widely used to achieve rapid hemostasis. Bovine thrombin, the major source of topical thrombin currently available for therapeutic use, is a concentrate of bovine plasma thrombin and contains various non-thrombin proteins. A small fraction of treated patients develop antibodies to these impurities that cross-react to native clotting factors, resulting in bleeding diatheses with occasionally fatal outcomes. Recombinant thrombin (rhThrombin), produced from a precursor derived from cell culture, is not expected to contain immunogenic proteins such as the Factor V found in bovine thrombin.
METHODS: Surface Plasmon Resonance technology was used to analyze rhThrombin samples and Thrombin JMI® (lots R114A510 (exp Mar 04) and R114A752 (exp Mar 05)). Anti-Bovine Factor V/Va (Haematologic Inc., lot LO918) was immobilized to the sensor surface. Samples of the above Thrombin JMI® lots were run by SDS-PAGE and transferred to PVDF membranes. Bands were excised and subjected to N-terminal Sequence analysis using Edman chemistry on Applied Biosystems' Procise instrumentation.
RESULTS: Biacore-SPR experiments detected material specifically reactive to Factor V/Va antibodies in two separate lots of bovine thrombin. No response was seen when testing rhThrombin. Additionally, N-terminal sequencing verified the presence of bovine Factor V in the above bovine product lots.
CONCLUSIONS: Several published articles document the immunogenic properties of bovine Factor V in commercially available bovine thrombin. The above studies indicate that there is no Factor V in rhThrombin. Therefore, rhThrombin may be a safer alternative to bovine thrombin for use in surgical hemostasis.

113. Safety evaluation of outpatient tinzaparin for bridge therapy to warfarin. *William Dager, Pharm.D.*, Stacy Chow, Pharm.D., Ruby Ferrer, Pharm.D., Sandy Pak, Pharm.D., Patti Togioka, Pharm.D., Jeff King, Pharm.D.; University of California, Davis Medical Center, Sacramento, CA.

PURPOSE: The use of low-molecular-weight heparin (LMWH)has been previously shown to be as effective as unfractionated heparin for the treatment of deep-vein thrombosis (DVT) and pulmonary embolism (PE). The convenience of patients being able to self inject LMWHs has made them an acceptable VTE treatment alternative in the outpatient setting while bridging to warfarin. The safety of using the LMWH, tinzaparin, for outpatient bridge therapy in the treatment of DVT and/or PE in a University Hospital setting is examined.
METHODS: A retrospective review of sequential, eligible patients receiving at least one outpatient tinzaparin dose for treatment of DVT and/or PE. Data were analyzed for recurrent venous VTE and bleeding complications within a 1 and 3 month period after initiation of tinzaparin.
RESULTS: A total of 90 patients (DVT-61%, PE alone 29%, DVT plus PE 9%) received outpatient tinzpaprin (175u/kg/day) for a mean of 7 +/- 5 days. The mean INR at discharge was 1.3, and 2.8 when stopping tinzaparin. No incidence of recurrent symptomatic VTE within the 1 and 3 months was observed. Three patients (3.8%) developed major bleeding complications within the 1-month period. No additional major bleeding complications were observed. Five minor bleeding events (6.3%) occurred at 1 month and one event (1.2%) at 3 months.
CONCLUSIONS: The recurrence rate of VTE and bleeding complications appears to be consistent with previous studies evaluating LMWH use with warfarin. Tinzaparin as outpatient bridge therapy to warfarin for the treatment of deep-vein thrombosis and/or pulmonary embolism appears to be safe.

114E. Cost-effectiveness of FEIBA vs NovoSeven as initial therapy for the treatment of mild-to-moderate bleeds in hemophilia patients with inhibitors. Ariel Berger, M.P.H.[1], John Edelsberg, M.D., M.P.H.[1], Ellis Neufeld, M.D., Ph.D.[2], *Karen C Chung, Pharm.D., M.S.*[3], Gerry Oster, Ph.D.[1]; (1)Policy Analysis, Inc., Brookline, MA; (2)Children's Hospital Boston, Boston, MA; (3)Baxter BioScience, Westlake Village, CA.

Presented at the 2004 Hemophilia Congress of the World Federation of Hemophilia, Bangkok, Thailand, October 17–21, 2004.

115. A retrospective review to identify causes of elevated INRs in outpatients on warfarin. *Andrew F. Kelliher, M.S., R.Ph., C.D.E., M.B.A.*, Robert G. Henault, R.Ph., C.D.E., George Alexis, M.S., R.Ph.; VA Boston Healthcare System, West Roxbury, MA.

PURPOSE: This descriptive report will identify outpatients with International Normalized Ratios (INRs) greater than 5.9 and examine the contributing causative factors that caused the elevations. Drug interactions, co-morbid conditions such as liver disease and congestive heart failure, warfarin dose noncompliance and alcohol abuse can acutely increase the INR. Our intent is to identify the causative factors and their percentage occurrence to use the knowledge gained to prevent elevated INRs and ultimately reduce morbidity, hospital visits, and/or admissions.
METHODS: Patients enrolled in one of the 6 anticoagulation clinics (approximately 1500 patients) within the VA Boston Healthcare System and having an INR greater than 5.9 over the last two years were identified using the VA database. Clinical pharmacists conducted a retrospective review of the patients' electronic medical record to determine and review causative factors. The percentage of each identified contributing factor was determined.
RESULTS: 207 occurrences of INR greater than 5.9 were identified. Based on current Chest guidelines (2001) we identified 159 patients with INR range of 2–3 and 48 with an INR range of 2.5–3.5. Major identified causes included: unknown cause (20.6%), drug/drug interaction (15.7%), alcohol abuse (13%), nonadherence to warfarin dose (13.9%), and nausea/vomiting/diarrhea (9.9%). Major identified drugs causing interactions were antiinfectives (37.1%), corticosteroids (31.4%), and NSAIDs/analgesics (25.7%).
CONCLUSIONS: Our findings of major identified causes of elevated INR and related classes of drugs can be used to enhance provider and patient education and awareness to improve identification of potential causes and reduce the number of incidences of elevated INR.

Herbal/Complementary Medicine

116. Herbal/dietary supplements marketed for recreational use on the Internet. *Amy E Miller, Pharm.D.*, Cathi E Dennehy, Pharm. D., Candy Tsourounis, Pharm. D.; University of California, San Francisco, San Francisco, CA.

PURPOSE: The purpose of this study was to characterize herbs and dietary supplements (DS) marketed over the Internet for recreational use.
METHODS: Four major search engines and the search terms "buy herbal high" and "buy legal high" were used to identify the sites. The first 20 sites from each search engine, excluding duplicates which distributed product to the United States (U.S.) were selected. Sites were characterized for country of origin, compliance with the Dietary Supplement Health and Education Act (DSHEA), ingredients, efficacy claims, comparisons to illicit drugs, side effects, and drug interactions. Up to five products per site were evaluated.
RESULTS: Twenty-eight web sites with 119 products were evaluated. Most sites were in the U.S. (54%), identified the product as a DS (73%) and carried a Food and Drug Administration (FDA) disclaimer (67%). Forty seven percent of products were likened to illicit drugs, typically marijuana (48%) or ecstasy (23%). The most common product ingredients were ephedra alkaloids (26%), *Salvia divinorum* (17%), kava (9%), guarana (9%), *Acorus calamus* (9%) and damiana (9%). Efficacy claims frequently involved the products use as a hallucinogen (51%) or stimulant (39%). Sixty-four percent of sites mentioned side effects and 54% mentioned drug interactions.
CONCLUSIONS: This study demonstrates that herbs and DS are being marketed for use as legal alternatives to illicit drugs of abuse. The use of ephedra as a stimulant and *Salvia divinorum* as a hallucinogen were the most prevalent. Health care professionals need to be aware of this trend and the products that are involved.

117. Chitosan augmenting the inhibitory effect of gymnemic acid on glucose absorption. *Hong LUO, M.D./Ph.D.*, Kazuo YAMADA, M.D./Ph.D.; Division of Medical Biochemistry,Department of Pathophysiological and Therapeutic Science,Faculty of Medicine,Tottori University, Yonago 683-8503, Japan.

PURPOSE: We have found that gymnemic acid (GA) extracted from *Gymnema sylvestre* and chitosan inhibited glucose absorption respectively. For more effectively nutrient control in diabetes and obesity, we compared the combinative and individual effect of GA and chitosan on glucose absorption.
METHODS: Absorption of 20 mmol/l glucose with or without 0.3~2.5 mg/ml chitosan (about 10, 100, 1000 kDa) and/or 5 mg/ml (near IC50) gymnema water extractor (containing GA) was studying in Wistar rat small intestine *in situ* loop (n=9~12) by recycle perfusion for an hour. To compare effective duration, the glucose was perfused following 30, 60, 90 and so on minutes rinse until the absorption recovered.
RESULTS: The maximum inhibitory rate of glucose absorption was achieved 56.7±7.5% by GA combining 0.3 mg/ml 100 kDa chitosan during the first 15 min, however only was 20.6±9% (P<0.05) in GA and no effect in the same dose chitosan only group simultaneously (the absorption of glucose without GA and chitosan as 100%). The maximum inhibitory rate was 40.4±3.2% at 60 min and 16.8±5.9% at 45 min in the GA and chitosan only group respectively. The inhibitory duration in combinative group was 210 min nearly same with the GA only (240 min). The effect disappeared in chitosan only group following 30 minutes rinse.
CONCLUSIONS: GA combining lower dose chitosan augmented the inhibitory effect on glucose absorption resulting in limited glucose and insulin peaks in blood, which could be a useful method for diet regimen in diabetes and obesity.

118. Adjunctive therapy in Alzheimer's disease: is vitamin E neuroprotective? *Michael Hitchcock, B.S.*[1], Joshua Caballero, Pharm.D.[1], David Beversdorf, M.D.[2], Douglas Scharre, M.D.[2], Milap C Nahata, Pharm.D.[1]; (1)The Ohio State University, College of Pharmacy, Columbus, OH; (2)The Ohio State University, Department of Neurology, Columbus, OH.

PURPOSE: Patients with Alzheimer's disease (AD) may be given Vitamin E as an antioxidant. Limited data are available on the claim of efficacy of Vitamin E. Therefore, the objective of our study was to determine the effects of Vitamin E on cognition in patients with AD.
METHODS: Data for a minimum of nine months were retrospectively collected from patients with AD receiving cholinesterase (ChE) inhibitors. Demographic information included age, gender, medication regimens, and Mini Mental State Exam scores (MMSE). Based on previous results, a minimum sample of 96 patients would yield a power of 0.8 and p-value <0.05. Data were analyzed to compare patients with AD taking Vitamin E and those not receiving Vitamin E using chi square and analysis of covariance.
RESULTS: Medical records of 100 patients were reviewed. Vitamin E (mean dose 1615 IU/day) was prescribed in 76% of patients. The baseline mean MMSE scores were similar between Vitamin E groups and non-Vitamin E groups. Those with mild AD (MMSE 18–26), taking vitamin E had a mean annual rate of decline of 0.67 ±0.46 compared to 3.14 ± 0.96 for patients not taking vitamin E (p=0.021). In the moderate (MMSE 10–17) and severe (MMSE <9) groups, rates of annual decline did not differ between patients receiving Vitamin E and those not taking Vitamin E (moderate AD p=0.188; severe AD p=0.825).
CONCLUSIONS: Vitamin E may provide neuroprotective benefits in mild AD but efficacy may be lost as AD progresses. Larger prospective randomized trials are needed to confirm these results.

HIV/AIDS

119E. Post-exposure prophylaxis (PEP) in health care workers (HCWs) after exposure to an HIV-infected source patient (SP). *Betty J. Dong, Pharm.D*, Ann Harvey, M.D., Richard A. Aranow, M.D., Larry Boly, M.D., Jennifer Cocohoba, Pharm.D., Jeff East, M.D., Cristina Gruta, Pharm.D., Nancy Nguyen, Pharm.D., Jason Tokumoto, M.D., Kirsten Balano, Pharm.D., Amy Kindrick, M.D., M.P.H., Janet Myers, M.P.H., Carl Thelin, AA, Ronald H. Goldschmidt, M.D.; National HIV/AIDS Clinicians' Consultation Center, University of California, San Francisco, San Francisco, CA.

Presented at the 11th Conference on Retroviruses and Opportunistic Infections of the Foundation for Retrovirology and Human Health, San Francisco, CA, February 2–11, 2004.

120. Clinically significant inter-patient variability in lopinavir pharmacokinetics in HIV-infected patients on salvage therapies. Lillian S. L. Ting, BSc.(Chem)[1], Chris S. Alexander, Ph.D.(Chem)[2], Richard P. Harrigan, Ph.D..(Biochem)[2], Julio Montaner, M.D., FRCPC[2], *Mary H. H. Ensom, B.S.(Pharm), Pharm.D.*[3]; (1)University of British Columbia, Vancouver, BC, Canada; (2)BC Centre for Excellence in HIV/AIDS, Vancouver, BC; (3)University of British Columbia and Children's & Women's Health Centre of British Columbia, Vancouver, BC, Canada.

PURPOSE: This retrospective study aims to characterize pharmacokinetic parameters of lopinavir (LPV) in HIV-infected individuals predominantly undergoing salvage therapies.
METHODS: Study patients were on steady-state twice-daily Kaletra® (LPV/ritonavir; 400/100 mg or 533/133 mg) plus ≥2 other antiretrovirals. Plasma samples were collected at pre-dose and at 1, 2, 4, 6, 8, 10 and 12 h post-dose. Lopinavir concentrations were determined by a validated HPLC-MS/MS assay, and LPV pharmacokinetic profiles were analyzed by non-compartmental modeling using WinNonlin 4.1. Apparent oral clearance (Clss/F), apparent volume of distribution(Vss/F), mean residence time(MRT), elimination rate constant(λ) and absorption rate constant(Ka) were calculated. Patients were stratified by Kaletra doses due to potential alteration in pharmacokinetic parameters caused by different doses of ritonavir (a potent CYP450 inhibitor; LPV-boosting agent).
RESULTS: Eighty-eight lopinavir pharmacokinetic profiles (with at least 6 concentrations each) from 73 patients who were predominantly on salvage antiretroviral therapies were analyzed. Sixty-two patients were taking at least one interacting antiretroviral. Pharmacokinetic variability was clinically significant (see Table).
Results in mean(%CV)

LPV dose	Clss/F (L/h)	Vss/F (L)	MRT (h)	l (1/h)	Ka (1/h)	N
400 mg	8.51	61.52	13.29	0.172	0.378	40
	(95.31%)	(60.60%)	(72.89%)	(73.70%)	(43.95%)	
533 mg	9.82	85.04	13.40	0.146	0.467	48
	(92.90%)	(67.52%)	(50.33%)	(73.30%)	(78.85%)	

CONCLUSIONS: Wide inter-patient variability exists in lopinavir pharmacokinetic parameters of patients on salvage antiretroviral therapies. Therapeutic drug monitoring is recommended and studies of TDM strategies are underway to ensure optimal clinical outcome.

121E. The efficacy of protease inhibitors in patients co-infected with HIV and hepatitis B or C. *Marie C. Vilme, Pharm.D.*, Shvawn McPherson-Baker, Pharm.D., M.P.H., BCPS, Deidree E. Edwards, Pharm.D.; Miami Veterans Affairs Medical Center, Miami, FL.

Presented at the 35th Annual Southeastern Residency Conference, Athens, GA, May 6–7, 2004.

Infectious Diseases

122. Does fluoroquinolone resistance affect the clinical outcomes of patients with *Escherichia coli* or *Klebsiella species* bacteremia?. *Leticia R. Villela, Pharm.D.*[1], Ronald G. Hall II, Pharm.D.[2], Robin H. Amirkhan, M.D.[3]; (1)Veterans Affairs North Texas Health Care System, Dallas, TX; (2)Texas Tech University Health Sciences Center, School of Pharmacy - Dallas/Fort Worth Regional Campus, Dallas, TX; (3)University of Texas Southwestern Medical Center at Dallas, Dallas, TX.

PURPOSE: This study evaluated the effects of fluoroquinolone resistance (FQR) in *E. coli* and *Klebsiella species* bacteremia on length of hospital stay (LOS) and mortality.
METHODS: Patients at the Dallas VA Medical Center with a positive *E. coli* or *Klebsiella species* blood culture from January 2001–June 2003 were included. FQR was defined by ciprofloxacin susceptibilities. A retrospective chart review was performed to collect demographics, comorbidities, treatment, and outcomes.
RESULTS: Twenty-three FQR patients and 112 fluoroquinolone-susceptible patients were included. FQR patients were more likely to be located in the intensive care unit (p=0.002) or a long-term care facility (p=0.001), have a central venous catheter (p=0.001), be mechanically ventilated (p<0.001), require dialysis (p=0.046), or have a diagnosis of congestive heart failure (p=0.048). However, APACHE II scores did not differ significantly between the two groups. FQR was associated with an increased LOS (46.7 vs. 21.6 days, p=0.008), 14-day mortality (34.8% vs. 12.5%, p=0.024), and 30-day mortality (43.5% vs. 19.6%, p=0.042). Inappropriate empiric treatment with a fluoroquinolone increased 14-day mortality compared to appropriate empiric therapy with a fluoroquinolone (71% vs. 6%, p<0.003).
CONCLUSIONS: This is the first study conducted in the United States to evaluate the effects of FQR on clinical outcomes for patients with *E. coli* or *Klebsiella species* bacteremia. LOS, 14-day, and 30-day mortality were significantly increased in patients with FQR. Although these findings may be confounded by differences between our patient groups, practitioners should note the consequences of inappropriate empiric fluoroquinolone treatment for *E. coli* or *Klebsiella species* bacteremia.

123. Heterogeneous glycopeptide resistance in *Staphylococcus aureus* associated with accessory gene regulator (agr) group II. *Brian T. Tsuji, Pharm.D.*, David Yoon, B.S., Michael J. Rybak, Pharm.D.; Anti-infective Research Laboratory, Wayne State University, Detroit, MI.

PURPOSE: Prolonged exposure to sub-therapeutic levels of vancomycin have been associated with the development of glycopeptide heteroresistance in patients with *S. aureus* infections. In vitro, sub-inhibitory concentrations of vancomycin have been shown to select for heteroresistance in agr-null group II *S. aureus*. We studied the effect of administering varying concentrations of vancomycin and the development heteroresistance in agr group II *S. aureus* using time kill experiments.
METHODS: One agr^+ group II (RN6607) and the respective agr^- group II, null derivate (RN9120) strain of *S. aureus* were obtained from the Network on Antimicrobial Resistance in Staphylococcus aureus (NARSA). Minimum inhibitory concentrations (MIC) were determined by Etest & microdilution according to NCCLS. Time-kill experiments were performed using vancomycin at 0.25, 0.5 & 1 X MIC over 48h. The development of heteroresistance and resistance was evaluated at multiple time points.
RESULTS: Pre-exposure vancomycin MIC were 1 against both agr^+ II and agr^- II strains. Against both strains, vancomycin treatment curves resembled growth curves, evident by limited bacterial reduction at all time points. Against agr^+ II, no heteroresistance was noted at all concentrations. Post-exposure MIC for all concentrations was 1 µg/ml. Against agr^- II, exposure to vancomycin at 0.5 and 1 x MIC produced heteroresistance at 48h. Post-exposure vancomycin MIC was 4 µg/ml.
CONCLUSIONS: Sub-inhibitory exposures of vancomycin resulted in heteroresistance in agr—null group II *S. aureus*. This may have implications to current recommended dosing guidelines for vancomycin. No heteroresistance was noted in agr^+ group II *S. aureus*.

124. Inaccurate susceptibility results with VITEK 1 may impair proper empiric antimicrobial selection for *Pseudomonas aeruginosa* infection. *Christopher D Miller, Pharm.D.*, Kelly Echevarria, Pharm.D., BCPS, Kimberly K Summers, Pharm.D., BCPS; South Texas Veterans Health Care System, San Antonio, TX.

PURPOSE: The VITEK 1 is an automated microbiology susceptibility testing system still in use by many laboratories despite growing inaccuracy data and the advent of the VITEK 2. This study was designed to measure the accuracy of the VITEK 1 against *Pseudomonas aeruginosa*, using disk diffusion methodology as a control comparison. The primary outcome measurement was percent susceptibility, as it would relate to antibiogram data.
METHODS: Consecutive *Pseudomonas aeruginosa* patient isolates received by the microbiology laboratory were tested using both the VITEK 1 and disk diffusion according to NCCLS guidelines. Antimicrobials analyzed included cefepime, ceftazidime, ciprofloxacin, gentamicin, imipenem, levofloxacin, and piperacillin/tazobactam. Error rates and percent susceptibility were logged and compared for overall and individual drugs. Differences in percent susceptibility of ≥ 10% were considered substantial, potentially resulting in important alterations in antibiogram data.
RESULTS: In total, 105 *Pseudomonas aeruginosa* bacterial isolates were tested against the above antimicrobial agents, with 726 susceptibility results available. For all susceptibility results combined, the percent agreement between testing methods was 86.0%. Cefepime, ceftazidime, and gentamicin displayed a ≥ 10% decrease in susceptibility using the VITEK 1 versus disk diffusion results. Respective differences in susceptibility rates between the VITEK 1 and disk diffusion were as follows: cefepime (63%, 85%), ceftazidime (72%, 88%), and gentamicin (52%, 63%).
CONCLUSIONS: Susceptibility results from the VITEK 1 varied from the control method for certain antibiotics. Such differences would convey dramatic effects upon antibiogram data and in turn may improperly guide empiric antimicrobial treatment selections.

125. Impact of culture site on antimicrobial pharmacodynamics. *Christopher R. Frei, Pharm.D., M.S., BCPS*, David S. Burgess, Pharm.D.; University of Texas at Austin, University of Texas Health Science Center at San Antonio, San Antonio, TX.

PURPOSE: Pharmacodynamic studies typically do not stratify microbiologic data by culture site. This study evaluated the pharmacodynamics of 2 antimicrobial regimens against 6 gram-negative bacteria from 3 culture sites.
METHODS: Blood, pulmonary, and wound MIC distributions for bacteria with >20 isolates for each site were extracted from the 2002 Intensive Care Unit Surveillance System (ISS) database. Pharmacokinetic parameters were obtained from healthy human studies for piperacillin/tazobactam (PTZ) 3.375g q4h and piperacillin (PIP) 3g q4h. Monte Carlo simulation was used to model 10,000 patients for each antimicrobial-MIC distribution pair. The probability of target attainment (TA) for a %T>MIC ≥50% was determined. A clinically significant difference in the probability of TA was defined as ≥10%.
RESULTS: For PTZ, the probability of TA varied <10% by culture site. Likewise, the probability of TA for PIP was similar among the 3 culture sites for *A. baumanii*, *K. pneumoniae*, *P. mirabilis*, and *P. aeruginosa*. However, the probability of TA against *E. coli* was significantly higher for PIP in pulmonary vs. wound cultures (59% vs. 43%). In addition, the probability of TA against *E. cloacae* was significantly higher for PIP in pulmonary vs. blood cultures (63% vs. 48%). The probability of TA agreed with the %S for PTZ and PIP regimens for all gram-negative bacteria except *P. aeruginosa* demonstrating that the NCCLS breakpoint of 16 µg/ml is appropriate for non-Pseudomonal gram-negative bacteria.
CONCLUSIONS: Culture site appears to be of minor importance for pharmacodynamic studies of piperacillin/tazobactam and piperacillin. Further investigations with additional antimicrobial regimens are warranted.

126. Macrolide pharmacodynamics in serum and epithelial lining for *Streptococcus pneumoniae*. *Christopher R. Frei, Pharm.D., M.S., BCPS*[1], David Burgess, Pharm.D.[2]; (1)University of Texas at Austin, University of Texas Health Science Center at San Antonio, San Antonio, TX; (2)University of Texas Health Science Center, San Antonio, TX.

PURPOSE: This study evaluated the pharmacodynamics of clarithromycin (CLA) and azithromycin (AZI) in serum and epithelial lining for S. pneumoniae.
METHODS: Susceptibility data were extracted from the 2002–2003 Global Respiratory Antimicrobial Surveillance Project (GRASP). Pharmacokinetic parameters in serum and epithelial lining were obtained from healthy human studies for CLA XL 1000mg q24h, CLA 500mg q12h, and AZI 500mg q24h x 1d plus 250mg q24h x 4d. Monte Carlo modeling was used to simulate 10,000 patients. Target attainment (TA) was determined for a free AUC_{0-24}/MIC ratio ≥ 25. A clinically significant difference was defined as a change in TA ≥ 10%.
RESULTS: S. pneumoniae isolates by penicillin (PCN) and erythromycin (ERY) susceptibilities were as follows: all (1,828), PCN-S (1,198), PCN-I (291), PCN-R (339), ERY-S (1,283), and ERY-R (545). Overall, the MIC50/90 revealed that CLA (≤ 0.06/8) was more potent than AZI (≤ 0.12/16). The AUC_{0-24} was significantly higher in epithelial lining than serum for all 3 regimens: CLA 500mg q12h (400 vs. 52), CLA XL 1000mg q24h (179 vs. 42), and AZI (30 vs. 1). Likewise, TA was consistently higher in epithelial lining compared to serum for all 3 regimens. CLA 500mg q12h and CLA XL

1000mg q24h achieved similar TA in serum (74% and 73%) and epithelial ling (88% and 84%). AZI TA was significantly lower than both CLA regimens in the serum (0%) and epithelial ling (71%). Finally, TA rates for CLA and AZI correlated with PCN and ERY susceptibilities.
CONCLUSIONS: Clarithromycin demonstrated better pharmacodynamics than azithromycin in both serum and epithelial lining.

127E. Pharmacodynamics of continuous infusion (CI) β-lactams against Gram-negative pulmonary isolates from ICU patients. *Christopher R. Frei, Pharm.D., M.S., BCPS*, David S. Burgess, Pharm.D.; University of Texas at Austin, University of Texas Health Science Center at San Antonio, San Antonio, TX.

Presented at the Annual Meeting of the Infectious Diseases Society of America, Boston, MA, September 30-October 3, 2004.

128E. Pharmacodynamics of piperacillin/tazobactam and piperacillin for Gram-negative bacteremia in ICU patients. *Christopher R. Frei, Pharm.D., M.S., BCPS*, David S. Burgess, Pharm.D.; University of Texas at Austin, University of Texas Health Science Center at San Antonio, San Antonio, TX.

Presented at the Annual Meeting of the Infectious Diseases Society of America, Boston, MA, September 30-October 3, 2004.

129. Lack of clinically significant hepatotoxicity following moxifloxacin therapy. Daniel Haverstock, M.S., *Shurjeel Choudhri, M.D.*; Bayer Pharmaceuticals Corporation, West Haven, CT.

PURPOSE: To evaluate the incidence of hepatic adverse events (AE) of PO/IV moxifloxacin vs. comparators antimicrobials.
METHODS: A retrospective search of the oral/IV moxifloxacin (Bayer) Phase II-IV database using CoSTART terminology for hepatic AE was conducted. Clinical events categorized as definitely, probably, or possibly-related to moxifloxacin were considered potential hepatotoxic events. Liver function test (LFT) abnormalities were also recorded.
RESULTS: Drug-related hepatic AE stratified by route of administration are shown below:

Drug-related AE	400 mg PO moxifloxacin (all studies) n=6,794	400 mg IV/PO moxifloxacin (CAP/cSSSI studies)* n=1,254	PO Comparators (all studies) n=5,961	IV/PO Comparators (CAP/cSSSI studies)* n=1,279
LFT abnormal	63 (0.9%)	50 (4.0%)	61 (1.0%)	39 (3.0%)
Gamma-GT increased	10 (0.1%)	18 (1.4%)	15 (0.3%)	22 (1.7%)
Cholestatic jaundice	3 (<0.1%)	0	1 (<0.1%)	2 (0.2%)
Liver damage	2 (<0.1%)	2 (0.2%)	1 (<0.1%)	2 (0.2%)
Biliary pain	1 (<0.1%)	0	0	0
Cholangitis	0 (0.0%)	1 (<0.1%)	0	0
Hepatic failure	0 (0.0%)	1 (<0.1%)	0	0
Jaundice	0 (0.0%)	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)
Hepatitis	0 (0.0%)	0	1 (<0.1%)	1 (<0.1%)

*CAP=community-acquired pneumonia
cSSSI=complicated-skin and skin structure infection

Overall, there were increased rates of drug-related hepatic AE/laboratory abnormalities in the IV/PO vs. oral studies. The incidence of hepatic AE following PO or IV/PO therapy was similar between the moxifloxacin and comparator groups.
CONCLUSIONS: Oral and IV moxifloxacin are associated with a low potential to induce clinically-significant hepatotoxicity.

130. Pharmacodynamics of β-lactams against 2,584 Gram-negative pulmonary isolates from ICU patiens. *David Burgess*, Christopher R. Frei, Pharm.D., M.S., BCPS[2]; (1)University of Texas Health Science Center, San Antonio, TX; (2)University of Texas at Austin, University of Texas Health Science Center at San Antonio, San Antonio, TX.

PURPOSE: Pulmonary infections remain a leading cause of morbidity and mortality among ICU patients. Most often, these infections are due to gram-negative organisms. This study compared the pharmacodynamics of 10 beta-lactam regimens against gram-negative isolates from ICU patients.
METHODS: Susceptibility data were extracted from the 2002 Intensive Care Unit Surveillance System (ISS) database. Pharmacokinetic parameters were obtained from peer-reviewed studies in healthy volunteers. Monte Carlo analysis was used to simulate 10,000 subjects for each bug-regimen combination. Target attainment (TA) was determined for %T>MIC as follows: carbapenems (≥ 30%), penicillins (≥ 40%), cephalosporins (≥ 50%), and aztreonam (≥ 50%).
RESULTS: Overall, the 2002 ISS database comprised susceptibility data from over 2,584 gram-negative pulmonary isolates including Enterobacteriaceae (N=1,606), *P. aeruginosa* (N=799), and *A. baumanii* (N=179). TA rates were as follows: imipenem 500mg Q6h (99%, 76%, 83%), ertapenem 1g Q24h (97%, NT, NT), cefepime 2g Q8h (96%, 89%, 55%), ceftazidime 2g Q8h (89%, 90%, 63%), aztreonam 2g Q8h (88%, 85%, 46%), piperacillin/tazobactam 3.375g Q4h (87%, 82%, 49%), ceftriaxone 2g Q24h (84%, NT, NT), ticarcillin/clavulanate 3g Q4h (82%, 59%, 55%), piperacillin 3g Q4h (69%, 79%, 37%), and ampicillin/sulbactam 3g Q6h (64%, NT, 73%), respectively.
CONCLUSIONS: This pharmacodynamic evaluation of pulmonary isolates from ICU patients, demonstrates that monotherapy with imipenem, ertapenem, or cefepime achieves a high probability of clinical success (TA >90%) against the Enterobacteriaceae; however, combination therapy should be administered for suspected P. aeruginosa or A. baumanii since none of the regimens tested achieved a TA >90% as monotherapy.

131E. Fluoroquinolone pharmacodynamics in serum and epithelial lining against *S. pneumoniae*. *David S. Burgess, Pharm.D.*, Christopher R. Frei, Pharm.D., M.S., BCPS; University of Texas at Austin, University of Texas Health Science Center at San Antonio, San Antonio, TX.

Presented at the Annual Meeting of the Infectious Diseases Society of America, Boston, MA, September 30–October 3, 2004.

132E. Gram-negative resistance in outpatients at an academic medical center. *David S. Burgess, Pharm.D.*, Christopher R. Frei, Pharm.D., M.S., BCPS; University of Texas at Austin, University of Texas Health Science Center at San Antonio, San Antonio, TX.

Presented at the Annual Meeting of the Infectious Diseases Society of America, Boston, MA, September 30–October 3, 2004.

133. Impact of ESBL enzyme and inoculum size on antimicrobial activity as measured by time-kill methodology. *David S. Burgess, Pharm.D.*[1], Ronald G. Hall II, Pharm.D.[2]; (1)University of Texas HSC, San Antonio, TX; (2)Texas Tech University Health Sciences Center, School of Pharmacy - Dallas/Fort Worth Regional Campus, Dallas, TX.

PURPOSE: ESBLs are an emerging infectious disease problem. This study evaluated the activity of meropenem (MEM), cefepime (CPM), piperacillin/tazobactam (PTZ), levofloxacin (LEV), and tobramycin (TOB) against 10 ESBLs with known genotypes at 2 inocula.
METHODS: NCCLS methodologies were used to determine MICs for 4 SHV and 6 TEM producing isolates. Time-kill curves were performed using standard ($5x10^5$ CFU/mL) and high ($1x10^7$ CFU/mL) inocula. Antimicrobial concentrations (µg/mL) were: MEM (4), CPM (20), PTZ (40/5), LEV (2), and TOB (4). Samples were withdrawn at 0, 2, 4, 6, 8, 12, and 24 hrs, plated and incubated for 24 hrs at 35°C.
RESULTS: Number of susceptible isolates was highest for MER (10) followed by LEV (8), CPM (6, MIC ≤ 8), PTZ (2) and TOB (1). Only MEM achieved and maintained bactericidal activity over 24 hrs for all isolates at both inoculum. For standard inoculum, CPM was more likely to maintain bactericidal activity against SHV than TEM (100% vs. 67%); whereas, LEV and PTZ were more likely against TEM than SHV (83% vs. 50% and 50% vs. 0%). TOB displayed poor bactericidal activity against TEM (0%) and SHV (0%). Bactericidal activity of PTZ and TOB was unaffected by inoculum size. However, CPM and LEV had a significant decline in bactericidal (standard vs high): CPM (80% vs. 0%), LEV (70% vs. 40%).
CONCLUSIONS: Meropenem was the most active antimicrobial irrespective of enzyme or inoculum size. Cefepime exhibited a significant inoculum effect. The clinical significance of these findings warrants further investigation in clinical studies.

134. Evaluation of the impact of educational efforts on the use of vancomycin in febrile neutropenic fever. *Olga H. DeTorres, Pharm.D., BCPS*, Donna R. Burgess, R.Ph., Debra A. Garza, R.Ph., M.B.A.; Southwest Texas Methodist Hospital, San Antonio, TX.

PURPOSE: The emergence of vancomycin resistant organisms has been associated with increased use of vancomycin. The objectives of this study were to evaluate how educational efforts and interventions impacted the use of vancomycin in febrile neutropenic patients and the rate of vancomycin-resistant *Enterococcus faecium* in our community hospital.
METHODS: All hospitalized febrile neutropenic patients (n=64) admitted between March–April 2001 initially started on vancomycin were evaluated for appropriateness based on the IDSA Neutropenic Fever Guidelines (Clin Infect Dis 1997;26:551–73). The results were presented to the hospital's Quality Improvement Committee and the Medical Board. Letters, educational posters, and pocket cards were developed and distributed to the hematologists/oncologists. A follow-up study was conducted in October–November 2002 (n=63) to evaluate the impact of the educational efforts. Finally, hospital-wide vancomycin-resistant *Enterococcus faecium* rates were evaluated for 2001–2003.
RESULTS: The appropriateness of vancomycin significantly increased from 49% in 2001 to 76% in 2002 for neutropenic fever patients. Overall, the number of *Enterococcus faecium* isolates increased from 163 in 2001 to 200 in 2003. However, vancomycin-resistant *Enterococcus faecium* decreased from 49% in 2001 to 29% in 2003.
CONCLUSIONS: Educational posters and interventions significantly improved the use of vancomycin in the treatment of neutropenic fever at our community hospital. Furthermore, the hospital-wide vancomycin-resistant *Enterococcus faecium* decreased during this 3 year period.

135E. Activity of tigecycline (GAR-936) tested against clinical isolates of *Haemophilus influenzae, Moraxella catarrhalis* and *Neisseria meningitidis,* a worldwide perspective. *Helio S. Sader, M.D., Ph.D.*, Thomas R. Fritsche, M.D.,

Ph.D., Ronald N. Jones, M.D.; The JONES Group/JMI Laboratories, North Liberty, IA.

Presented at the European Congress of Clinical Microbiology and Infectious Disease, Prague, Czech Republic, May 1–4, 2004.

136. Influence of a urinary tract infection empiric treatment pathway on physician prescribing in an academic medical center. *Ibis Lopez, Pharm.D.*, Aimee Leclaire, Pharm.D., Robert Kuhn, Pharm.D., Robert Rapp, Pharm.D., Kelly Smith, Pharm.D., Craig Martin, Pharm.D.; University of Kentucky Chandler Medical Center, Lexington, KY.

PURPOSE: In an attempt to maintain or improve patient outcomes and control health care costs, treatment algorithms are often implemented by health care institutions or organizations. In July 2002, a guide to empiric antimicrobial therapy, which includes a urinary tract infection (UTI) algorithm, was distributed to all hospital physicians in an academic medical center. The primary objective of the study was to assess the impact of the guide on physician prescribing of empiric antimicrobial therapy for UTIs.
METHODS: A retrospective patient chart review for three months prior to implementation of the guide and the corresponding three months one year after implementation was conducted for patients with a primary or secondary diagnosis of UTI or acute pyelonephritis. Patients who were < 18 years of age, did not receive any antimicrobial agent, lacked laboratory or subjective parameters confirming UTI diagnosis, had a concomitant infection, or had a diagnosis of urosepsis were excluded. Descriptive statistics, primarily incidence rates and percentages, and χ^2 analysis were used to describe data.
RESULTS: Prior to the implementation of the guide, 45% of (n=52) patients with UTIs were treated consistently with the algorithm. Consistency increased to 51% (n=44) after the implementation of the guide; however, this was not a statistically significant improvement (p=0.35).
CONCLUSIONS: The implementation of a guide to empiric antimicrobial therapy did not influence physician prescribing habits regarding UTIs. Educational sessions at implementation along with reinforcement of guidelines are essential for impacting prescribing habits.

137. Effects of formulary addition of cefepime on susceptibility of select Gram-negative pathogens to ceftazidime and imipenem: analysis by interrupted time series analysis. *John A. Bosso, Pharm.D.*, Patrick D. Mauldin, Ph.D.; Medical University of South Carolina, Charleston, SC.

PURPOSE: The addition of cefepime (CEF) to the antibiotic formulary may have salutatory effects on susceptibility patterns of other β-lactam antibiotics, especially when used as a substitute agent.
METHODS: To assess these potential effects in our institution, quarterly susceptibility rates (SR) of 3 organisms [Pseudomonas aeruginosa (PA), *Escherichia coli* (EC), *Klebsiella pneumoniae* (KP)] to ceftazidime (CTZ) and imipenem (IMI) from 1993 through 2003 were considered. Segmented regression analysis for interrupted time series was used to compare slopes over time before and after the introduction of CEF. The Durbin-Watson statistic was used to test for autocorrelation.
RESULTS: No effects on SR of KP to CTZ or IMI were observed related to introduction of CEF. With PA, significant negative changes (p=0.0029 and 0.0315, respectively) in slope trend in CTZ and IMI SR were detected (R^2=0.75 and 0.26, respectively). With EC, a significant negative change (p=0.0078) in the already downward slope of CTZ SR after introduction of CEF (R^2=0.47) was detected. However, there were no significant effects on IMI SR with EC.
CONCLUSIONS: These results should be interpreted with caution. Although some of the detected relationships were statistically significant, the low coefficients of determination suggest a lack of explanatory value for these models. Although utilization of cefepime has risen substantially over the study period (9.54 and 1.32 Gm/1000 patient days for 4th quarter of 2003 for adults and pediatric patients, respectively), it may be that cefepime needs to completely replace the use of other cephalosporins to appreciate positive effects on susceptibility trends.

138. Potential effects on methicillin-resistant *Staphylococcus aureus* (MRSA) isolation rate assessed by time series analysis. *John A. Bosso, Pharm.D.*, Patrick D. Mauldin, Ph.D.; Medical University of South Carolina, Charleston, SC.

PURPOSE: The introduction or use of certain antibiotics has been linked to changes in MRSA isolation rates in hospitals.
METHODS: Using Isolate Rates (IR) of hospital-acquired MRSA over time as a marker, we assessed the affect of introduction of new antibiotics onto our formulary. Quarterly IRs of MRSA for 1993 through 2003 were considered. Segmented regression analysis for interrupted time series was used to determine significance for the difference in levels and slopes over time due to three interventions: 1) addition of levofloxacin (L) to the formulary in 1999, with 2) a subsequent switch from L to gatifloxacin in 2001, and 3) addition of cefepime (C) to formulary in 2000. The Durbin-Watson statistic was used to test for autocorrelation.
RESULTS: A significant positive change (p=0.0109) in the already upward slope trend of MRSA IR was observed related to introduction of L. However, during the later change from L to G, a strong negative change (p=0.0001) was observed (R^2=0.79). With C, there was no significant change in the overall slope trend (p=0.1141) from the pre-C period (R^2=0.72), although there was a change in slope from positive to negative.
CONCLUSIONS: While changes in MRSA IR are likely affected my many factors, the introduction and/or use of certain antibiotics may play an important role. These effects may be related to total quantity of an antibiotic class used, although they may also be specific-antibiotic-dependent. Assessment of quantity of use should provide further insight into the nature of these apparent relationships.

139. A multidisciplinary approach to decrease post-cardiac surgical infections through antibiotic timing. *John Noviasky, Pharm.D.*[1], Linda Kokoszki, R.N.[1], Lorraine Circelli, R.N.[1], Stacey Morosco, R.N.[1], James Bramley, M.D.[1], Kathy Ward, R.N.[1], Nicole Myers, Pharm.D., Candidate[2]; (1)St Elizabeth Medical Center, Utica, NY; (2)Albany College of Pharmacy, Albany, NY.

PURPOSE: Post-cardiac surgical infections increase patient's morbidity, length of stay, and resource utilization. This project attempted to decrease infection rate through multiple interventions (e.g. mupirocin application, intense blood-glucose control, and improving antibiotic time to incision (TTI)). Of these interventions, TTI is the first to be implemented.
METHODS: Infection rate, antibiotic TTI, and other variables of Cardiac Risk Index I patients having cardiac surgery were collected.
RESULTS: At baseline, our monthly TTI mean (± S.D.) for 48 patients was 76.9 (± 42.6) minutes and additional five patients either received no antibiotic or antibiotic was given after incision. The most common antibiotic delivered was cefazolin 1 gram (88.5%). After intervention, our TTI for 43 patients decreased to 43.5 (± 45.6) minutes (p<0.001) and only one patient received antibiotic after incision. The most common antibiotic given was cefazolin 2 gm (40.4%) and cefazolin 1 gram (25%). Our rates of post-cardiac surgical infection in 2002 and 2003 were 4.5% and 4.5%. This is above the National Nosocomial Infections Surveillance (NNIS) rate of 3.51%. While our year-to-date (2004) infection rate is above the NNIS rate at 4.13%, our infection rate for the past 4 months (post-TTI implementation) is much improved at 2.8%, 4%, 0% and 0%.
CONCLUSIONS: Increased awareness of the importance of antibiotic timing and the incorporation of anesthesiologists in antibiotic administration have led to significantly decreased TTI and use of weight-adjusted antibiotic dosing (cefazolin 2 gram for patients >70kg). An additional early trend of this intervention is a decrease in post-operative infection rate.

140E. Three-year national analysis of outpatient antimicrobial prescribing. *Katie J Suda, Pharm.D.*[1], Kevin W. Garey, Pharm.D.[2], Carl T. Bertram, Pharm.D.[3], Larry H. Danziger, Pharm.D.[4]; (1)Baptist Memorial Health Care, Memphis, TN; (2)University of Houston College of Pharmacy, houston, TX; (3)Walgreens Health Initiatives, Deerfield, IL; (4)UIC College of Pharmacy, Chicago, IL.

Presented at the Annual Meeting of the Infectious Diseases Society of American, Boston, MA, September 30–October 3, 2004.

141E. Relationship of inoculum and beta-lactam (BL) exposure on mutation selection in *P. aeruginosa*. *Krystal K. Haase, Pharm.D.*, Ronda L. Akins, Pharm.D., Carolyn L. Bouma, Ph.D., Andrea J. Morris, B.S.; Texas Tech University Health Sciences Center School of Pharmacy, Amarillo, TX.

Presented at the 43rd Interscience Conference on Antimicrobial Agents and Chemotherapy, Chicago, IL, September 14–17, 2003.

142E. Compliance with NCCLS antibiogram (AB) criteria: benchmarking of South Carolina (SC) hospitals (H). *Kiran K. Ubhi, Pharm.D.*, Roger L. White, Pharm.D.; Medical University of South Carolina, Charleston, SC.

Presented at the 42nd Annual Meeting of the Infectious Diseases Society of America, Boston, MA, September 30–October 3, 2004

143E. Declining susceptibility (S) to Gram-negative aerobes: analysis of data from 2000–2003 for 24 South Carolina (SC) hospitals. *Kiran K. Ubhi, Pharm.D.*, Roger L. White, Pharm.D.; Medical University of South Carolina, Charleston, SC.

Presented at the 42nd Annual Meeting of the Infectious Diseases Society of America, Boston, MA, September 30–October 3, 2004.

144. Comparing phenotypic expression of community and hospital associated methicillin-resistant *Staphylococcus aureus* (MRSA) on the basis of SCCmec type. *Kerry L. LaPlante, Pharm, D.*, Anna Ponomareva, Pharm D candidate, Michael J. Rybak, Pharm, D.; Wayne State University, Detroit, MI.

PURPOSE: MRSA resistance to beta-lactams is mediated through the mecA gene located on staphylococcal-chromosomal-cassette mec (SCCmec). Four different Sccmec types, subdivided into types I, II, III and IV have been described. SCCmecIV is found in CA-MRSA and tends to be susceptible to many non-beta lactam antibiotics. SCCmecII is found in HA-MRSA and tends to be multi-drug resistant. We evaluated the MIC50 for 11 different

antibiotics according to SCCmec type.
METHODS: CA-MRSA isolates (n=40) and HA (n=56), strains were defined by CDC definition, then molecular SCCmec type. MIC50's were completed in accordance to NCCLS for cefaclor, clindamycin, ciprofloxacin, daptomycin, doxycycline, erythromycin, imipenem, linezolid, oxacillin, trimethoprim/sulfamethoxazole and vancomycin.
RESULTS: For CA-MRSA and HA-MRSA we identified 12 and 18 mec II, and 25 and 30 mec IV respectively. When comparing CA and HA-MRSA irrespective of mec type, clindamycin's MIC50 of HA-MRSA was at least 256 fold greater than CA-MRSA and for oxacillin, the MIC50 of HA-MRSA was 2 fold greater than CA-MRSA. When comparing mec types, mecII demonstrated a >256, 128, 8, 32, and 4 fold difference in MIC50 against clindamycin, ciprofloxacin, doxycycline, imipenem and oxacillin respectively. SCCmec type II and IV isolates were susceptible to daptomycin, linezolid, trimethoprim/sulfamethoxazole and vancomycin.
CONCLUSIONS: SCCmecII is associated with significant resistance to multiple antibiotics, whereas SCCmecIV was susceptible to most antibiotics tested. Both SCCmec type II and IV were susceptible to daptomycin, linezolid, trimethoprim/sulfamethoxazole and vancomycin. We conclude that there is a significantly different resistance pattern seen between mecII and mecIV for both beta-lactam and non-beta-antibiotics.

145. Evaluation of empiric treatment and patient outcomes in patients with Candida blood isolates at John Cochran VA Medical Center. *Laura E. Hamblin, Pharm.D.*[1], Kristi Theobald, Pharm.D.[1], Rodney Lusk, M.D.[2]; (1)St. Louis College of Pharmacy, St. Louis, MO; (2)John Cochran VA Medical Center, St. Louis, MO.

PURPOSE: This study was conducted to 1) determine the epidemiology of *Candida* blood isolates at John Cochran VA Medical Center (JCVAMC) in St. Louis, Missouri, 2) delineate prescribing practices of empiric antifungal therapy, and 3) analyze patient outcomes regarding fungal isolate and empiric therapy.
METHODS: Records of inpatients with speciated *Candida* blood isolates obtained between January–December 2003 were reviewed, including patient demographics, risk factors, empiric therapy, directed therapy, mortality, and species of each isolate. Data was extracted from the VA Computerized Patient Record System and laboratory records. Empiric treatment was evaluated based on the 2004 IDSA Guidelines for Treatment of Candidiasis. Criteria in determining appropriateness of therapy included dosage, patient clinical stability, recent azole use, and organism identified.
RESULTS: Fifteen of the nineteen study patients received fluconazole empirically, while four patients received no therapy. Twelve patients (63%) grew non-*albicans Candida* species (*C. tropicalis*, *T. glabrata*, and *C. parapsilosis*). Mortality occurred in nine patients, including seven with non-*albicans* and two with *C. albicans* infections. Thirteen patients (68%) empirically received inappropriate therapy with six patient deaths. Based on the species identified, empiric therapy was inappropriate in fifteen patients with eight patient deaths.
CONCLUSIONS: Most study patients received inappropriate empiric treatment based on national guidelines, and the incidence of inappropriate treatment increased when applied to JCVAMC fungal epidemiology. With a majority of non-*albicans Candida* isolates, particularly species with reduced sensitivity or resistance to fluconazole, these results suggest that fluconazole (particularly at inadequate doses) may not be the optimal empiric therapy at JCVAMC.

146. Evaluation of levofloxacin 750 mg pharmacodynamic target attainment rates in organisms causing nosocomial pneumonia at an academic medical center with comparisons to surveillance data for *Pseudomonas aeruginosa*. *Brian A. Potoski, Pharm.D.*[1], David L. Paterson, M.D.[2], Ronald N. Jones, M.D.[3], George L. Drusano, M.D.[4]; (1)University of Pittsburgh School of Pharmacy, Pittsburgh, PA; (2)University of Pittsburgh Department of Medicine, Division of Infectious Diseases, Pittsburgh, PA; (3)The JONES Group/JMI Laboratories, North Liberty, IA; (4)Ordway Research Institute, Albany, NY.

PURPOSE: To simulate the pharmacodynamic target attainment (TA) rates correlated with pathogen eradication in hospitalized patients being treated for nosocomial pneumonia (NP) with levofloxacin 750mg once daily.
METHODS: A 10,000 subject Monte Carlo simulation was performed. Pharmacodynamic TA values and pharmacokinetic parameters of levofloxacin 750mg in patients treated for NP were previously identified. Antibiotic susceptibility and minimum inhibitory concentration (MIC) distribution data were collected over the last 4 years at this institution for Gram-negative organisms causing NP. SENTRY and MYSTIC surveillance data were also queried for susceptibility and MIC distribution data for *Pseudomonas aeruginosa* (PA).
RESULTS: Empiric TA rates in NP were PA (41.1%); *Klebsiella* spp. (84.1%); E. coli (85.5%); *Serratia* spp. (74.3%); *Enterobacter* spp. (74.3%); *Acinetobacter* spp. (65.3%) and *Stenotrophomonas* (56.7%). TA rates were >90% for all organisms after susceptibility was confirmed except PA (87.7%) and *Stenotrophomonas* (76%). Empiric TA rates using SENTRY and MYSTIC microbiology data for PA were higher than our institution, 64.1% ($p<0.0001$) and 60% ($p<0.0001$) respectively.
CONCLUSIONS: The low TA rate for PA is a direct reflection of the high resistance rate and high MIC values in a large percentage of the isolates at this institution. Comparable TA rates using surveillance data are higher, yet relatively low when considering levofloxacin for monotherapy in NP when PA is suspected. Good TA rates were attained once susceptibility was confirmed in most infecting organisms. Patients with NP where PA is strongly suspected should not be empirically treated with levofloxacin at this institution when other alternatives exist.

147. Bactericidal activity of telithromycin against penicillin-nonsusceptible, macrolide-resistant, and levofloxacin-resistant *Streptococcus pneumoniae* by time-kill methodology. *Michael B. Kays, Pharm.D.*, Christopher R. Lisek, Pharm.D.; Purdue University School of Pharmacy, Indianapolis, IN.

PURPOSE: To determine the bactericidal activity of telithromycin against penicillin-nonsusceptible, macrolide-resistant, and levofloxacin-resistant *S. pneumoniae*.
METHODS: Ten clinical, non-duplicate isolates of *S. pneumoniae* were tested. Triplicate MICs (NCCLS) and time-kill (TK) studies were performed using cation-adjusted Mueller-Hinton broth with 5% lysed horse blood and an inoculum of 10^6 CFU/ml. TK studies were performed at 35∞C in a shaking water bath. Telithromycin concentrations of 1, 2, 4, and 8xMIC were tested. Colony counts were determined at 0, 4, 8, 12, and 24 h, and recovery plates were incubated at 35°C in 5% CO_2 up to 48 h. Bactericidal activity was defined as a $\geq 3\text{-}\log_{10}$ reduction in CFU/ml.
RESULTS: All of the isolates were telithromycin-susceptible (MIC ≤ 0.5 µg/ml), penicillin-nonsusceptible (6 Pen-I, 4 Pen-R), macrolide-resistant (7 M-phenotype [*mefA*], 3 MLS_B-phenotype [*ermB*]), and levofloxacin-resistant (MIC ≥ 8 µg/ml). At 24 h, telithromycin was bactericidal for 0/10, 2/10, 6/10, and 6/10 isolates at 1xMIC, 2xMIC, 4xMIC, and 8xMIC, respectively. At 4-8xMIC, telithromycin was bactericidal for 6/7 M-phenotype isolates and 0/3 MLS_B-phenotype isolates. At 24 h, colony counts were decreased by 2.52 and 2.57 $\log_{10}$ CFU/ml at 4xMIC and 8xMIC, respectively, for the M-phenotype isolate that bactericidal activity was not achieved. For the MLS_B-phenotype isolates, colony counts were decreased by 1.32 to 2.09 $\log_{10}$ CFU/ml after 24 h at 8xMIC.
CONCLUSIONS: Telithromycin was bactericidal at clinically achievable concentrations for 6 of the 10 penicillin-nonsusceptible, macrolide-resistant, and levofloxacin-resistant *S. pneumoniae*. Telithromycin should be a useful treatment option for respiratory infections caused by resistant pneumococci.

148E. Antitoxin effects of clindamycin against α-hemolysin exotoxin released by methicillin-resistant *Staphylococcus aureus* (MRSA): could MIC make a difference? *Elizabeth A Coyle, Pharm., D.*, Russell E. Lewis, Pharm., D., Randall A. Prince, Pharm. D.; University of Houston College of Pharmacy, Houston, TX.

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149E. Genome-wide expression profile analysis reveals genes coordinately regulated with *CDR1* and *CDR2* in association with the acquisition of azole resistance in clinical isolates of *Candida albicans*. *P. David Rogers, Pharm.D., Ph.D.*[1], Katherine S. Barker, Ph.D.[1], Lai Wei[1], Ramin Homayouni, Ph.D.[1], Joachim Morschh‰user, Ph.D.[2]; (1)University of Tennessee, Memphis, TN; (2)Universit‰t W¸rzburg, W¸rzburg, Germany.

Presented at the 7th Conference on Candida and Candidiasis of the American Society for Microbiology, Austin, TX, March 18–22, 2004.

150E. Analysis of daptomycin (D) population susceptibility profiles and killing activity against two clinical strains of vancomycin-resistant *Staphylococcus aureus* in an in vitro simulated endocardial vegetation infection model (SEVM). *Ronda L. Akins, Pharm.D.*, Krystal K. Haase, Pharm.D., Carolyn L. Bouma, Ph.D., Andrea J. Morris, B.S,; Texas Tech University Health Sciences Center School of Pharmacy, Amarillo, TX.

Presented at the 104th General Meeting of the American Society for Microbiology, New Orleans, LA, May 23–27, 2004.

151E. MIC creep: early detection with geometric mean (GM) and E-test (ET) MICs. *Roger L. White, Pharm.D.*[1], Lawrence Friedrich, Pharm.D.[2], Kiran K. Ubhi, Pharm.D.[1], Gregory Steinkraus, Ph.D.[3]; (1)Medical University of South Carolina, Charleston, SC; (2)Bristol-Myers Squibb, Charleston, SC; (3)New Hanover Regional Medical Center, Wilmington, NC.

Presented at the 11th International Congress on Infectious Diseases, Cancun, Mexico, March 4–7, 2004.

152E. Antimicrobial activity of tigecycline (GAR-936) tested against enterobacteriaceae, and selected non-fermentative Gram-negative bacilli, a worldwide sample. *Ronald N. Jones, M.D.*, Thomas R. Fritsche, M.D., Ph.D., Helio S. Sader, M.D., Ph.D.; The JONES Group/JMI Laboratories, North Liberty, IA.

Presented at the European Congress of Clinical Microbiology and Infectious Disease, Prague, Czech Republic, May 1–4, 2004.

153. Evaluation of fluoroquinolone-induced hypoglycemia in a community hospital system. *Shannon M. Lee, Pharm.D., BCPP*[1], Katherine C. Herndon, Pharm.D., BCPS[2]; (1)Princeton Baptist Medical Center, Birmingham, AL; (2)Pfizer Inc., Birmingham, AL.

PURPOSE: This project was designed to evaluate and compare the occurrence of hypoglycemia in patients receiving gatifloxacin and levofloxacin following a change in the fluoroquinolone formulary in a seven-member community hospital system.
METHODS: A retrospective medical record review was conducted in patients receiving intravenous or oral levofloxacin (n = 96) before the formulary conversion and gatifloxacin (n = 104) after the formulary conversion. Patients were excluded from the review if blood glucose levels were not documented prior to and during three or more of the first five days of fluoroquinolone therapy. Demographics, medical history, concomitant drug therapies, and hypoglycemic episodes (blood glucose < 70 mg/dL or > 40% decrease from baseline) were documented.
RESULTS: Hypoglycemia was documented in 26% and 15.6% of gatifloxacin and levofloxacin patients, respectively (p=0.073). The mean time to the development of hypoglycemia was 2.3 days in gatifloxacin patients (mean glucose = 58.7 mg/dL) and 3.7 days in levofloxacin patients (mean glucose = 56.5 mg/dL). Hypoglycemia was documented in 45.5% and 22% of gatifloxacin and levofloxacin patients with diabetes, respectively (p=0.022). Oral hypoglycemic medication ± insulin was prescribed in 55.2% of patients with hypoglycemia and 26.7% of patients without hypoglycemia (p=0.010).
CONCLUSIONS: Hypoglycemia was documented with both gatifloxacin and levofloxacin, however it appears to be more common in patients with diabetes receiving gatifloxacin in this retrospective review. Prospective studies are needed to further differentiate and determine the clinical significance of the glycemic effects of the fluoroquinolones.

154. Determinants of costs for patients with complicated skin and soft-tissue infections due to suspected or proven methicillin-resistant *Staphylococcus aureus*. *Sonja V. Sorensen, M.P.H.*[1], Christopher S. Hollenbeak, Ph.D.[1], Larry Z. Liu, M.D., Ph.D.[2], Timothy M. Baker, B.S.[1], Peggy McKinnon, Pharm.D.[3]; (1)MEDTAP International Inc., Bethesda, M.D.; (2)Pfizer Inc., New York, NY; (3)Detroit Receiving Hospital, Detroit, MI.

PURPOSE: Using data from a recent clinical trial, this analysis was performed to identify determinants of treatment cost for complicated skin and soft-tissue infections (cSSTI).
METHODS: Costs per patient were estimated by applying representative per diem hospital costs (in 2003 US Dollars) for days spent in medical/surgical, ICU, or step-down units. Intravenous (IV) administration costs were applied to the duration of IV therapy; study medication was valued at wholesale acquisition cost. Cost of admission was estimated using multivariate regression controlling for patient factors, infection site, adverse events, and death.
RESULTS: A total of 717 patients (366 linezolid, 351 vancomycin) admitted to United States hospitals with suspected or proven methicillin-resistant *Staphylococcus aureus* (MRSA) cSSTI were included in the study. These patients had diagnoses of cellulitis (42%), major skin abscess (30%), and surgical/wound infections (14%). MRSA was confirmed in 32% of all patients. Patients receiving linezolid and vancomycin were similar in terms of age, gender, and race. Regression analyses showed that hospital cost was $787 lower for patients receiving linezolid vs. vancomycin (P = 0.0004). Other factors significantly associated with increased cost include age (P = 0.0113), confirmed MRSA infection (P = 0.0262), comorbid diabetes (P = 0.0118), number of procedures (P<0.0001), presence of serious adverse event (P<0.0001), and death (P = 0.0026).
CONCLUSIONS: Cost of hospital care for patients with cSSTI is associated with patient demographics, comorbidities, and antibiotic treatment. After adjusting for all other factors, treatment with linezolid resulted in significantly lower treatment costs vs. vancomycin.

155E. In vitro activity of the glycylcycline tigecycline (GAR-936) tested against a worldwide collection of 10,127 contemporary Staphylococci, Streptococci and Enterococci. *Thomas R. Fritsche, M.D., Ph.D.*, Helio S. Sader, M.D., Ph.D., Ronald N. Jones, M.D.; The JONES Group/JMI Laboratories, North Liberty, IA.

Presented at the European Congress of Clinical Microbiology and Infectious Disease, Prague, Czech Republic, May 1–4, 2004.

156. Community-associated MRSA displaying glycopeptide heteroresistance. *Vanthida Huang, Pharm.D.*, Gladys S. Dabaja, Pharm.D., Candidate, Michael J. Rybak, M.S., Pharm.D.; Anti-Infective Research Laboratory, Eugene Applebaum College of Pharmacy & Health Sciences, Wayne State University, Detroit, MI.

PURPOSE: We describe a case of a 24-year-old male from county prison with multiple lower extremity abscesses. The patient had been previously treated with multiple antimicrobials for the previous 3 months. The lesions improved with treatment but returned. Cultures grew *S. aureus* resistant to methicillin but, susceptible to clindamycin, gentamicin, rifampin, vancomycin (V), ciprofloxacin, and levofloxacin. This isolate was identified as part of a larger study evaluating molecular characteristics and risk factors for CA-MRSA per CDC definitions. Repeat V and teicoplanin (TP) MIC by microtiter revealed an MIC of 32 and 128, respectively.
METHODS: CA-MRSA (R2617), Mu3, and Mu50 were utilized. MICs were performed according to NCCLS. Molecular typing was performed. Subpopulation profiles were evaluated using BHI plates containing various concentrations (0.25–32µg/mL) of V and TP.
RESULTS: R2617 was identified as SCC*mec* type IV. MICs for non-pressurized R2617 for V and TP were 1–4 and 0.5–4µg/ml, respectively. When pressurized on 2–6µg/ml antibiotic plates, MICs were ≥32 and >64µg/ml, respectively. V and TP E-tests exhibited colonies of subpopulation growth that varied in sizes. Population analysis for R2617 revealed varying organism growth across 0.25–16µg/ml similar to that found with the control hGISA and GISA strains. Selective pressure shifted greater bacterial densities to higher concentrations compared to no pressure.
CONCLUSIONS: We demonstrated that R2617, CA-MRSA isolate, has hGISA characteristics similar to that of Mu3, a well described hGISA isolated from patient who failed V therapy. Discovery of hGISA in CA-MRSA is of significant importance since it further complicates potential therapy options for patients infected with these isolates.

157. Monte Carlo simulation of bactericidal activity versus urinary tract infection *E. coli* of ciprofloxacin 500 mg every 12 Hours, gatifloxacin 200 mg and 400 mg once daily and levofloxacin 500 mg, 750 mg and 1000 mg once daily administered to hospital. *Ayman M. Noreddin, M.Sc.., Ph.D.*[1], Nancy Laing, TD.[2], Tamiko Hisanaga, M.Sc..[3], Loraine Palatnick, TD.[2], Daryl J. Hoban, Ph.D.[2], George G. Zhanel, Pharm.D., Ph.D.[2]; (1)College of Pharmacy, Univeristy of Minnesota, Duluth, MN; (2)Univeristy of Manitoba, Winnipeg, MB, Canada; (3)University of Manitoba, Winnipeg, MB, Canada.

PURPOSE: Probability of Ciprofloxacin (Cipro) compared to Gatifloxacin (Gati) and Levofloxacin (Levo) achieving favorable pharmacodynamic (PD) targets for bacterial eradication and prevention of resistance development in *E. coli*. Cipro 500mg BID along with various doses of Gati and Levo were simulated and target attainment potential was estimated in hospitalized patients.
METHODS: Previously described and validated population pharmacokinetic (PK) models of Cipro, Gati and Levo in hospitalized patients were utilized to simulate Cipro, Gati and Levo PKs. Free-drug AUC_{0-24} were simulated in Plasma (P) using Cipro 500mg BID, Gati 200mg and 400mg OD as well as Levo 500mg, 750mg and 1000mg OD. Use of Monte Carlo Simulation allowed for the full variability of encountered drug clearance to be accounted. E.coli susceptibility data were obtained from the North American Urinary Tract Infection Surveillance Study (NAUTICA).
RESULTS: Probability of target attainment (free AUC_{0-24}/MIC of 125 and 250) of Cipro, Gati and Levo versus Canadian and US outpatient E.coli are shown in the following table:

CANADA	US PD Target	125	250	125	250
Cipro	500mg BID	98.5%	98.4%	93.1%	92.9%
Gati	200mg	98.7%	98.4%	95.3%	94.7%
	400mg	98.8%	98.7%	95.3%	95.1%
Levo	500mg	96.8%	95.9%	91.8%	90.8%
	750mg	97.5%	96.4%	93.1%	91.7%
	1000mg	98.3%	96.8%	94.0%	93.0%

CONCLUSIONS: In hospitalized patients, Cipro 500mg BID, Gati 400mg OD and Levo 750mg OD showed high probability for target attainment of free AUC_{0-24}/MIC of 125 or 250 against *E. coli*. Compared to CANADA, US isolates showed lower probability of achieving favorable outcome.

158. Antimicrobial activity of tigecycline against clinical isolates of Gram-negative bacteria from a single academic medical center. *Alicia M. Reese, Pharm.D., M.S.*, David S. Burgess, Pharm.D.; University of Texas at Austin, University of Texas Health Science Center at San Antonio, San Antonio, TX.

PURPOSE: Tigecycline (formerly GAR-936; Wyeth Pharmaceuticals, Radnor, PA) is a novel glycylcycline that is being evaluated for complicated skin and skin structure, intra-abdominal, and lower respiratory tract infections. Since these are indications for which gram-negative coverage is essential, this study examined the in vitro activity of tigecycline against several gram-negative organisms.
METHODS: A total of 97 clinical non-duplicate isolates (26 *E.coli*, 18 *K.pneumoniae*, 21 *E. cloacae*, and 32 ESBL-producing organisms) were obtained from the Clinical Microbiology Laboratory at University Hospital in San Antonio, Texas. MICs were determined in triplicate using broth microdilution according to NCCLS guidelines for tigecycline and thirteen comparator agents (minocycline, tetracycline, ceftriaxone, cefepime, piperacillin/tazobactam, imipenem, meropenem, ertapenem, gentamicin, tobramycin, ciprofloxacin, levofloxacin, and gatifloxacin). Established NCCLS susceptibility breakpoints were used, and a breakpoint of 2 µg/mL was used for tigecycline.
RESULTS: Tigecycline was most potent against *E. coli* and *K. pneumoniae*, followed by *E. cloacae*, and ESBL-producing organisms (MIC_{90}, 2 µg/mL, 2

µg/mL, 8 µg/mL, and 16 µg/mL, respectively). Tigecycline exhibited similar activity as cefepime, the carbapenems, aminoglycosides, and fluoroquinolones against *E. coli*, *K. pneumoniae*, and *E. cloacae*. Against ESBL-producing organisms, tigecycline was more active than all other antimicrobials tested, except the carbapenems.
CONCLUSIONS: Tigecycline exhibited in vitro activity against these enteric gram-negative isolates, including ESBL-producing isolates.

Managed Care

159. Angiotensin-II receptor blocker (ARB) use without previous angiotensin converting enzyme inhibitor (ACEI) trial in a large managed care population: opportunity for member and plan savings. *Brent W. Gunderson, Pharm.D.*[1], Patrick P Gleason, Pharm.D., BCPS[1], Alan H. Heaton, Pharm.D.[2]; (1)Prime Therapeutics, LLC, St Paul, MN; (2)Blue Cross Blue Shield of Minnesota, Eagan, MN.

PURPOSE: This retrospective analysis described current trends of ACEI trial before ARB and projected member/health plan savings.
METHODS: Using 18-months continuous enrollment (JUL2002–DEC2003), from a BCBS plan, member files were created with ≥ 1 ARB claim 1JUL2003–30SEP2003 and ≥ 1 ACEI claim 1JUL2002–30JUN2003. Members with a new ARB start 1JUL2003–30SEP2003 and no ARB claim during previous 12-months were identified.
RESULTS: 1,754 members newly started an ARB; 996 (56.8%) did not have a previous ACEI claim. During the 3-month analysis period, the 996 members had 1,665 ARB claims: median days supply 30, mean plan paid $33, and mean member copay $26. Median days supply, mean plan paid cost and mean member copay for lisinopril were 30, $7 and $10, respectively. Assuming 100% persistence, ARB members without an ACEI trial would result in an annual plan paid per member (PPPM) cost of $396 or $394,416 as a group, with an annual member copay of $312. If members instead had begun therapy with and persisted on lisinopril, annual PPPM would be $84 or $83,664 as a group, with an annual member copay of $120. Maximal potential plan paid annual savings is $310,752 and an annual member copay savings potential $192.
CONCLUSIONS: Members are frequently newly initiated on ARB therapy without an ACEI trial. Persistence is more likely when copays are lower; generic lisinopril copay is 330% less than ARBs. Savings potential exists for health plans and members if mechanisms are put in place to require an ACEI trial prior to initiating ARB therapy.

160. Off-label use of topiramate (Topamax): analysis of a large health plan's medical and pharmacy claims. *Patrick P Gleason, Pharm.D., BCPS*[1], Brent W. Gunderson, Pharm.D.[1], Alan Heaton, Pharm.D.[2], Steven V. Johnson, Pharm.D., BCPS[3]; (1)Prime Therapeutics, LLC, St Paul, MN; (2)Blue Cross Blue Shield of Minnesota, Eagan, MN; (3)Prime Therapeutics, LLC, Eagan, MN.

PURPOSE: Quantify and characterize the frequency of off-label topiramate use. Topiramate is currently FDA approved for epilepsy treatment. Topiramate therapy is associated with considerable serious adverse events such as markedly low serum bicarbonate (up to 3%–11% of patients exposed), nephrolithiasis, ataxia, oligohidrosis, and ocular syndromes.
METHODS: Medical and pharmacy claims from a midwestern health plan with 1.7 million members were analyzed in 2003 to identify members with a miscellaneous antiepileptic drug (MiscAED) (AHFS code 281292) claim. Identified members ICD-9 diagnosis codes for all outpatient medical encounters were evaluated. Epilepsy diagnosis defined as ICD-9 code 345.XX or 780.3X and all other medical diagnoses were described using validated Schneeweiss diagnostic clustering.
RESULTS: Of 1.7 million members, 34,563 (2.0%) had 205,736 MiscAED claims. 4,309 (12.5%) of 34,563 members had 20,931 topiramate claims at a total plan paid cost of $3,498,006 ($167.10 per claim). 113 members had an invalid ICD-9 code, of the remaining 4,196 topiramate utilizing members, 583 (13.9%) had an epilepsy diagnosis. Of the 3,613 (86.1%) without an epilepsy diagnosis, the top three Schneeweiss diagnostic clusters were: headaches - 2031 members (56.2%), depression, anxiety, and neuroses - 1954 members (54.1%), and fibrositis, myalgia, and arthralgia - 1696 members (46.9%).
CONCLUSIONS: Integrating medical and pharmacy claims identified the vast majority of topiramate utilization appears to be for an off-label indication. This inappropriate use may expose patients to unnecessary risks and costs for unproven benefits. Plans should considering implementing programs to ensure safe appropriate use of topiramate.

161. Letters of medical necessity: value and potential in the managed care environment. Donna L. Zarycranski, M.S., Mlada Kamenshchik, B.S., *Kiumars Q. Vadiei, Ph.D., RPh, FCP*; Cephalon, Inc., West Chester, PA.

PURPOSE: Physicians frequently seek out specialized tools and services to address operational and financial challenges to patient care. One such service is the Letter of Medical Necessity (LMN), a template document designed to facilitate reimbursement for requested treatments. The LMN document includes relevant supporting medical information, and can be tailored to each patient's medical history. Because the quality and utility of these types of services have not been thoroughly explored, we conducted a survey of physicians to ascertain the value Cephalon's LMN service.
METHODS: The survey was mailed and made available via a dedicated Web site to 4014 physicians who made unsolicited request for LMNs over a 1-year period. No incentive was offered for completing the survey. A satisfactory outcome was defined as reimbursement by the health plan for the requested treatment.
RESULTS: A total of 273 (6.7%) respondents completed the survey. Respondents most often (54.5%) requested LMNs to appeal denied reimbursement. Respondents rated the timeliness of response and overall quality of the service very highly. The majority (73%) experienced a satisfactory outcome ≥51% of the time. Furthermore, the primary reason for a negative outcome was use of the requested treatment for an unapproved indication.
CONCLUSIONS: Respondents indicated a very high level of satisfaction with the LMN service. Although the immediate value of the LMN service lies in its ability to expedite reimbursement for a requested treatment, this type of service may indirectly improve patient care. Further research is required to quantify the effects of LMNs on patient care.

162. Specialty pharmacy utilization and cost in a large managed care population: analysis of medical and pharmacy benefit claims. *Patrick P Gleason, Pharm.D., BCPS*[1], Alan H. Heaton, Pharm.D.[2]; (1)Prime Therapeutics, LLC, St Paul, MN; (2)Blue Cross Blue Shield of Minnesota, Eagan, MN.

PURPOSE: Describe specialty pharmacy utilization and plan paid costs through an evaluation of both medical and pharmacy claims.
METHODS: Specialty pharmaceuticals were defined as therapies that require complex care and special handling or administration. Claims from a 1.7 million member midwestern health plan were analyzed during 2003 identifying all medical benefit processed J-code claims and pharmacy benefit processed claims for 121 retail specialty pharmacy products.
RESULTS: Of 1.7 million members, 141,177 (8.3%) had 568,083 medical processed J-code claims at a plan paid amount of $64,119,166. The top three J-code expense categories were: injectable oncology chemotherapeutics (J9000-J9999) $28,574,885 for 68,823 claims; infliximab a tumor necrosis factor blocker (TNF-blocker) (J1745) $8,604,266 for 4885 claims; and miscellaneous unclassified drugs (J3490) $3,603,449.89 for 13,782 claims. 11,187 (0.7%) members had 51,444 retail specialty pharmacy claims at a plan paid amount of $59,705,702. The top three retail specialty pharmacy expense categories were: multiple sclerosis $16,027,079 for 14,564 claims; TNF-blockers (etanercept or adalimumab) $11,435,348 for 9407 claims; and antihemophilic factors $7,152,534 for 960 claims.
CONCLUSIONS: For this plan, expenses, approximately evenly divided between the medical and pharmacy benefits, totalled $123,824,868 or approximately $6.07 per member per month. With plans being challenged by specialty pharmacy, comprehensively assessing medical and pharmacy benefit claims is important, as only one specialty drug class was in the top three of both the medical and pharmacy benefits. These integrated medical and pharmacy claims evaluations are a necessary precursor to the development of management strategies.

Medication Safety

163. Implementation of a self-administered questionnaire to identify patients at risk for medication-related problems in a family medicine clinic. *Bradley J. Langford, BScPhm*, Derek Jorgenson, Pharm.D., Debora Kwan, BScPhm, M.Sc., Christine Papoushek, Pharm.D.; Toronto Western Hospital, University Health Network, Toronto, ON, Canada.

PURPOSE: Methods to quickly and systematically identify patients at-risk of MRPs are currently lacking in the ambulatory setting. The usual method for pharmacist referral at the Family Health Centre is largely based on health care professional referral. We hypothesized that this method may under-refer patients at high risk for MRPs. This study assessed if a medication-risk questionnaire can more appropriately identify patients at-risk for MRPs compared to usual methods of referral.
METHODS: Ambulatory patients ≥ 18 years old, taking ≥ 2 medications were eligible to complete the questionnaire. A pre-validated modified five-item self-administered questionnaire statistically correlated with MRP-risk was used. All patients completed the questionnaire and were subsequently randomized for pharmacist-referral by one of two methods; 1) referral by usual methods or 2) referral according to questionnaire score. Primary outcomes were rate of referral and to compare the questionnaire risk scores of the patients in both groups. MRPs of patients in each group were characterized.
RESULTS: A total of 194 patients completed the questionnaire; 105 randomized to the questionnaire referral group and 89 to the usual referral group. More patients were referred to a pharmacist using the questionnaire (n=21; 20.0%) compared to usual methods (n=5; 5.6%), (P=0.003). The number of MRPs detected was similar in both groups. The most common MRPs documented by pharmacists for both groups were subtherapeutic dose,

drug interaction and adverse drug reaction.
CONCLUSIONS: A self-administered medication-risk questionnaire is an effective complement to usual referral practices for the identification of patients at risk for MRPs.

164. Preliminary evaluation of the impact of clinician order entry on medication errors in an inpatient oncology unit in a community teaching hospital. *Dianne M Brundage, Pharm.D.*, Kelly Becicka, Pharm.D., Judy Wilson, R.N.; Methodist Hospital/Park Nicollet Health Services, Minneapolis, MN.

PURPOSE: Clinician order entry (COE) should decrease medical errors. Methodist Hospital has 51 beds for patients with cancer, an on-line system of self-reporting adverse events, and electronic medication administration records. This preliminary study examines medication errors that could be prevented by COE during a 6-month baseline period, and medication errors attributable to COE for 6 weeks after implementation (started 4/19/04). Standardized paper order sets were used for TPN and chemotherapy.
METHODS: Adverse medication events (AMEs) were extracted from Quality Resources database for a 6-month period prior to COE, and for 6 weeks after COE was implemented. Medication events that could be prevented by or attributed to COE were separated from all other AMEs. Two pharmacists independently reviewed events to determine if the event could be prevented by COE (during baseline period), or attributed to COE (COE phase). Patient days were obtained from nursing administration.
RESULTS: During the baseline period of 7517 patient days, 59 medication events were considered preventable by COE (8 per 1000 patient days). Four COE-related medication events occurred in the first 6 weeks (2 per 1000 patient days) of COE. Drug categories associated with COE-related events include: electrolytes 1, insulin 1, opioids 1, and all meds (wrong account). Changes were developed to prevent the opioid event from occurring.
CONCLUSIONS: COE decreases medication errors that occur in an inpatient oncology unit. Since COE was new, and the evaluation covered the first 6 weeks, some errors could be attributed to part of the learning process.

165. Evaluating sample medication use in primary care: a sub-study of applied strategies for improving patient safety. *Donald S Nuzum, Pharm.D.*, Laura B Hansen, Pharm.D., Joseph J Saseen, Pharm.D., Sherry Holcomb, ASc, Wilson D Pace, M.D.; University of Colorado Health Sciences Center, Denver, CO.

PURPOSE: This study assessed the frequency, motivation and safety of sample medication use in primary care practices. Sample medication processes were evaluated and compared to Institute for Safe Medication Practices (ISMP) standards.
METHODS: Eighteen urban and rural Colorado primary care practices participated in a one-day prospective, observational evaluation. A card study assessed provider motivation and sample dispensing. A simultaneous card study assessed patient knowledge of their sample(s). Sample inventories and distribution policies/procedures were documented for each practice.
RESULTS: During 18 days of evaluation, 57 samples were dispensed during 54 of 585 (9.2%) patient encounters. Sixty-five percent were new medications. Motivations for dispensing included availability (57.1%), cost (20%), and patient request (20%). Providers also stated their plan to continue the medication was through written prescriptions (54.9%) and more samples (28.6%). Seventy-two percent of patient card studies were returned and indicated verbal instruction alone was the primary means of patient education for dose and frequency of use (68%), precautions (68%) and side effects (60%). Twelve percent of patients received no education related to side effects. Of 1,233 samples inventoried, antihypertensives were most prevalent (17.7%) followed by cold/allergy (9.0%), dyslipidemia (6.9%), bacterial infections (6.8%), asthma (6.7%), diabetes (5.4%), and depression (5.3%). Labels were either absent or incomplete in all 18 practices.
CONCLUSIONS: These data suggest that sample medications are dispensed during approximately 9% of primary care visits with availability being the strongest impetus for use. Patient education and labeling were not compliant with ISMP standards and potentially increase risk for medication errors.

166. Effectiveness and impact of an admitting pharmacist on patient care. *Estela M Trimino, Pharm.D.*, Janelle M Berg, Pharm.D., Fernando J Zaldivar, R.Ph.; Mercy Hospital, Miami, FL.

PURPOSE: To evaluate the effectiveness and impact of an admitting pharmacist in a community hospital setting. This position was added with the following goals: impact patient care by preventing or reducing potential medication adverse events, control cost through formulary management, review medication histories and initial admitting orders, provide patient education and counseling, improve diagnostic test utilization, provide recommendations to enhance initial therapies, and serve as a drug information specialist to all members of the clinical staff.
METHODS: The admitting pharmacist position was proposed, approved, and implemented in August 2002. All interventions and outcomes are recorded on a PDA using Pendragonô software. Data analysis occurs quarterly and is submitted to the Pharmacy and Therapeutics Committee.
RESULTS: Medication histories have been reviewed for 2,492 patients, and a total of 2,965 interventions documented from August 2002 to December 2003. Interventions were categorized as: medication omissions, discontinuations, additions, renal dose adjustment, wrong drug or dose, wrong frequency, diagnostic tests, non-formulary drugs, automatic therapeutic substitutions, drug information, herbal consultation, smoking cessation, warfarin teaching, adverse drug reaction reporting, and improved documentation of JCAHO Core Measures required by Medicare.
CONCLUSIONS: The addition of the admitting pharmacist has provided us with a measurable benefit, as well as substantial improvement in patient care. Ongoing consults in the medical records for the "pharmacist" to evaluate medication regimens attest to its value, as well as returning patients requesting to see "their pharmacist." In addition, time to receive the first dose of medication is expedited and patient satisfaction greatly improved.

167E. Voluntary reporting of medication errors in critical access hospitals compared to MEDMARX℠. Katherine J. Jones, M.S., PT[1], *Gary L. Cochran, SM, Pharm.D.*[1], Rodney W. Hicks, R.N., MSN, MPA[2], Keith J. Mueller, Ph.D.[1]; (1)University of Nebraska Medical Center, Omaha, NE; (2)USP Center for the Advancement of Patient Safety, Rockville, M.D.

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Nephrology

168E. Influence of ultrafiltrate production rate on sieving coefficient (SC) in continuous venovenous hemofiltration (CVVH). *Deborah A. Pasko, Pharm.D.*, Mariann D. Churchwell, Pharm.D., Bruce A. Mueller, Pharm.D.; University of Michigan College of Pharmacy, Ann Arbor, MI.

Presented at the 9th International Conference on Continuous Renal Replacement Therapies, San Diego, CA, February 26–28, 2004.

169. *N*-Acetylcysteine and its protective role in a murine model of gentamicin nephrotoxicity. *George Mathew, M.D.*, David Sundin, Ph.D., Edward Nehus, B.S.; From the Division of Infectious Disease ,Department of Medicine, Indiana University School of Medicine, indianapolis, IN.

PURPOSE: Gentamicin is an aminoglycoside antibiotic that is used predominantly to treat gram negative infections .In 10–50% of cases nephrotoxicity can develop. It is unlikely that there is one single mechanism but rather a net result of disruptions in several cellular pathways.In rats gentamicin affects renal mitochondria and increases the production of reactive oxygen metabolites such as hydrogen peroxide, superoxide and hydroxyl radical. The aim of this study is to find out if *N*-actetylcysteine (NAC) a free oxygen radical scavenger can decrease gentamicin(Gent)induced nephrotoxicity in a rat model
METHODS: Male Sprague Dawley rats were randomised to 6 groups and were treated for 12 days. Group 1 (n= 2) received Gent vehicle control at 100mg/kg/d, group 2(n=4) received NAC 100mg /kg/d, group 3 received Gent at 100mg/kg/d(n= 8) , group 4 (n= 9) received NAC at 100 m g/kg/d and Gent 100mg /kg/d , group 5 (n= 7)received Gent at 150mg/kg/d and Group 6 (n=7)received NAC at 100mg /kg/d and Gent at 150 mg/kg/d.
RESULTS: At peak nephrotoxicity day 8–10 the mean peak serum creatinine for gp (1) was 0.1 mg/dl, gp (2) 0.3 mg/dl, gp (3) 0.8 , gp (4) 0.4, gp(5) 1.22 mg /dl and gp(6) 0.7 mg/dl.
CONCLUSIONS: This showed that there was a tendency for decreased nephrotoxicity in rats that were treated with gentamicin and NAC than rats that got gentamicin alone and that this protective benefit increased as the gentamicin dose increased. These results show that NAC ameliorates gentamicin nephrotoxicity in a murine model.

170. Comparison of hemoglobin response in hospitalized hemodialysis patients receiving either epoetin alfa or darbepoetin alfa in an integrated health care system. *Indu Lew, Pharm.D.*, Robert Adamson, Pharm.D.; Saint Barnabas Health Care System, West Orange, NJ.

PURPOSE: To measure the hemoglobin response of epoetin alfa (EA) and darbepoetin alfa (DA) in hospitalized hemodialysis patients.
METHODS: Patients for review were identified through an electronic billing system, using the ICD-9 code for hemodialysis and charge codes for EA and DA. The measurement period was from September 2003 to April 2004. Patient charts, 47 EA and 56 DA were requested and abstracted for: demographic information, co-morbidities, admission and discharge hemoglobin, length of stay (LOS), dose, frequency, total number of doses administered of the erythropoietic growth factor and transfusions.
RESULTS: Demographic information was well matched in each group: average age was 66.7, 70.6 years, females 47.8%, 39.3%, diabetes 40.4%, 41%, HTN 46.8%, 42.8%, CAD 29.8%, 39.3% for EA and DA respectively. The average LOS for EA was 17.4 days versus 13.6 days for DA. EA administration frequency was 57.4% three times a week, 31.9% twice a week and 10.7% weekly. All patients in DA cohort received therapy weekly. The average weekly dose of EA was 14,914 units versus 42.9 µg for DA. The total number of doses administered was 154 for EA and 71 for DA. The decline between admission and discharge hemoglobin was (0.78) and (0.89) gm/dL for EA and

DA respectively. Patients requiring transfusion were similar for each group, 34% and 37.5% for EA and DA respectively.
CONCLUSIONS: Overall, minimal difference in hemoglobin response was observed between EA and DA patients. It appears that EA and DA can be used interchangeably in this patient population.

171. Anemia management in patients with chronic kidney disease. *James M Hoffman, Pharm.D., M.S.*[1], Lee C Vermeulen, M.S.[2], Curtis A Johnson, Pharm.D.[3], Kimberly E Holdener, Pharm.D.[1], Bryan N Becker, M.D.[4]; (1)Department of Pharmacy, University of Wisconsin Hospital and Clinics, Madison, WI; (2)Department of Pharmacy, University of Wisconsin Hospital and Clinics; School of Pharmacy, University of Wisconsin - Madison, Madison, WI; (3)Schools of Pharmacy and Medicine, University of Wisconsin - Madison, Madison, WI; (4)School of Medicine, University of Wisconsin - Madison, Madison, WI.

PURPOSE: This study described patterns of anemia management in patients with stage 3 and 4 chronic kidney disease (CKD) and compared these patterns of care to the NKF K/DOQI guidelines and other literature.
METHODS: Using administrative and clinical data, we identified patients from an academic medical center with an outpatient visit for kidney disease or associated conditions from January 1, 2002 to July 31, 2003. Estimated glomerular filtration rate (eGFR) was calculated using the abbreviated Modification of Diet in Renal Disease (MDRD) formula and subjects were stratified by stage of CKD. We evaluated process of care measures including nephrologist referral and anemia assessment. We also determined the prevalence of anemia, and patterns of epoetin/darbepoetin use.
RESULTS: 879 patients met the inclusion criteria, and 482 of these patients were in stage 3 or 4. Only 57.8% of stage 4 patients had a documented nephrologist evaluation during the year after their index creatinine value. Using measurement of hemoglobin as a proxy for anemia assessment, 98.1% of stage 3 and 4 patients were evaluated for anemia. Anemia, defined as hemoglobin less than 11g/dL, was present in 42.2% of stage 3 patients and 78.0% of stage 4 patients (56.0% overall). At some time during the study, 67.5% of anemic stage 3 and 4 patients were treated with epoetin or darbepoetin.
CONCLUSIONS: Efforts to improve the care of CKD patients should focus on nephrologist referral and the use of erythropoietic agents in CKD patients with anemia.

172E. Influence of race on cyclosporine pharmacokinetics in stable renal transplant recipients. *Kiran Dole, Pharm.D.., B.S.*[1], Kathryn Gillis, Pharm.D.[1], Nicolae Leca, M.D.[2], Samir Yassa, M.D.[2], Rocco Venuto, M.D.[2], Kathleen Tornatore, Pharm.D.[1]; (1)University at Buffalo, Pharmacy Practice, School of Pharmacy, Buffalo, NY; (2)University at Buffalo, Department of Medicine, Buffalo, NY.

Presently being considered for publication in American Society of Nephrology (ASN).

173E. Comparison of diffusive and convective transmembrane clearance with AN69 and polysulfone hemodiafilters in CVVH and CVVHD. *Mariann D. Churchwell, Pharm.D.*, Deborah A. Pasko, Pharm.D., Bruce A. Mueller, Pharm.D.; University of Michigan College of Pharmacy, Ann Arbor, MI.

Presented at the 9th International Conference on Continuous Renal Replacement Therapies, San Diego, CA February 26–28, 2004.

174. CVVH transmembrane clearance of daptomycin with two different hemofilters. *Mariann D. Churchwell, Pharm.D.*, Deborah A. Pasko, Pharm.D., Bruce A. Mueller, Pharm.D.; University of Michigan College of Pharmacy, Ann Arbor, MI.

PURPOSE: Daptomycin will be used to treat Gram positive infections in critically ill patients receiving continuous venovenous hemofiltration (CVVH), but daptomycin's transmembrane clearance (Cl) by CVVH has not been previously studied.
METHODS: Daptomycin CVVH Cl was assessed using an in vitro CVVH model with 2 common hemodiafilters, polysulfone (Optiflux 160NR) and AN69 (Multiflow 100) at four different ultrafiltration (UF) rates of 1, 2, 3, & 6 L/hr. Blood flow rate was adjusted to maintain UF rates. Each experiment was run 5 times with a new hemodiafilter. Daptomycin & urea concentrations were assayed from blood sampled at the pre-filter port (A) and UF samples from the UF sampling port of the Diapact™ CVVH circuit. Daptomycin concentrations were determined by HPLC. Daptomycin & urea calculations were: sieving coefficient (SC) = UF/A and Cl = SC x UF rate.
RESULTS: The mean (±SD) Daptomycin Cl (mL/min) at each respective UF rate with the M100 was 2.52 ±0.15 (1L/hr), 5.3±0.50 (2L/hr), 7.0±0.88 (3L/hr), 13.8±1.3 (6L/hr). Daptomycin Cl at each respective UF rate with the F-160 was 2.72±0.26 (1L/hr), 6.3±0.74 (2L/hr), 9.8±0.88 (3L/hr), 19.4±2.1 (6L/hr). Daptomycin SC & Cl demonstrated a significant difference between filters for UF rates of 2L/h, 3L/h & 6L/h. Daptomycin & urea SC were consistent for each filter type regardless of UF rate. Urea Cl approximated UF rate.
CONCLUSIONS: Daptomycin Cl was significantly greater with the F160NR than the M100 but never exceeded 20% of UF rate. CVVH is unlikely to result in appreciable daptomycin Cl at any UF rate.

175E. The safety and efficacy of an accelerated iron sucrose dosing regimen in patients with chronic kidney disease. *Michael H. Schwenk, Pharm, D*[1], Daniel A. Blaustein, M.D.[2], Jyoti Chattopadhyay, Ph.D.[2], Rachid Daoui, M.D.[2], Harinder Singh, M.D.[2], Radjeep Gadh, M.D.[2], Morrell M. Avram, M.D.[2]; (1)The New York Hospital Medical Center of Queens, Flushing, NY; (2)The Long Island College Hospital, Brookyln, NY.

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176. Stability of cefepime in icodextrin peritoneal dialysis solution. *Rowland J. Elwell, Pharm.D.*[1], Lucio Volino, Pharm.D.[1], Reginald F. Frye, Pharm.D., Ph.D.[2]; (1)Albany College of Pharmacy, Albany, NY; (2)College of Pharmacy and Center for Pharmacogenomics, University of Florida, Gainesville, FL.

PURPOSE: To determine the chemical stability of cefepime in icodextrin peritoneal dialysis (PD) solution over a 7-day period.
METHODS: Samples were prepared by adding 1000 mg cefepime HCl to commercially available 2.0 liter bags of icodextrin 7.5% PD solution. Nine bags were prepared and stored at the following conditions: 3 under refrigeration (4°C), 3 at room temperature (20°C), and 3 at body temperature (37°C). Study samples were withdrawn from each bag immediately after preparation and at predetermined intervals over the subsequent 7 days. Solutions were visually inspected for precipitation, cloudiness and discoloration at each sampling interval. Total concentration of cefepime in dialysate fluid was determined by liquid chromatography-tandem mass spectrometry.
RESULTS: The mixtures were clear in appearance and no color change or precipitation was observed during the study. Under refrigeration, a mean of 95.7 ± 4.2% of the initial cefepime concentration remained at 168 hours (7 days). At room temperature, 92.0 ± 17.9% remained at 48 hours. At body temperature, 92.2 ± 4.7% remained at 4 hours. Beyond these respective time points, less than 90% of the initial cefepime concentrations remained.
CONCLUSIONS: Pre-mixed cefepime-icodextrin PD solutions stored at room temperature were stable for up to 48 hours. However, it is recommended that these be kept refrigerated whenever possible. When refrigerated, cefepime-icodextrin solutions were found to be stable for up to 7 days. Solutions stored at body temperature were stable up to 4 hours permitting the practice of pre-warming solutions prior to administration.

177E. Lanthanum carbonate, the new non-aluminum, non-calcium phosphate binder, is not genotoxic. Stephen J.P. Damment, Ph.D.[1], C. Beevers, Ph.D.[2], D.G. Gatehouse, Ph.D.[2], *Larry Segars, Pharm.D., BCPS*[3]; (1)Shire Pharmaceutical Development, Ltd., Basingstoke, United Kingdom; (2)Covance Laboratories Ltd, Harrogate, United Kingdom; (3)Shire, Medical Science Liaison/Medical Information Services, Newport, KY.

Presented at the Clinical Meeting of the National Kidney Foundation, Chicago, IL, April 28–May 2, 2004.

178. Assessment of the accuracy of renal dosing recommendations made by pharmacists. *Toby Trujillo, Pharm.D., BCPS*, Christine A. Gongleski, Pharm.D., Andrew M. Levitsky, Pharm.D.; Boston Medical Center, Boston, MA.

PURPOSE: Adjustment of doses of renally eliminated medications is a core function of a pharmacist. We conducted an analysis of renal dosing recommendations made by our pharmacy staff to assess their accuracy.
METHODS: A retrospective analysis of pharmacy renal dosing recommendations over a 1-month period of time was conducted. Recommendations were identified from the pharmacy intervention database. Information collected for each intervention included patient demographics and labs, prescribed medication and dose, calculated creatinine clearance (CLcr) and dose recommended by the pharmacist, and physician acceptance of the intervention. Each intervention was reviewed for whether CLcr was calculated appropriately and if the recommended dose was correct.
RESULTS: A total of 159 interventions were assessed from November 2003. The rate of physician acceptance was 99.4%. Antibiotics (n=101) and H2 receptor antagonists (n=45) were the most common medication classes. Creatinine clearance was calculated incorrectly 44% of the time resulting in an incorrect dose recommendation in 15% of patients. The most common errors seen with calculation of CLcr was failure to use ideal body weight (38%) or multiply by 0.85 for females (38%).
CONCLUSIONS: Pharmacists at our institution routinely do not calculate CLcr correctly, which can result in inappropriate dosing recommendations. In addition, pharmacists may not be routinely adjusting doses of renally eliminated medications that are not antibiotics or H2 antagonists. Based on these findings we are developing an education program and resource materials on the appropriate use of the Cockcroft and Gault equation and dosing of renally eliminated medications.

178A. Comparison of GFR estimates by MDRD and Cockcroft-Gault with 24-hour urine collection. *S. Casey Laizure, Pharm.D.*[1], Gary E. Arwood, B.S.[2]; (1)University of Tennessee Dept of Pharmacy, Memphis, TN; (2)Arlington Developmental Center, Arlington, TN.

PURPOSE: The MDRD and a simplified version of the MDRD (MDRD-S) have been proposed as better methods for the estimation of glomerular filtration rate (GFR) than the Cockcroft-Gault (C-G) equation. This report compares the estimation of GFR using the MDRD, MDRD-S, and C-G equations with GFR estimated from a 24-hour urine collection.
METHODS: Nine citizens at a long-term care facility for the mentally disabled had 24-hour urine collections as part of their clinical care. Urine output over a 24-hour period was collected after catheterization, and GFR estimated from the amount of creatinine excreted. The GFR was also estimated from the Scr using the MDRD, MDRD-S, and C-G equations. The body surface area (BSA) was calculated as $0.0235 \times \text{Height}^{0.42246} \times \text{Wt}^{0.51456}$. GFR computations by the MDRD equations were adjusted for citizen's BSA before statistical comparison using the Wilcoxon signed rank test.
RESULTS: The mean ±standard deviation of the GFR estimates from the 24-hour urine collection, MDRD Eqn, MDRD-S Eqn, and C-G Eqn were 75±31, 96±31, 105±37, and 71±21 ml/minute, respectively. The mean±standard deviation of the percent difference for MDRD, MDRD-S, and C-G from the 24-hour urine estimate were 36±58, 52±80, and 1±35%, respectively. The GFR estimate using C-G did not differ from the 24-hour urine collection ($p = 0.359$), while the MDRD and MDRD-S estimations of GFR were high compared to the 24-hour urine collection ($p = 0.02$ and 0.012, respectively).
CONCLUSIONS: Using the Cockcroft-Gault equation provided a better estimate of GFR than MDRD or MDRD-S in this population.

179E. Intravenous (IV) iron trends in U.S. dialysis patients (1994-2001). *Wendy L. St. Peter, Pharm.D.*[1], Gregorio T. Obrador, M.D.[2], Tricia L. Roberts, M.S.[3], Brian J. G. Pereira, M.D.[4], Allan J. Collins, M.D.[1]; (1)University of Minnesota and Chronic Disease Research Group, Minneapolis, MN; (2)University of Panamericana, Insurgentes Mixcoac, Mexico; (3)Chronic Disease Research Group, Minneapolis, MN; (4)Tufts-New England Medical Center, Boston, MA.

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180E. The effects of lanthanum carbonate and calcium carbonate on bone in patients with chronic kidney disease. Anthony J. Freemont, M.D.[1], J. Denton, M.D.[1], *Chris Paap, Pharm.D.*[2]; (1)The Medical School, University of Manchester, Manchester, United Kingdom; (2)Shire, National Medical Science Liaison Manager/Medical Information, Newport, KY.

Presented at the Clinical Meeting of the National Kidney Foundation, Chicago, IL, April 28–May 2, 2004.

181E. Optimal sampling for international normalized ratios in hemodialysis patients with central venous catheters. *Alex V. Boyd, B.S.*[1], Amy B. Pai, Pharm.D.[1], Anne Tinklenberg, R.N., BSN[2], Kelly Townsend, B.S.[3], Charles T. Spalding, M.D., Ph.D.[1]; (1)University of New Mexico, Albuquerque, NM; (2)Dialysis Clinic Inc, Albuquerque, NM; (3)TriCore Laboratories, Albuquerque, NM.

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Neurology

182E. Fluoxetine-induced orobuccolingual dyskinesia and persistent mandibular dystonia treated with botulinim toxin type-A. *Jack J. Chen, Pharm.D.*[1], David M. Swope, M.D.[2]; (1)Western University of Health Sciences and Movement Disorders Clinic, Loma Linda University, Pomona, CA; (2)Loma Linda University, Loma Linda, CA.

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183. Rasagiline, a selective, second-generation, irreversible inhibitor of monoamine oxidase type-B, is effective in patients older and younger than 65 years of age with early-to-advanced Parkinson's disease (PD). *Jack J. Chen, Pharm.D.*[1], Richard C. Berchou, Pharm.D.[2]; (1)Western University of Health Sciences and Movement Disorders Clinic, Loma Linda University, Pomona, CA; (2)Wayne State University, Detroit, MI.

PURPOSE: Rasagiline is an investigational drug demonstrating efficacy in patients with early-to-advanced PD. Age-related differences in clinical effects are unknown and warrants investigation.
METHODS: Data from three multicentered, randomized, placebo-controlled trials were pooled and reanalyzed for differences in efficacy between patients ≥ 65 or < 65 years of age. Only patients receiving rasagiline 1mg daily were included. One trial assessed early PD patients for baseline change in Total Unified Parkinsons Disease Rating Scale (UPDRS), which measures mental/motor function and ADL (Activities of Daily Living). Two trials studied advanced PD patients for improvments in daily OFF time (poor function/mobility), UPDRS ADL while OFF, global impression, and UPDRS motor while ON (good function/mobility).
RESULTS: Data from a total of 1040 PD patients were analyzed: 272 (118 older and 154 younger) with early PD (mean duration 0.94±1.2 yrs) and 768 (378 older and 390 younger) with advanced PD (mean duration 8.95±5.0 yrs). Rasagiline monotherapy improved total UPDRS, ADL, and motor subscales, as compared to placebo (all ≤ 0.005), with no significant age effect on rasagiline response ($p = 0.68$). As adjunctive therapy to carbidopa/levodopa, rasagiline reduced daily OFF time, improved UPDRS ADL OFF, motor ON,and global impression (all $p < 0.0001$ vs placebo) with no significant age effect on efficacy ($p = 0.08$) or safety. Rasagiline was well tolerated across age groups.
CONCLUSIONS: In early-to-advanced PD, once-daily rasagiline 1mg, as initial monotherapy or adjunctive therapy, is efficacious and well tolerated across age groups. This study was supported by Teva Neuroscience Inc., in partnership with Eisai Inc., and H. Lundbeck A/S.

184E. Study design and baseline characteristics of patients in the AFFIRM study, an efficacy and safety study of natalizumab in patients with multiple sclerosis. *J. Theodore Phillips, M.D., Ph.D.*[1], Chris H. Polman, M.D.[2], Eva Havrdova, M.D.[3], Michael Hutchinson, M.D.[4], Ludwig Kappos, M.D.[5], David Miller, M.D.[6], Paul O'Connor, M.D.[7], Allison J. Willmer-Hulme, Ph.D.[8], Michael A. Panzara, M.D., M.P.H.[9], Alfred Sandrock, M.D., Ph.D.[9]; (1)Multiple Sclerosis Center at Texas Neurology, Baylor University Medical Center, Dallas, TX; (2)Free University Hospital, Amsterdam, Netherlands; (3)General Teaching Hospital, Prague, Czech Republic; (4)St. Vincent's Hospital, Dublin, Ireland; (5)University Hospital, Kantonsspital, Basel, Switzerland; (6)Institute of Neurology, London, United Kingdom; (7)St. Michael's Hospital, Toronto, ON; (8)Elan Pharmaceuticals, Inc., San Diego, CA; (9)Biogen Idec, Inc., Cambridge, MA.

Presented at Mult Scler 2003;9(suppl 1):S142).

185. Antiepileptic drug saliva concentration stability in the postal system. *Mikael D. Jones, Pharm.D.*[1], Melody Ryan, Pharm.D.[1], Michael V. Miles, Pharm.D.[2], Peter Tang, Ph.D.[2], Toufic A. Fakhoury, M.D.[3], Robert J. Baumann, M.D.[3]; (1)University of Kentucky College of Pharmacy, Lexington, KY; (2)Cincinnati Children's Hospital Medical Center, Cincinnati, OH; (3)University of Kentucky College of Medicine, Lexington, KY.

PURPOSE: Saliva antiepileptic drug (AED) concentrations strongly correlate with serum concentrations and offer an alternative to venipuncture. Remote patients could mail saliva samples to a laboratory for monitoring. The purpose of this study is to assess the stability of saliva AED concentrations sent through the United States Postal Service (USPS) and the reliability of patients and the USPS to return samples in a timely manner.
METHODS: Saliva samples were obtained from patients currently taking one of the targeted AEDs. Samples were split into 2 storage vials. One sample was sealed in an addressed envelope which the patient mailed from home while the other sample was frozen immediately. Saliva concentrations were determined using HPLC. Wilcoxon rank sum tests were used to compare the immediately-frozen and mailed sample means. Correlations were determined by the Spearman test.
RESULTS: Forty-six patients were enrolled in the study. The median time between collection and postmark was 1 day (range 0-8 days); and between collection and receipt was 4 days (range 1-160 days). The mean concentrations for mailed and immediately frozen samples were similar for each AED ($p > 0.15$):

AED	Mailed Concentration (µg/mL± SD)	Immediately Frozen (µg/mL± SD)	r_s
Lamotrigine (n=10)	4±2.8	4.1±2.9	1
Levetiracetam (n=7)	21.1±17.3	21.1±17.3	1
Oxcarbazepine (n=7)	24.4±8.4	24.3±8.9	0.964
Topiramate (n=5)	4.9±2	4.7±1.9	0.90
Zonisamide (n=6)	14.3±11.8	13.8±10.9	1

CONCLUSIONS: Saliva samples mailed by patients maintain stability and can be returned in a reasonable length of time. Further studies are needed to assess patient/caretaker capability of obtaining an adequate sample.

186. Rasagiline, a novel, potent, second-generation, selective, irreversible inhibitor of monoamine oxidase-B (MAO-B), improves freezing of gait (FOG) in advanced Parkinson's disease (PD) patients receiving levodopa/carbidopa (LD/CD). Richard C. Berchou, Pharm.D.[1], *Jack J. Chen, Pharm.D.*[2]; (1)Wayne State University, Detroit, MI; (2)Western University of Health Sciences and Movement Disorders Clinic, Loma Linda University, Pomona, CA.

PURPOSE: FOG is a disabling PD symptom that is generally unresponsive to dopaminergic therapy. MAO-B inhibition has shown promise and we investigated the effect of rasagiline on FOG in advanced PD patients.
METHODS: A 10-week, double-blinded, trial of PD patients with motor fluctuations despite optimized LD/CD. Patients (n=412) randomized to adjunctive rasagiline (1mg QD, n=135), entacapone (200mg with each LD/CD dose, n=136), or placebo (n=141). Primary efficacy measured as decrease from baseline in FOG-Questionnaire (FOG-Q, range 0 to 24). Additionally, correlations explored between change from baseline FOG-Q score and baseline FOG severity; Beck Depression Inventory (BDI); changes from baseline in total daily OFF duration (poor function/mobility); and in Total Unified Parkinsons Disease Rating Scale (UPDRS, mental/motor function measure).

RESULTS: Mean overall baseline FOG-Q score was 12. Rasagiline+LD/CD produced a significant mean 1.2 point decrease from baseline in FOG-Q versus placebo+LD/CD (0.5 decrease, p=0.045). Entacapone+LD/CD showed a 1.1 point reduction from baseline (p=0.066) versus placebo+LD/CD. FOG-Q reductions with rasagiline+LD/CD correlated significantly with BDI but non-significantly with baseline FOG severity, improvements in total daily OFF time, or total UPDRS. FOG-Q reductions with entacapone+LD/CD correlated significantly with baseline FOG severity and improvements in total daily OFF time and total UPDRS.
CONCLUSIONS: Significant improvement in FOG with once-daily rasagiline 1mg in advanced PD was independent of symptomatic effects, suggesting additional non-dopaminergic actions. Conversely, the effect of entacapone on FOG appears to be dependent on symptomatic effects. This study was supported by Teva Neuroscience Inc., in partnership with Eisai Inc., and H. Lundbeck A/S.

187. Characterization of acute and delayed headache in migraineurs following sublingual nitroglycerin challenge. *Tyler M. Smith-Strutz, Pharm.D.-Candidate*[1], Edward M. Bednarczyk, Pharm.D.[1], Linda Hershy, M.D., Ph.D.[2], Ellana Eberhardt, CCRC, R.N.[2]; (1)State University of New York at Buffalo, Buffalo, NY; (2)Veteran's Affairs Medical Center of Buffalo, Buffalo, NY.

PURPOSE: Nitroglycerin is well recognized as a headache inducer. Literature has asserted that migraineurs experience ëspontaneous' migraines within twenty-four hours of nitroglycerin challenge. The purpose of this study was to characterize acute and delayed headache in migraineurs following sublingual nitroglycerin challenge.
METHODS: Migraineurs, with and without aura (IHS criteria), recruited from the general population received 0.3 mg of sublingual nitroglycerin. They reported headache occurrence and similarity to their usual migraines on a 0–10 scale immediately following dosing, with 10 being exactly like usual migraine. Volunteers were asked about the presence of laterality, pulsatility, nausea, photophobia, and phonophobia in their induced headache. Volunteers were contacted approximately twenty-four hours later and queried regarding headache reoccurrence and similarity to usual migraine.
RESULTS: Seventeen migraineurs were enrolled. All experienced acute headache following sublingual nitroglycerin. The median similarity rating of headaches was 4.5 and 4 for patients with aura (N=4) and without aura (N=13), respectively. Seventy and six-tenths percent (70.6%), 64.7%, 52.9%, 35.3%, and 52.9% of migraineurs experienced the same symptoms of laterality, pulsatility, nausea, photophobia, and phonophobia, during headache after nitroglycerin challenge, respectively. Twenty-four hours following nitroglycerin, 35.3% experienced headache with a median similarity score of 6.5. Volunteers with aura and without aura reported 24 hour headache recurrence rates of 50% and 30.8% with similarity ratings of 8 and 6.5, respectively.
CONCLUSIONS: Sublingual nitroglycerin reliably provokes acute headache in migraineurs; however, it does not necessarily induce migraine within twenty-four hours. Even when headache forms, either acute or delayed, these headaches are dissimilar to migraines.

188E. National survey of high-dose steroid prescribing practices following spinal cord injury (SCI). *Denise H. Rhoney, Pharm.D.*, Marissa Didonato, Pharm.D., Lisa L. Larive, Pharm.D.; Wayne State University, Detroit, MI.

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189. Double blind crossover study of topiramate for the treatment of tinnitus. *Edward M. Bednarczyk, Pharm., D.*, Ellana Eberhardt, B.S., Mary Lou Coad, B.S., Richard Salvi, Ph.D., Robert F Burkard, Ph.D., Alan H Lockwood, M.D.; University at Buffalo, Buffalo, NY.

PURPOSE: It has been estimated that 5% of the US population suffers from tinnitus severe enough to seek medical attention. In spite of this, no effective pharmacotherapy has been identified, and few drugs have been carefully studied. The purpose of this study was to evaluate topiramate for the treatment of subjective idiopathic tinnitus.
METHODS: A randomized double blind, placebo controlled, crossover trial of topiramate was conducted. Patients age 18–75 with history of subjective tinnitus > 1 year were recruited via a local tinnitus support group and newspaper advertisements. Patients were excluded based on the presence of significant neurologic or psychiatric disease, previous use of topiramate, concomitant pharmacotherapy of tinnitus or ototoxic drugs, or use of investigational drugs within 30 days. A 10 point visual analog scale (VAS) was used to assess tinnitus. Topiramate was administered at 25mg day, with dose escalation to 200mg/day over an 8 week period. A 1 week placebo run-in preceded each arm of the study
RESULTS: Ten subjects were enrolled in the study; 4 continued the study through completion of both arms. Median tinnitus VAS scores were 5, 5.3 and 7 for baseline, post topiramate and placebo respectively. Reasons for withdrawal included family emergency (1, topiramate), increasing tinnitus (1, placebo, topiramate), confusion (1, topiramate) and paresthesias (1, placebo) a final subject was withdrawn by the investigators for misrepresenting their age.
CONCLUSIONS: While the high drop out rate precludes a definitive conclusion, topiramate does not appear to offer significant symptomatic benefit to patients with subjective tinnitus.

Nutrition

190. The Lifestyle Challenge Program: a collaborative therapy management approach for obesity. *Margaret Malone, Ph.D., FCCP*[1], Sharon Alger-Mayer, M.D.[2], Drew Anderson, Ph.D.[3]; (1)Albany College of Pharmacy, Albany, NY; (2)Albany Medical College, Albany, NY; (3)Dept of Psychology-SUNY, Albany, NY.

PURPOSE: To establish an outcome based cost effective multidisciplinary obesity program.
METHODS: Adult patients >18yr were recruited from an out patient university based setting to participate in a 20 week structured weight management program incorporating behavioral techniques and diet/exercise and disease management. Faculty involved include a physician (responsible for overall patient care), pharmacist (responsible for medication management and data collection/analysis), and behavioral psychologist (small group facilitator/educator). Specialist consultant such as a dietitian and exercise physiologist participate as needed. Clinical outcomes such as weight change, metabolic fitness, health related QOL, depression scores and binge eating severity are documented.
RESULTS: All data are expressed as mean (SD). 90 patients (74 Female), mean age 48 +/-10 yrs started the program. At the start of the program weight was 228 +/-46 lbs (BMI 37 +/- 6 kg/m^2). At 10 weeks 83/90 (92%) remained in the program, % wt loss was 3 (3). At 20 weeks the % wt loss of completers (n=59) was 4.8 (5.0). Beck Depression Inventory (BDI) scores improved from 13 (19) at baseline to 5 (6) at completion. Binge eating scores were reduced from 18 (10) to 11 (7). SF-36 Physical (PCS) and Mental (MCS) component summary scores improved from 44 (11) and 46 (11) at baseline to 50 (7) and 52 (9) respectively.
CONCLUSIONS: This program is a successful model of collaborative therapy management, each faculty team member contributes within their area of expertise to achieve positive patient outcomes.

191. Adverse events associated with parenteral nutrition systems. *Gordon S. Sacks, Pharm.D., B.S.*, Steve Rough, M.S., RPh, Kenneth A. Kudsk, M.D.; The University of Wisconsin - Madison, Madison, WI.

PURPOSE: Parenteral nutrition (PN) has the potential for serious adverse events involving various health-care system breakdowns, yet many institutions have no standardized method for capturing these adverse events. This study describes the use of a computerized database to record the frequency and type of adverse events related to PN in a large, teaching university hospital.
METHODS: Data was prospectively collected for any patient receiving PN between November 2002 to May 2004. Data was entered into the UHC Patient Safety Net™ System, a real-time, Web-based reporting tool that is used for adverse event reporting. Data collection included errors related to wrong formulation preparation, operational system errors, order entry problems with automated technology, and incorrect administration practices. Each event was assigned a harm score (A-I)to assess severity of the adverse event.
RESULTS: The overall error rate was calculated at 15.9 errors per 1000 PN prescriptions filled. The majority of errors (33%) were associated with incorrect administration practices, followed by 23% order entry errors, 12% operational system errors, 9% preparation errors, and 23% miscellaneous errors. The event distribution included 11 (15%) near-miss events (harm scores A, B1, B2), 58 (77%) no-harm events (harm scores C,D), and 6 (8%) harmful events (harm scores E-I).
CONCLUSIONS: Serious adverse events related to PN occurred at a relatively high rate in a large, teaching university institution. Many of the adverse events were related to errors in the ordering process and administration of PN. A standardized ordering process should be created to reduce PN administration and preparation errors.

192. Incidence of medication associated with weight gain by participants in a weight loss program. *Margaret Malone, Ph.D., FCCP*[1], Sharon Alger-Mayer, M.D.[2], Drew Anderson, Ph.D.[3]; (1)Albany College of Pharmacy, Albany, NY; (2)Albany Medical College, Albany, NY; (3)Dept of Psychology-SUNY, Albany, NY.

PURPOSE: to determine the frequency of use of medication associated with weight gain (WGD) by participants in a weight loss program
METHODS: Adult patients >18yr were recruited from an out patient university based setting to participate in a 20 week structured weight management program. All data are reported as mean + SD.
RESULTS: Ninety patients (74 female) were recruited. Age 48 + 10 years, BMI 37 + 6 kg/m2. Patients had multiple diseases including: type 2 diabetes mellitus (n=23); hypertension (n=48); depression (n=18) and dyslipidemia (n=9). The total # of drugs per patient was 4.9+3.3 (range 0–15). The # of WGD was 0.8+1.0 per patient (range 0–3). Forty-three (48%) patients were taking at least one WGD. WGD included beta blockers (n=18), SSRI's (n=18), sulfonylureas (n=7), insulin (n=9), and TZD's (n=6). Seven patients

completed 6 weeks or less were excluded from further analysis. Eight-three patients completed 10 weeks (40 on WGD), 38/83 (46%) had lost <2% of their initial weight, 23/38 (61%) were on WGD. Fifty-nine patients completed 20 weeks (27 on WGD at start), 21/59 (36%) had lost <2% of whom 10/21 (48%) were on WGD. Overall weight loss of completers was 4.8+5.0% (range -5.9 to17.1%) at 20 weeks.
CONCLUSIONS: A large number of patients were taking WGD. Attention should be given to prescribing of WGD to obese patients as this may negatively influence their weight management but does not appear to affect outcome within the program.

193. A comparison between ICU and LTCF nurses in delivering medications through enteral feeding catheters. *Charles F. Seifert, Pharm.D., FCCP, BCPS*, Barbara A. Johnston, R.N., Ph.D.; Schools of Pharmacy & Nursing, Texas Tech University Health Sciences Center, Lubbock, TX.

PURPOSE: To compare ICU & LTCF nursing practices with regard to the delivery of medications through enteral feeding catheters (EFCs).
METHODS: Two large national surveys (ICU = 1278, LTCF = 1177) of nurses were compared regarding predetermined delivery techniques for administering medications through EFCs.
RESULTS: Significantly more patients received medications through EFCs in the ICU setting (35.3%) than the LTCF setting (8.6%) (p<0.0001). There were more medications administered per day in the LTCF setting (8.8 vs 6.3, p<0.0001) but more doses administered per day in the ICU setting (9.3 vs 7.3, p<0.0001). Significantly more LTCF nurses were aware of guidelines in their facility (70.6% vs 36.4%, p<0.0001) and had attended an in-service (50.0% vs 19.2%, p<0.0001) than the ICU nurses. ICU nurses estimated a higher overall medication obstruction rate (15.4%) than LTCF nurses (5.2%) (p<0.0001). Out of eight pre-determined techniques, a significantly higher percentage of ICU nurses (45.1%) utilized three or more inappropriate techniques than LTCF nurses (11.6%) (p<0.0001).
CONCLUSIONS: Significant differences exist between ICU & LTCF nurses regarding administration techniques for delivering medications through EFCs. ICU nurses utilized a significantly greater number of inappropriate techniques than LTCF nurses. ICU nurses had a sifnificantly higher medication obstruction rate than LTCF nurses.

Oncology

194. Effect of modified front-load dosing of darbepoetin alfa for chemotherapy-associated anemia. *Adrian L. Goram, Pharm., D.*; Sacred Heart Health System, Pensacola, FL.

PURPOSE: This study evaluated 1) the hematopoietic response of darbepoetin alfa, 2) determined the effect of modified front-load, weight-based dosing every 3 weeks and 3) assessed the patient's quality of life (QOL).
METHODS: This open-labeled, non-randomized pilot study recruited women receiving chemotherapy for gynecologic tumors who met study criteria. Study was approved by SHHS IRB and started 6/2003. Patient accrual ended 3/2004. Initial dose was 6.75 µg/kg SC followed by 4.5 µg/kg SC every 3 weeks, up to 15 weeks. Actual body weight was used to calculate doses then rounded to nearest vial size. Functional Assessment in Cancer Therapy-Anemia (FACT-An) was self-administered before and after study completion. Hematopoietic and iron parameters (response predictors) were used per protocol.
RESULTS: The mean age and mean weight for 14 patients recruited (12 assessable) were 52.1 years and 64.6 kg, respectively. Average initial and follow-up doses were 442 µg; CI 368.7, 551.4 and 301.6 µg; CI 296.2, 307, respectively. Overall hematopoietic response was 71.5% (complete 28.6%, partial 42.9%). Peak response occurred at weeks 9 and 12. Mean Hb change was 1.3 g/dL; CI 0.60, 2.00. Response failure to treatment was predicted by week 9 (n=2). Follow-up doses were withheld if Hb > 12 g/dL (n=3). Mean point differential for pre and post FACT-An scores was 5.8; CI 1.9, 9.7 (n = 6).
CONCLUSIONS: A hematopoietic response was achieved using this dosing approach. Extended 3-week dosing with compliance to response predictors and CMS guidelines were safe, convenient and cost-effective. Improvement in QOL was documented.

195. Inpatient dosing and cost analysis of erythropoietic stimulating therapies (EST) for treatment of chemotherapy-related anemia from community hospitals nationwide. *Aaron Killian, Pharm.D., BCPS*, Vikas Gupta, Pharm.D., BCPS, Alisa Goetz, Pharm.D.; Cardinal Health, Data & Clinical Information, Houston, TX.

PURPOSE: Treatment guidelines for chemotherapy-related anemia recommend an initial epoetin alfa (EPO) regimen of 40,000 units weekly (QW) or 10,000 units thrice weekly (TIW) (NCCN 2004). Given the financial burden that hospitals confront, assessing EST dosing patterns is useful in managing EST costs.
METHODS: A retrospective analysis of a multi-institutional database (Diagnosis RX™, CHDCI) was performed evaluating EPO regimens among inpatient oncology diagnostic related group (DRG) discharges during 2003. For discharges receiving EPO ≥40,000 units QW, an EST cost analysis was conducted to estimate drug costs of switching to an EPO TIW or darbepoetin alfa (DARB) QW regimen using 2003 wholesale acquisition costs.
RESULTS: The eligible dataset included 677 unique discharges, 34 oncology DRGs, and 30 hospitals. Overall, there were 1,410 EPO doses with a median dose of 20,000 units (IQR: 10,000–40,000) and median length of stay of 8.0 days (IQR: 4.4–15.0). The cost analysis was performed on 450 EPO QW doses of ≥40,000 units (311 discharges). Switching to EPO TIW could have resulted in savings of 9,642,667 units (31,005 units/discharge) or $107,323 ($345/discharge). Compared to EPO QW, switching to DARB QW (260:1 EPO:DARB conversion ratio) resulted in an increased cost of $82,932 ($267/discharge). Sensitivity analyses varying the EPO:DARB conversion ratio from 260:1 to 400:1 resulted in higher costs for DARB QW compared to EPO TIW ($272–612/discharge).
CONCLUSIONS: Assuming comparable efficacy, this analysis suggests EPO TIW results in lower EST costs compared to EPO QW or DARB QW in the supportive care of oncology inpatients.

196. The effect of iron supplementation on hematologic response in hematology/oncology patients receiving epoetin. *Amber P. Lawson, Pharm.D.*, John A. Armitstead, M.S., FASHP, Kelly M. Smith, Pharm.D., Heather Cashman, Pharm.D., Val R. Adams, Pharm.D., BCOP; University of Kentucky, Lexington, KY.

PURPOSE: To determine if hematology/oncology patients prescribed epoetin receiving iron supplementation or have proven adequate iron stores have higher hematologic response rates than patients with unknown iron status not receiving iron.
METHODS: A billing database was utilized to identify hematology/oncology patients receiving three consecutive weekly doses of epoetin 40,000 units in a hematology/oncology clinic. A retrospective chart review was conducted to categorize patients as having proven adequate iron availability for erythrocytosis or unknown iron stores. The primary endpoint was the rate of hematologic response (an increase in hemoglobin of ≥1g/dL over 4 weeks in absence of blood transfusions) for each group. Secondary endpoints included mean change in hemoglobin and the median number of units of packed red blood cells transfused monthly in both groups at 4 weeks and at 8 weeks.
RESULTS: Fifty-one patients were included in data analysis. Fifteen had adequate iron availability with a hematologic response rate of 60% compared to 36 patients not receiving iron supplementation (response rate of 31%). Increases in hemoglobin concentration were statistically significant by 8 weeks of therapy. Patients who received blood transfusions in the adequate iron availability group did so at a median rate of 2 units/patient/month at 4 weeks and 1 unit/patient/month at 8 weeks. Patients who received blood transfusions in the unknown iron status group were transfused at a median rate of 2 units/patient/month at 4 weeks which decreased to zero units/patient/month by 8 weeks.
CONCLUSIONS: Iron supplementation contributes to increased rate of hematologic response in hematology/oncology patients receiving epoetin.

197E. Iron and B12 parameters in anemic cancer patients on chemotherapy presenting for epoetin-α (EPO) therapy. David H. Henry, M.D.[1], *Naomi V. Dahl, Pharm.D.*[2], Ferrlecit Cancer Study Group, various[2]; (1)Pennsylvania Hospital, Philadelphia, PA; (2)Watson Laboratories, Morristown, NJ.

Presented at the Annual Meeting of the American Society of Clinical Oncology, New Orleans, LA, June 5–8, 2004.

198. A single-center, observational study comparing neutropenic event rates for patients receiving pegfilgrastim on the same day or the day after chemotherapy administration. *David M Baribeault, B.S., BCOP*, Rita Blanchard, M.D.; Boston Medical Center, Boston, MA.

PURPOSE: Pegfilgrastim can be administered once-per-chemotherapy-cycle to provide the same protection against neutropenia as daily injections of Filgrastim. Pegfilgrastim administration on the same day as chemotherapy would further reduce the need for clinic visits; however, limited data are available on the safety and efficacy of same-day administration.
METHODS: Data were prospectively collected for 53 adult cancer patients who received chemotherapy and subsequent pegfilgrastim between April 2003 and July 2003. According to physician preference, a single dose of pegfilgrastim (6 mg subcutaneously) was given either on the same day as chemotherapy (n = 31) or on the day after chemotherapy (n=22). A neutropenic event (NE) was defined as: grade 4 neutropenia (ANC <0.5 ◊ 109/L), febrile neutropenia (FN), or a neutropenia-related delay in treatment.
RESULTS: Same-day and next-day treatment groups were well matched with respect to age and gender. Various solid and hematologic malignancies represented in each group were treated with standard chemotherapy regimens based on the tumor type. There were no significant differences in NE in the 2 groups (3 in the same-day group and 6 in the next-day group, [p=0.2851]). In the same-day vs next-day treatment groups, grade 4 neutropenia was observed in 1 vs 4 patients, FN in 0 vs 1 patient, and neutropenia-related delay in 2 vs 1 patients.
CONCLUSIONS: Results of this observational study suggest that administration of pegfilgrastim on the same day as chemotherapy may be as safe and effective as the administration of pegfilgrastim subsequent to chemotherapy administration. Further studies are warranted.

200. Implementation of a therapeutic substitution program for erythropoietic agents. *Holly Chan, Pharm.D.*, Sally Htoy, Pharm.D., Scott Drugan, Pharm.D.; City of Hope, Duarte, CA.

PURPOSE: City of Hope implemented a pharmacist-managed therapeutic substitution program to automatically substitute darbepoetin alfa for epoetin alfa. All adult patients were converted to darbepoetin alfa. A retrospective drug use evaluation (DUE) was conducted.
METHODS: Consecutively treated patients with a diagnosis of cancer and chemotherapy-induced anemia (CIA) who received at least three doses of darbepoetin alfa between January 1, 2003 to June 30, 2003 were eligible. Patient demographics, darbepoetin alfa dose, hematopoietic response, and transfusion data were collected retrospectively for 12 weeks following the first dose of darbepoetin alfa. Both intent-to-treat (ITT) and available data approaches were used for data analysis. For ITT, missing hemoglobin values were imputed with the last-value-carried-forward method. For the available data method, no imputation was used. Hemoglobin values within 28 days of a transfusion were excluded.
RESULTS: One hundred patients were eligible for the study. Twenty-eight percent of patients received platinum-containing chemotherapy. The starting darbepoetin dose was 200 µg every 2 weeks. Patients received an average of 4.6 doses during the 12 week study period. The average dose administered was 203 µg. The percentage of patients who received a transfusion during the first, second and third month was 40, 18 and 11, respectively. Completed results including average increase from baseline in hemoglobin at 4, 8, and 12 weeks will be presented.
CONCLUSIONS: The implementation of a pharmacist-run therapeutic substitution program for erythropoietic agents successfully converted all patients from epoetin alfa to darbepoetin alfa.

201. Evaluation of the variability in chemotherapy pharmacokinetic (PK) parameters obtained in oncology phase I clinical trials. *Judith A. Smith, Pharm.D., BCOP*[1], Marisa Navo, Pharm.D.[1], Hop Ngo, Pharm.D.[2], Fredrick Hausheer, M.D.[3]; (1)The University of Texas, M.D. Anderson Cancer Center, Houston, TX; (2)Univerisity of Houston College of Pharmacy, Hosuton, TX; (3)BioNumerik Pharmaceuticals, INC, San Antonio, TX.

PURPOSE: Establish the range of variability on PK parameters of 20 chemotherapy agents commonly used in the treatment of solid tumors. And determine what study parameters influenced degree of variability such as sample size, treatment regimen, patient selection criteria, number of PK samples, or tool for data analysis (PK modeling).
METHODS: Medline was used to search the primary medical research published from 1966 to present. Selected Chemotherapy agents included: Paclitaxel, docetaxel, cisplatin, carboplatin, oxaliplatin, doxorubicin, liposomal doxorubicin, topotecan, irinotecan, 9-aminocamptothecin, 9-nitrocamptothecin, gemcitabine, etoposide, melphalan, cyclophosphamide, ifosfamide, 5-fluorouracil, capcetabine, vinca alkaloids. Search terms: pharmacokinetics, phase I, cancer, each by agent name, antineoplastic, half-life, clearance, or volume of distribution. Search Limits included: clinical trial, human, English language.
RESULTS: A total of 2140 citations were returned from the 20 med-line searches. After eliminate duplicate citations, wrong drug or wrong citation, a total of 798 articles were selected and reviewed. A total of 768 were included in the data analysis, of these 575 reported PK parameters. The inter-study variability on half-life, clearance, volume of distribution, and area under the curve (AUC) ranged from 50.2%–180.5%, 5.9%–219.5%, 45.3%–168.1%, and 52.6%–348.9%, respectively.
CONCLUSIONS: Phase I studies have traditionally been conducted to determine appropriate doses for phase II studies. Our evaluation of the oncology phase I pharmacokinetic studies provided data to support that considerable variability exists in the estimated PK parameters. To optimize drug development and patient safety, attention should focus on the design of phase I studies including adequate PK sampling schemes and data analysis tools.

202. Costs and outcomes of hospitalized patients with cancer. *John C Kuth, Pharm.D.*[1], Amy H. Manguso, Pharm.D.[1], Susannah E. Motl, Pharm.D.[2], Katie J. Suda, Pharm.D.[1]; (1)Baptist Memorial Healthcare - Memphis, Memphis, TN; (2)University of Tennessee Drug Information Center, Memphis, TN.

PURPOSE: Cancer patients receive costly medications and treatment interventions. Recent changes to outpatient chemotherapy reimbursement will make inpatient chemotherapy more common. The purpose of this study is to compare hospital costs and outcomes of patients with a principal diagnosis of cancer to all other diagnoses.
METHODS: Outcomes of cancer inpatients in a large tertiary care hospital were compared to other primary diagnoses from 10/1/02–9/30/03. Cost data was extracted from hospital financial data. Diagnoses were obtained from an aggregated DRG coding system (Medicode-DRG Expert). Student's *t*-test and Chi Squared were used for statistical analysis; $p<0.05$ was considered significant.
RESULTS: 1286 cancer patients were identified (6.4% of admissions). When compared to patients in all other diagnoses, cancer patients did not have significantly higher total hospital costs ($10,331 vs. $9,772), but had higher case mix indices (CMI) (1.85 vs. 1.66), medication costs ($1,232 vs. $901), and length of stay (LOS) (7.84 vs. 6.42 days) ($p<0.0002$ for all). Cancer patients were discharged home less frequently (71.4%) than cardiac (87.1%), gastrointestinal (86.4%), or pulmonary patients (79%) and required continuing health services after discharge more frequently (15.3%) than cardiac (10%) or gastrointestinal (9.8%) patients. Compared to other diagnoses, cancer patients utilized hospice services (3.2% vs. 0.5%; $p<0.05$) or expired more frequently (9.6% vs. 3.8%; $p<0.05$). Laboratory, radiology, physical therapy, and surgery costs were not statistically significant.
CONCLUSIONS: Compared to other principal diagnoses, cancer patients had higher CMI, LOS, medication costs, and poorer outcomes. Future inpatient cost analysis is warranted given the economic changes currently underway.

203E. Darbepoetin-α (DA) 200 µg every 2 weeks (Q2W) vs epoetin-α (Epo) 40,000 U weekly (QW) in anemic patients receiving chemotherapy (ctx). *Lee Schwartzberg, M.D.*[1], Lorrin Yee, M.D.[2], Frank Senecal, M.D.[2], Veena Charu, M.D.[3], Dianne K. Tomita, M.P.H.[4], Gregory Rossi, Ph.D.[4]; (1)The West Clinic, Memphis, TN; (2)Northwest Medical Specialties, Tacoma, WA; (3)Pacific Cancer Medical Center, Inc., Anaheim, CA; (4)Amgen Inc., Thousand Oaks, CA.

Presented at the Annual Meeting of the American Society of Clinical Oncology, New Orleans, LA, June 5–8, 2004.

204E. A meta-analysis of filgrastim dosing duration for chemotherapy-induced neutropenia in nonmyeloid malignancies. *Michael D Green, M.D.*[1], Roy Baynes, M.D., Ph.D.[2]; (1)Royal Melbourne Hospital, Department of Haematology and Medical Oncology, Parkville, VIC, Australia; (2)Amgen Inc, Thousand Oaks, CA.

Presented at the European Hematology Association Meeting, Geneva, Switzerland, June 10–13, 2004.

205E. A pharmacist-run phone triage system to reduce hospital admissions from chemotherapy related adverse events. *Maryann Hawes, Pharm.D.*, David Baribeault, RPh, BCOP; Boston Medical Center, Boston, MA.

Presented at 22nd Annual Eastern States Conference, Baltimore, M.D., May 1–3, 2003.

206. Contribution of anti-DT IgG from platelet transfusions and FFP. *Philip D. Hall, Pharm.D.*[1], Anne Patala, Pharm.D. student[1], Arthur Frankel, M.D.[2]; (1)Medical University of South Carolina, Box 250142, Charleston, SC; (2)Wake Forest University, Winston-Salem, NC.

PURPOSE: We are developing two fusion proteins consisting of a diphtheria toxin (DT) linked to either granuolocyte macrophage colony stimulating factor (DT-GMCSF) or interleukin-3 (DT-IL3). In trials, patients with anti-DT IgG concentrations > 2 µg/ml had significantly lower concentrations of either fusion protein. We noted increased concentrations of anti-DT IgG after fresh frozen plasma (FFP) and platelets (PLT) transfusions. Therefore, we measured the anti-DT IgG content of FFP and PLT.
METHODS: We assayed 14 bags of FFP and 12 bags of single-donor PLT for anti-DT IgG by an enzymoimmunoassay (Clin Immunol 2001;100:191–7) against DT-GMCSF and DT-IL3.
RESULTS: The median (range) anti-DT IgG concentration in PLT against DT-GMCSF and DT-IL3 was 0.6 µg/ml (0.2–11.2) and 0.65 µg/ml (0.2–9.4), respectively. The median (range) anti-DT IgG concentration in FFP against DT-GMCSF and DT-IL3 was 2.1 µg/ml (0.2–10.6) and 1.9 µg/ml (0.2–6.2), respectively. There was a strong correlation between anti-DT IgG content in FFP cross-reacting with DT-GMCSF and DT-IL3 (Rho=0.895, p=0.0013), and a strong correlation between anti-DT IgG content in PLT cross-reacting with DT-GMCSF and DT-IL3 (Rho=0.624, p=0.04). Assuming a plasma volume of 50 ml/kg in a 70 kg patient, a single FFP unit (median volume: 275 ml and anti-DT IgG content of 2 µg/ml) would increase the plasma anti-DT IgG content by 0.2 µg/ml. For PLT (median volume: 261 mls with anti-DT IgG content of 0.6 µg/ml) would increase the plasma anti-DT IgG concentration by 0.04 µg/ml.
CONCLUSIONS: One FFP or PLT transfusion should minimally increase anti-DT IgG concentrations, but multiple transfusions maybe significant.

207E. A phase II study of pegfilgrastim to support ACE 14 chemotherapy for the treatment of patients with small cell lung cancer (SCLC; extensive disease). *Robert Pirker, M.D.*[1], E Ulsperger, M.D.[2], J Messner, M.D.[3], K Aigner, M.D.[4], V Easton, Ph.D.[5], P Bacon, Ph.D.[5]; (1)Division of Oncology, Department of Internal Medicine I, Medical University Vienna, Vienna, Austria; (2)Krankenhaus Lainz, Vienna, Austria; (3)Landesklinik f¸r Lungenkrankheiten, Salzburg, Austria; (4)Krankenhaus der Elisabethinen, Linz, Austria; (5)Amgen Ltd, Cambridge, United Kingdom.

Presented at the Annual Meeting of the American Society of Clinical Oncology, New Orleans, LA, June 10–13, 2004.

208E. Epoetin-α (EPO) 40,000 U QW vs darbepoetin-α (DARB) 200 µg Q2W in anemic cancer patients receiving chemotherapy: preliminary results of a phase 3 randomized trial. Roger Waltzman, M.D.[1], Mark Fesen, M.D.[2], Glenn R Justice, M.D.[3], Christopher Croot, M.D.[4], *Denise Williams,*

M.D.[5]; (1)St. Vincent's Comprehensive Cancer Center, New York, NY; (2)Hutchinson Clinic, Hutchinson, KS; (3)Pacific Coast Hematology/Oncology Medical, Fountain Valley, CA; (4)North Mississippi Hematology & Oncology, Ltd, Tupelo, MS; (5)Ortho Biotech Clinical Affairs, LLC, Bridgewater, NJ.

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209. Retrospective study of the appropriate utilization of epoetin alfa and darbepoetin alfa in cancer patients with anemia. *Siu-Fun Wong, Pharm.D.*, Megan L. Brown, Pharm.D., Rozalin Sarkisian, Pharm.D.; Western University of Health Sciences, College of Pharmacy and Hematology Oncology Medical Group of Orange County, Inc., Pomona, CA.

PURPOSE: Epoetin alfa and darbepoetin alfa have been proven similar in efficacy, yet darbepoetin alfa offers advantage in dosing schedule. This study assessed the feasibility of formulary conversion by monitoring the prescribing pattern, efficacy, safety, and costs of epoetin alfa and darbepoetin alfa in a community oncology practice.
METHODS: Retrospective chart reviews were conducted in anemic cancer outpatients who were prescribed epoetin alfa or darbepoetin alfa per Medicare guidelines. The efficacy endpoints assessed were hemoglobin response, hemoglobin correction, hematopoietic response, mean change in hemoglobin, and RBC transfusions up to 16 weeks. The secondary objectives assessed were safety and cost.
RESULTS: Seventy-three (70 epoetin alfa and 3 darbepoetin alfa) of 140 patients screened were evaluated. Mean age was 66 years. Lymphoma (26%) and gastrointestinal cancer (20%) were the most common cancer types. Inappropriate dosing occurred in 43% of the patients. In the epoetin alfa group, 52.8% achieved hematopoietic response with a mean change of hemoglobin of 1.3 g/dL at week 6. Baseline hemoglobin level significantly affected the response to epoetin (p=0.003). RBC transfusion occurred in 11.4% of patients from week 5 to EOTP in the epoetin group and none in the darbepoetin group. Diarrhea (8.6%) and headache (1.4%) were reported in the epoetin group. The 2-week cost analysis comparison showed benefits with darbepoetin alfa.
CONCLUSIONS: Based on the data collected, additional prescribing education is indicated to optimize the utilization of the erythropoietic agents. Considering the cost benefit of darbepoetin alfa, a formulary conversion to darbepoetin alfa in these patients appears appropriate.

210E. Clinical and biological activity of soy protein powder (SPP) in healthy male volunteers: effect on testosterone and luteinizing hormone (LH). *Susan Goodin, Pharm.D.*, Weichung J. Shih, Ph.D., Michael Kane, B.S., Robert S. DiPaola, M.D.; Cancer Institute of New Jersey, New Brunswick, NJ.

Presented at the Annual Meeting of the American Society of Clinical Oncology, New Orleans, LA, June 5–8, 2004.

211E. Better early and overall hematologic outcomes and lower drug cost with epoetin alfa (EPO) compared with darbepoetin alfa (DARB) in patients with chemotherapy-related anemia. Tami L Mark, Ph.D.[1], *R. Scott McKenzie, M.D.*[2], Catherine T. Piech, M.B.A.[3]; (1)Medstat Group, Inc, Washington, DC; (2)Ortho Biotech Clinical Affairs LLC, Dallas, TX; (3)Ortho Biotech Clinical Affairs LLC, Bridgewater, NJ.

Presented at the 16th Annual Meeting and Showcase of the Academy of Managed Care Pharmacy, San Francisco CA, March 31–April 3, 2004.

212E. Results of a randomized study of every three-week dosing (Q3W) of darbepoetin-α for chemotherapy-induced anemia (CIA). *Timothy Rearden, M.D.*[1], Veena Charu, M.D.[2], Bruce Saidman, M.D.[3], Ali Ben-Jacob, M.D.[4], Glen R Justice, M.D.[5], Ajit S Manaim, M.D.[2], Danica Katz, M.D.[6], Dianne K. Tomita, M.P.H.[6], Gregory Rossi, Ph.D.[6]; (1)Hematology Oncology Consultants, Inc., St. Louis, MO; (2)Pacific Cancer Medical Center, Inc., Anaheim, CA; (3)Medical Oncology Associates, Kingston, PA; (4)Cache Valley Cancer Treatment and Research Center, Logan, UT; (5)Pacific Coast Hematology Oncology Medical, Fountain Valley, CA; (6)Amgen Inc., Thousand Oaks, CA.

Presented at the Annual Meeting of the American Society of Clinical Oncology, New Orleans, LA, June 5–8, 2004.

213E. Phase I study of CC-5013 (CC), a thalidomide (T) derivative, in patients with refractory metastatic cancer. *Tanyifor Tohnya, Pharm.D.*, James Gulley, M.D., Ph.D., Philip M. Arlen, M.D., Catherine Parker, R.N., William Dahut, M.D., William Figg Sr., Pharm.D.; National Cancer Intitute/National Institutes of Health, Bethesda, M.D.

Published in Proc Am Soc Clin Oncol 2003;22:231.

214E. A controlled, randomized, open-label study to evaluate the effect of every-2-week darbepoetin alfa for anemia of cancer. *Veena Charu, M.D.*[1], Chandra P. Belani, M.D.[2], Ahmad N. Gill, M.D.[3], Mukesh Bhatt, M.D.[4], Ali Ben-Jacob, M.D.[5], Dianne Tomita, M.P.H.[6], Danica Katz, MA[6]; (1)Pacific Cancer Medical Center, Anaheim, CA; (2)University of Pittsburgh Cancer Institute, Pittsburgh, PA; (3)Carolina Cancer Center, Aiken, SC; (4)Medina General Hospital, Medina, OH; (5)Cache Valley Center Treatment and Research Center, Logan, UT; (6)Amgen Inc., Thousand Oaks, CA.

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215. Cost-effectiveness analysis of amifostine in combination with paclitaxel or cisplatin in Korean gynecologic cancer patients. *Young Joo Chun, M.S.*[1], Jung Mi Oh, Pharm.D.[2]; (1)Department of Pharmacy, Asan Medical Center, Seoul, South Korea; (2)Graduate School of Clinical Pharmacy, Sookmyung Women's University, Seoul, South Korea.

PURPOSE: To perform the cost-effectiveness analysis (CEA) of amifostine given in combination with paclitaxel or cisplatin in Korean gynecologic cancer patients.
METHODS: Forty-one patients with gynecological cancer receiving cisplatin or paclitaxel with or without amifostine (910 μ•/μ³≥) every 3 weeks for six cycles were evaluated. The 'effectiveness' of amifostine was determined by evaluating the frequency and the severity of hematologic, neurologic, and renal toxicities. The 'cost' of the treatment was determined by including the expenses from the drugs, laboratory tests, and any additional medical expenses for treating the chemotherapy-induced adverse effects. C/E ratio, incremental cost-effectiveness ratio (ICER), and ICER graph were evaluated.
RESULTS: The cost per frequency of episode or C/E ratio for toxicity-grade 3, 4 neutropenia was ≤ 20,329 (Korean won)/percent, ≤ 18,454/percent, \16,840/percent, \5,058/percent, and \5,058/percent in TAP, TP, cTAP, and cTP group, respectively. C/E ratio of neuropathy was \8,600/percent, \1,905/percent, \11,032/percent, and \726/percent in TAP, TP, cTAP, and cTP group, respectively. ICER of neutropenia and neuropathy between TAP and TP was 547,730/22.06 and 512,611/-9.07, respectively. ICER of neutropenia and neuropathy between cTAP and cTP was 466,275/-0.16 and 497,061/4.49, respectively. ICER graph indicated that the groups treated with amifostine were inferior than control groups. All ICER except ICER of neuropathy between cTAP and cTP was located in IV area, indicating pre-treatment of amifostine was less effective and more costly than no amifostine.
CONCLUSIONS: Pre-treatment of amifostine was inferior to that of control groups in pharmacoeconomic analysis.

216. Health and economic outcomes of patients with febrile neutropenia. *Amy H Manguso, Pharm.D.*[1], Susannah E Motl, Pharm.D.[2], John C Kuth, Pharm.D.[1], Katie J Suda, Pharm.D.[1]; (1)Baptist Memorial Healthcare - Memphis, Memphis, TN; (2)University of Tennessee College of Pharmacy, Memphis, TN.

PURPOSE: Febrile neutropenia (FN) following antineoplastic chemotherapy or stem cell transplant is a common problem associated with substantial morbidity, mortality, and cost. Considered to be a medical urgency, FN necessitates inpatient evaluation and immediate initiation of broad-spectrum antibiotics. The purpose of this study was to examine hospital costs, length of stay (LOS), and overall patient outcomes of patients with FN compared to all oncology patients hospitalized at the same facility during the same time period.
METHODS: FN patients and matched controls were evaluated from 10/1/02–9/30/03. Cost data was extracted from hospital financial data. Diagnosis categories were obtained from an aggregated DRG coding system (Medicode-DRG Expert). A Student's *t*-test and χ^2 were used for statistical analysis; p-value < 0.05 was considered significant.
RESULTS: 208 FN patients (age (mean±SD)=59.2±15.6) were compared to 1286 controls (age=64.3±13.3) (p<0.05). FN patients had increased total hospital costs ($17,516 vs. $10,331), medication costs ($4,106 vs. $1,232), and LOS (12.6 vs. 7.8 days) (p<0.0001 for all). There was no difference in ICU LOS (0.7 vs 1.1 days) and severity of illness (CMI=1.9 vs. 1.7) between study and control groups. Interestingly, FN patients had lower mortality rates (6.3% vs. 9.6%), were more likely to be discharged home (72.1% vs 71.4%), and were less likely to be discharged with hospice (1% vs 3.2%) than controls (p<0.0001 for all).
CONCLUSIONS: Febrile neutropenia patients had a longer length of stay, higher total hospital costs and higher medication costs despite having improved overall outcomes compared to matched oncology patients.

217. An evaluation of the different methods used to estimate creatinine clearance for patients receiving carboplatin. *Audrea Hotsko, Pharm.D.*[1], Deborah A. Blamble, Pharm.D.[1], Amy Hatfield, Pharm.D.[1], Helen McFarland, Pharm.D.[1], Michelle Rudek, Pharm.D., Ph.D.[2]; (1)The Johns Hopkins Hospital, Carnegie 180, Baltimore, M.D.; (2)The Johns Hopkins Hospital, Room 1M85, Baltimore, M.D.

PURPOSE: Differences in physician practice allow for estimating creatinine clearance through a number of methods including the Jelliffe and Cockcroft-Gault equations. The weight parameter used within these equations may be the actual, ideal or corrected body weight of the patient. Providers may also correct creatinine to 0.8 –1 mg/dL or correct the Jelliffe equation for BSA. The objective of this study was to determine the frequency that practitioners adjust for these parameters and whether this affects carboplatin toxicities.
METHODS: Retrospective chart review of adult patients with head/neck, lung, or gynecologic malignancies who received carboplatin for at least 1 cycle and with at least 1 dose of the 2nd cycle ordered. Toxicities of the 1st cycle were evaluated Day #1 of the 2nd cycle and include: grade of

myelosuppression, thrombocytopenia, and change in creatinine.
RESULTS: Seventy-nine patients were included in this analysis. Only 8.8% of patients had ideal or corrected body weight used within the Cockcroft-Gault equation; no physician corrected for BSA within the Jelliffe equation; and only 19% of patients had their serum creatinine adjusted to 0.8–1.0mg/dL in either of these equations. A concise trend between type of weight used and carboplatin associated myelosuppression could not be made. However, adjusting serum creatinine resulted in less clinically significant thrombocytopenia (14% vs 18%).
CONCLUSIONS: Results warrant further investigation with greater patient accrual per parameter category. Adjusting serum creatinine to 1mg/dL in patients with serum creatinines < 0.8mg/dL may reduce the incidence of thrombocytopenia but not neutropenia.

Pediatrics

218. Antiproteinuric effect of benazepril in pediatric patients: evaluation after formulary change. *Irving Steinberg, Pharm.D.*[1], Jaspreet Bains, Pharm.D.[2]; (1)Division of Pediatric Pharmacotherapy, Department of Pediatrics, LAC+USC Medical Center; USC Schools of Pharmacy & Medicine, Los Angeles, CA; (2)USC School of Pharmacy, Los Angeles, CA.

PURPOSE: We examined the initial and maintained antiproteinuric effect of ACE-inhibitor therapy when medical center formulary preference shifted from enalapril and captopril (large pediatric experience) to benazepril.
METHODS: Retrospective evaluation was conducted of 45 patients from the pediatric renal clinic who were initiated on or switched to benazepril. Of these, 23 were retained for analysis having initial and multiple follow-up urine protein:creatinine ratios (Pr:Cr) measured, and compliance with therapy. Two patients had clear therapeutic failure with progressive renal disease. Parametric and nonparametric tests were applied to comparisons.
RESULTS: The mean ± s.d. age = 13.6 ± 3.0 years. The mean Pr:Cr (n = 21) at initiation of benazepril = 3.6 ± 4.6 (range 0.55 to 19.2) fell to 1.5 ± 1.5 (0.19 to 5.8; *p=0.016*) over a follow-up period of 453 ± 241 days. Nephrotic-level proteinuria (≥ 1000 mg/m2/day correlating to Pr:Cr ≥ 1.58) was observed in 13 patients when starting benazepril versus 6 at the final follow-up measurement (*p=0.03*). The median change in Pr:Cr in patients switched from another ACE-inhibitor (n = 7) was +10% (*p=0.87 vs zero change*), versus -60.6% (*p=0.003*) for patients initiated on benazepril (n = 14).
CONCLUSIONS: Benazepril maintained and provided antiproteinuric effects in patients switched to or initiated on this ACE-inhibitor in similar magnitude to published prospective pediatric studies of enalapril and ramapril. It is important to assess therapeutic response in subpopulations potentially affected by global formulary changes, where less published or practice experience exists.

219. Pentoxifylline pharmacokinetics following two novel delivery techniques. *Kim G. Adcock, Pharm.D.*[1], Patrick B. Kyle, B.S.[2], Jennifer S. Deaton, R.N., B.S.N.[2], Jake Olivier, Ph.D.[2]; (1)University of Mississippi, Jackson, MS; (2)University of Mississippi Medical Center, Jackson, MS.

PURPOSE: Pentoxifylline, an agent with anti-inflammatory activity, may have a role in preventing or treating chronic lung disease in premature neonates. Pentoxifylline is currently available in the US as an oral tablet, a dosage formulation not applicable in this population. This pilot study investigated the pharmacokinetic profile of pentoxifylline following two novel delivery techniques, intranasal and intratracheal.
METHODS: This pharmacokinetic study, utilizing 20 New Zealand white rabbits, consisted of 4 study groups. Group I was a control group and did not receive study medication. Groups II, III, and IV evaluated intravenous, intranasal and intratracheal routes of administration, respectively. A single 20 mg/kg pentoxifylline dose was administered to each rabbit followed by collection of blood samples over a 24-hour period. The pharmacokinetic parameters analyzed included area under the curve (AUC), maximum concentration (C_{max}), time of maximum concentration (T_{max}), elimination rate constant (Kel), and half-life ($T_{1/2}$).
RESULTS: The pentoxifylline pharmacokinetic parameters following the intravenous administration included AUC 5458 ng/ml*hr, C_{max} 15106 ng/ml, T_{max} 5.4 minutes, Kel 0.036 min-1 and $T_{1/2}$ 19 minutes. The pharmacokinetic parameters following intranasal and intratracheal administration included AUC 4451 ng/ml*hr and 6622 ng/ml*hr, C_{max} 10734 ng/ml and 15707 ng/ml, Tmax 5.4 minutes and 5 minutes, Kel 0.027 min-1 and 0.031 min-1, and $T_{1/2}$ 25 minutes and 22 minutes, respectively.
CONCLUSIONS: The pharmacokinetic profiles following intranasal and intratracheal administration appear similar to that following intravenous administration. This data provides support for development of pentoxifylline intranasal and intratracheal dosage formulations that would be suitable for use in premature neonates.

220. Effectiveness of a bronchiolitis pathway on length of stay in a community hospital. *Mary E. Temple, B.S., Pharm.D.*, Susan G. Arden, MSN, R.N., CPNP, Mary Bartos, MSN, R.N., Jeffrey H. Jinks, M.D.; Hillcrest Hospital - CCHS East, Mayfield Heights, OH.

Introduction: The American Academy of Pediatrics has no defined criteria for treating bronchiolitis in children. Some studies demonstrate use of a bronchiolitis care path (BCP) does reduce length of stay (LOS).
PURPOSE: To determine if LOS is reduced in pediatric patients by following a BCP in a private practice - based community hospital.
METHODS: A comparative retrospective chart review was conducted to compare LOS before (2002–2003) and after (2003–2004) implementation of a BCP. Additionally, LOS during 2003–2004 was compared between patients on the BCP versus LOS in those where physicians did not use the BCP. Secondary endpoints included comparisons in medication usage, suctioning, education documentation, diagnostic tool utilization and adverse events (ADEs). Statistical analysis was performed using SYSTAT. Sample size was based on a 20% decrease in LOS. Statistical significance was set at P<0.05.Chi square tests for nominal data and t tests for continuous data were used in the analysis. Descriptive statistics were also reported.
RESULTS: The LOS for patients in 2002–2003 was 1.8 days (N=68) versus 1.3 days (N=64) in 2003–2004 (p<0.03). Those patients who were on the BCP in 2003–2004 had a LOS of 1.19 (N=45) days versus 1.78 days (n=19) in those not on the BCP. Medications usage was decreased and documented suctioning, and education increased substantially in 2003–2004 versus 2002–2003. No differences in reported ADEs were found.
CONCLUSIONS: Utilization of a BCP may be effective in reducing LOS in private practice-based community hospitals.

221. Efficacy and safety of cyclosporine therapy in children with nephrotic syndrome. Myoung-Hun Chon, RPH[1], *Kie Ho Sohn, RPH, PHD*[1], Dong-Kyu Jin, M.D., PHD[1], Kyung-Eob Choi, Pharm.D.[1], Suk-Hyang Lee, Pharm.D., PHD[2]; (1)Samsung Medical Center, Kang-Nam Gu, Seoul, South Korea; (2)Graduate School of Clinical Pharmacy, Sookmyung Women's University, Yong-San Ku, Seoul, IA, South Korea.

PURPOSE: to assess the therapeutic efficacy and safety of six-month cyclosporine treatment with the low-dose deflazacort therapy in children with nephrotic syndrome.
METHODS: Thirty children with steroid dependence (SD), frequent relapse (FR) and steroid resistance (SR) were enrolled. They were treated with 6-month oral cyclosporine plus the low-dose deflazacort therapy from September 2002. The dosage of cyclosporine was started at 5 mg/kg/day and was monthly adjusted to maintain clinical remission and/or a trough blood level, while deflazacort dosage was reduced gradually. Clinical evaluation and monitoring of cyclosporine toxicity were performed every 2–4 weeks. Outcomes were compared to the latest six-month period of steroid only therapy before cyclosporine treatment. Student's *t*-test and ANOVA were used for statistical analysis.
RESULTS: Out of 28 children with SD and FR, 23 sustained remission, and 5 (17.9%) experienced 1 or 2 relapses during therapy. Out of 2 children with SR, 1 child sustained remission, and 1 child showed no response. The mean duration of remission and occurrence of relapse were significantly improved (p <.0001). In addition, the mean dosage of steroid was significantly reduced (p =.003). No nephrotoxicity was observed. Twenty out of the 28 children who had been in remission relapsed after withdrawal of cyclosporine. Fifteen of these children showed relapse within a month.
CONCLUSIONS: These results demonstrated that the combination of cyclosporine with the low-dose deflazacort was efficient and safe in children with SD and FR during the six-month treatment.

222E. Establishing a limited sampling strategy for cyclosporine (Neoral®) for pediatric renal transplant patients. *Mary H. H. Ensom, B.S.(Pharm), Pharm.D.*[1], Amanda Lai, B.Sc.(Pharm), student[2], David S. Lirenman, M.D.[3], James Carter, M.D.[3], Morrison Hurley, M.D.[3], Colin White, M.D.[3], Dawn K. Strong, B.Sc.(Pharm), Pharm.D.[3]; (1)University of British Columbia and Children's & Women's Health Centre of British Columbia, Vancouver, BC, Canada; (2)University of British Columbia, Vancouver, BC; (3)Children's & Women's Health Centre of British Columbia, Vancouver, BC.

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223E. Utility of anti-Xa monitoring in children receiving enoxaparin for therapeutic anticoagulation. *Mary H. H. Ensom, B.S.(Pharm), Pharm.D.*[1], Marianna Leung, BScPhm, Pharm.D.[2], Sharon H. Ho, BScPhm[2], Donald P. Hamilton, BScPhm[2], John K. Wu, MBBS, M.Sc.[2], David D. Dix, MBChB[2], Louis D. Wadsworth, MB, ChB[2]; (1)University of British Columbia and Children's & Women's Health Centre of British Columbia, Vancouver, BC, Canada; (2)Children's & Women's Health Centre of British Columbia, Vancouver, BC.

Presented at the 35th Professional Practice Conference of the Canadian Society of Hospital Pharmacists, Toronto, Ontario, Canada, Jan 31–Feb 4, 2004.

224. Clinical experience with spironolactone in infants and children. *Marcia L. Buck, Pharm.D., FCCP*; University of Virginia Medical Center, Charlottesville, VA.

PURPOSE: In 2003, the Food and Drug Administration placed spironolactone on its priority list for pediatric studies. The purpose of this study was to describe the use of spironolactone in a large group of children and identify

areas for future research.
METHODS: A prospective observational study was conducted. Patient demographic information was collected, as well as spironolactone dose, use of other diuretics and potassium supplements, and serum potassium concentrations. Data from patients with congenital heart defects (CHD) and chronic lung disease (CLD) were compared with a *t*-test.
RESULTS: A total of 100 patients were evaluated. Average patient age was 20.7±49.8 months and weight was 9.5±16.8 kg. Seventy-eight patients were infants. Sixty-eight were male. The average initial dose was 1.8±0.7 mg/kg/day (range 0.5–4.2 mg/kg/day) with a twice daily interval in 53 patients and once daily in 43. Sixty-six patients received furosemide; 37 received thiazides. Average serum potassium after initiation was 4.4±0.8 mmol/L. Potassium supplements were required by 29 patients. Mild hyperkalemia occurred in 19 patients, including nine given supplements. No other adverse effects were noted. The average length of treatment was 14±13 days. Of the 90 patients discharged, 65 (72%) continued on spironolactone. Sixty-two patients had CHD. Twenty-nine had CLD. Patients with CLD were treated with a higher initial dose than those with CHD (2.0±0.8 versus 1.7±0.5 mg/kg/day, p=0.04). There was no difference in serum potassium.
CONCLUSIONS: Future research should focus on defining the optimal pediatric spironolactone dosing regimen. Twice daily dosing may not be necessary. The use of potassium supplements should also be re-examined.

225. Pamidronate therapy in children with osteogenesis imperfecta and idiopathic juvenile osteoporosis. *Roxane R. Carr, Pharm.D.*[1], Renee F. Robinson, Pharm.D.[2], John D. Mahan, M.D.[2], Milap C Nahata, Pharm.D., FCCP[1]; (1)The Ohio State University College of Pharmacy, Columbus, OH; (2)The Ohio State University College of Medicine, Children's Hospital, Department of Pediatrics, Division of Nephrology, Columbus, OH.

PURPOSE: Pamidronate therapy (PT) may increase bone mineral density (BMD) and decrease fracture rates in children with osteogenesis imperfecta (OI) and idiopathic juvenile osteoporosis (IJO). The purpose of this study was to evaluate the relationship between dose, change in linear growth, and BMD in children with OI and IJO.
METHODS: Medical records of all children with OI and IJO receiving PT between 1999 and 2003 were retrospectively reviewed and analyzed via students *t*-test.
RESULTS: Twenty-six children (50% female) were studied; 58% OI Type I, 23% Type III, four percent Type IV, and 15% IJO. Mean age at initiation of PT was 9.7±4.4 yrs. Median dose of PT was 12 mg/kg/yr (range 9–24 mg/kg/yr) given as 1 mg/kg/d per three-day cycle every 3–4 months. Mean baseline height 111.0±27.3 cm, BMD 0.382±0.192 g/cm2, and BMD Z score -4.286±2.558. Change in height was 7.58±6.15 cm/yr (p <0.001), BMD 0.166±0.127 g/cm2/yr (p=0.006) and BMD Z score 2.607 ± 1.551 /yr (p <0.001). No association between dose and response (p=0.731, r = 0.076), or significant difference in response between groups based on gender (p >0.49), age at initiation (≥12 years versus <12 years) (p >0.10), baseline BMD Z score (p >0.253), or baseline average number of fractures/yr (≥3 versus <3) (p >0.277) was found.
CONCLUSIONS: PT may be effective in increasing BMD at doses of 9–24 mg/kg/yr in children with OI or IJO. Gender, age at initiation, and severity of disease at baseline did not appear to affect clinical outcomes.

226. Evaluation of gentamicin pharmacokinetics in neonates greater than seven days post partum. *Brady S. Moffett, Pharm.D.*[1], Susan W. Aucott, M.D.[2], Carlton K.K. Lee, Pharm.D., M.P.H.[3]; (1)Texas Children's Hospital, Department of Pharmacy, Houston, TX; (2)Department of Pediatrics, Division of Neonatology, The Johns Hopkins University, Baltimore, M.D.; (3)Department of Pediatrics, Johns Hopkins University & Department of Pharmacy, The Johns Hopkins Hospital, Baltimore, M.D.

PURPOSE: The lack of gentamicin pharmacokinetic (PK) data in neonates > 7 days old has resulted in dosing guidelines requiring serum sampling monitoring after each first dose for dosage individualization. The goal of this study is to evaluate gentamicin PK in neonates >7 days old so that more complete empiric dosing guidelines can be developed.
METHODS: Neonates > 7 days old receiving gentamicin were stratified into the following post-menstrual age (PMA) groups: < 29 wks & 8–28 days; < 29 wks & > 28 days; 30–33 wks; 34–37 wks; and > 38 wks. Kel (hr-1), $T_{1/2}$ (hr), and Vd (L/kg) were calculated using standard equations for the one-compartment first order elimination model. Variables affecting clearance, such as patent ductus arteriosus (PDA), were also evaluated.
RESULTS: Vd was 0.5 L/kg for all of the 5 age groups (n=23). Kel (hr-1) and T1/2 (hr) were similar among all 3 age groups > 30 wks (n=16); 0.16+0.06 and 4.94+1.94, respectively. Five of 7 patients in the age groups < 30 wks had PDAs resulting in lower Kel (p<0.005) and higher T1/2 (p<0.0001) compared to all other patients.
CONCLUSIONS: Patients with a PDA have reduced elimination similar to previous reports. All patients, regardless of PDA status, had a Vd of 0.5 L/kg; suggesting a uniform empiric gentamicin dosage of 4 mg/kg/dose. Patients > 30 wks PMA and > 7 days old have similar elimination characteristics, which may suggest a uniform empiric dosing interval of every 12–18 hours for these patients.

227. Pharmacokinetics of ganciclovir in children following the administration of valganciclovir. *Cristine Hogue, Pharm.D.*[1], Janelle A Hickey, Pharm.D.[1], Carolyn Henkin, Pharm.D., BCPS[2], Hasan S. Jafri, M.D.[3]; (1)Children's Medical Center, Dallas, Dallas, TX; (2)Methodist Medical Center of Dallas, Dallas, TX; (3)University of Texas Southwestern Medical Center, Dallas, TX.

PURPOSE: The steady state pharmacokinetic parameters and safety of ganciclovir was evaluated in children taking valganciclovir.
METHODS: Eligible study subjects must have received 48 hours of valganciclovir therapy with no IV or PO ganciclovir within this time period. Twelve children (0.9 to 13 years) qualified for the study. Eleven patients were solid organ transplant recipients, and one patient was treated for EBV encephalitis. The average valganciclovir dose was 14 mg/kg/dose given either every 12 hours (n=6) or 24 hours (n=6). For 12 hour dosing, ganciclovir levels were obtained at 0, 0.75, 1.5, 2.5, 5, and 12 hours. For 24 hour dosing, levels were obtained at 0, 0.75, 1.5, 2.5, 6, 15, and 24 hours. Drug levels were assayed by HPLC methods and pharmacokinetics were analyzed by non-compartmental methods.
RESULTS: Ganciclovir pharmacokinetic parameters (mean +/- SD) in children on 12 hour dosing were: peak ganciclovir concentration 6.9 µg/mL (+/-3.8) and area under the curve 39.0 µg/ml x hr (+/-23.5). The ganciclovir peak concentration and area under the curve for 24 hour dosing were 6.6 µg/mL (+/- 3.3) and 42.0 µg/mL(+/- 22.6), respectively. Peak ganciclovir concentrations were 9.5 µg/ml (+/- 2.7) for fed patients and 4.1 µg/ml (+/- 1.0) for unfed patients. The time to maximum serum concentration for all patients was 1.7 hr (+/-0.6). The terminal half-life was 4.6 hr (+/- 2.4). Neutropenia was reported in 2 patients and nausea and vomiting in 1 patient.
CONCLUSIONS: Valganciclovir was rapidly absorbed and converted to ganciclovir. Pharmacokinetic parameters varied greatly between pediatric subjects.

Pharmacoeconomics/Outcomes

228. Temporal effect of argatroban administration on budgetary impact of heparin-induced thrombocytopenia. *Renee J. G. Arnold, Pharm.D.*[1], Renee Kim, M.P.H.[1], Yonglong Zhou, M.S.[1], Boxiong Tang, M.D., Ph.D.[2]; (1)Pharmacon International, Inc., New York, NY; (2)GlaxoSmithKline PLC, Collegeville, PA.

PURPOSE: We evaluated the financial implications of using the direct thrombin inhibitor argatroban for early treatment (<48 hours after thrombocytopenia onset), compared with delayed treatment (≥48 hours after thrombocytopenia onset), of heparin-induced thrombocytopenia (HIT) with or without thrombosis.
METHODS: A cost analysis model was developed using data from argatroban clinical trials, medical literature, an expert panel, 2003 Physician's Fee Reference, Healthcare Cost and Utilization Project 2000, and drug costs from 2003 Drug Topics RedBook. The total per-patient cost included: hospital days, diagnostic tests, heparin, argatroban, major hemorrhagic events and patient outcomes (i.e., amputation, new thrombosis, stroke, or death), multiplied by the probability of each event.
RESULTS: The mean cost per patient having HIT without thrombosis who did not receive argatroban was $38,046. For such patients treated early with argatroban therapy, the mean cost decreased by 6.9%, representing a $2,605 savings per patient. For those receiving delayed argatroban therapy, the mean cost increased by $6,419 per patient. The mean cost for patients having HIT with thrombosis who did not receive argatroban was $48,101, which was 9.0% greater than those receiving early argatroban therapy, representing a $3,957 savings per patient. Mean costs increased by 18.2% (to $52,164) in patients whose argatroban was delayed, representing a cost increase of $8,020 per patient compared with early treatment.
CONCLUSIONS: Early initiation of argatroban therapy upon suspicion of HIT is recommended to reduce the prothrombotic consequences of HIT and associated healthcare costs. Argatroban therapy should not be delayed pending the results of HIT diagnostic tests.

229E. A predictive model of hospitalization and potential cost savings associated with oxandrolone in cancer patients with IWL. Hind T. Hatoum, Ph.D.[1], A. Simon Pickard, Ph.D.[2], Faith D. Ottery, M.D., Ph.D.[3], *Karin A. Greenberg, Pharm.D., BCPS*[3]; (1)Hind Hatoum & Co., Chicago, IL; (2)University of Illinois College of Pharmacy, Chicago, IL; (3)Savient Pharmaceuticals, Inc., East Brunswick, NJ.

Presented at the 40th Annual Meeting of the American Society of Clinical Oncology, New Orleans, LA, June 5–8, 2004.

230E. Short-term treatment of posttraumatic stress disorder: venlafaxine XR vs sertraline or placebo. Jonathan Davidson, M.D.[1], Alan Lipschitz, M.D.[2], *Jeff Musgnung, MT*[2]; (1)Duke University Medical Center, Durham, NC; (2)Wyeth Research, Collegeville, PA.

Presented at the International Congress of The World Federation of Societies of Biological Psychiatry, Sydney, Australia, February 9–13, 2004.

231. Quantifying the impact of an automatic antibiotic pharmacy intravenous to oral interchange program across all diagnoses: the physician 'spillover' effect. *John Dougherty, M.B.A., Pharm.D.*[1], James Pridemore, BA, CPhT[2], Violeta Barac, CPhT[2], Philip Sanchez, M.D.[2], Lee Adler, M.D.[2], Judy McManus, Pharm.D.[3]; (1)Orlando Regional Medical Center, Orlando, FL; (2)Florida Hospital, Orlando, FL; (3)Pfizer, Orlando, FL.

BACKGROUND: In 2001, physicians were reluctant to switch inpatients from intravenous (IV) to oral (PO) antibiotics. In 2002, a highly debated pilot program at Florida Hospital assessed an IV to PO automatic interchange. With a successful pilot program, a protocol endorsed by Infectious Disease physician champions allowed pharmacists to initiate an automatic switch of antibiotics from IV to PO.
PURPOSE: Evaluation of pharmacist-generated versus physician-generated "spillover" conversions, assessment of program cost-minimization, and cost-savings from physician "spillover".
METHODS: A retrospective study was conducted on 203 randomly sampled conversions between March - December 2003. Reviews utilized Palm® based Pendragon® forms to evaluate: pharmacist and physician conversions, conversion candidacy and actual conversion time, drugs converted, physicians involved, discharge time, and drug cost.
RESULTS: Two hundred-three conversions (171 patients) were evaluated. Eighty-seven (43%) conversions were initiated by pharmacists, 116 by physicians. Conversion candidacy versus actual conversion time was 1.56 days (pharmacists) versus 1.95 days (physicians). Forty percent of physician-generated conversions did not meet criteria. Pharmacist conversions had 1.2 greater days on PO versus IV compared to physicians. Annual savings realized from pharmacy interventions are $137,932. Including physician conversions, savings are $282,872 annually. Additional savings ($68,000) are realized if patients are converted upon meeting protocol criteria.
CONCLUSIONS: Pharmacist-directed IV to PO conversions led to cost-savings that doubled when factoring in a physician "spillover" effect. High numbers of physician-generated IV to PO conversions not meeting criteria suggests the protocol may be conservative and therefore a greater proportion of patients could safely be intervened upon by pharmacists.

232. Medication persistency with long-acting stimulants in children with ADHD. *Jason E. Kemner, M.P.H.*, George J. Wan, Ph.D., M.P.H.; McNeil Consumer & Specialty Pharmaceuticals, Fort Washington, PA.

PURPOSE: To evaluate medication persistency with OROS methylphenidate (M.P.H.) [#91;Concerta], mixed amphetamine salts extended-release (MAS XR) [Adderall XR], or Extended-Release (ER) M.P.H. [Metadate CD] in the treatment of patients (ages 6–12) with attention-deficit/hyperactivity disorder (ADHD).
METHODS: This was a 9-month retrospective longitudinal study of pharmacy claims data from Verispan for the period October 2002 to June 2003. Patients (ages 6–12) included in the analysis were required to have a new prescription (no prior ADHD medication use in 12 months) for OROS M.P.H., MAS XR, or ER M.P.H. Persistency was defined as a period <= the days of medication supplied plus a 30-day grace period between prescription fills.
RESULTS: Of the 20,089 patients included in this study, 9,110 were prescribed OROS M.P.H., 9,343 were prescribed MAS XR, and 1,636 were prescribed ER M.P.H.. Patients prescribed OROS M.P.H. or MAS XR were 1.47 times (95% CI = 1.29, 1.67; p<0.0001) and 1.44 times (95% CI = 1.27, 1.64; p<0.0001) more likely to persist on their medication than those prescribed ER M.P.H.. No significant differences in persistency rates were observed with OROS M.P.H. or MAS XR.
CONCLUSIONS: In patients with ADHD, OROS M.P.H. and MAS XR were associated with significantly greater persistency than ER M.P.H. and were not significantly different from each other. Medication persistency is an important factor to consider when selecting ADHD therapy.

233. Analysis and comparison of brand and generic drug price trends among four therapeutic classes. *Jeff J. Guo, B.Pharm., Ph.D.*, Brian Baker, Pharm.D., Aaron Dershak, Pharm.D., Amjad Iqbal, Pharm.D., Wael Safi, Pharm.D.; University of Cincinnati College of Pharmacy, cincinnati, OH.

PURPOSE: To identify how new brand or generic drug entrants affect drug prices of those already in the market.
METHODS: Using the First Databank file, average wholesaler price (AWP) data for each drug NDC were analyzed from 1986 to 2002. Study drugs were focused on four therapeutic classes: atypical antipsychotics, SSRI antidepressants, ACE inhibitors, and statins. Drug prices were calculated and compared as the monthly average AWP of daily dose for each brand and generic drug using time-series trend analysis.
RESULTS: Drug prices for all brand names of four therapeutic classes increased overtime. Drug prices for all generic drugs decreased overtime. Drug prices for all atypical antipsychotics, SSRI and ACEI brand names increased overtime regardless new brand or generic entry. Pravachol remained higher price while Lipitor price was the lowest. Lovastatin price was introduced at 60% below its brand and decreased sharply later. A little impact on drug price after Baycol withdrawal in August 2001. The first generic ACEI captopril was introduced as the same price as its brand in 1994 and decreased dramatically. Enalapril as the second generics introduced as 50% below its brand Vasotec. Risperdal price increased sharply in mid-1999 due to new dose formulation. Clozapine generic drug price introduced at 90% of brand Clozaril and decreased sharply later.
CONCLUSIONS: Brand-name drug prices didn't decrease when another new brand or generic drug was introduced. Drug prices for generic drugs decreased overtime due to market competition.

234E. A comparison of depression remission rates using treatment algorithms: venlafaxine XR versus SSRIs. *Jeff Musgnung, MT*, Isma Benattia, Ph.D., Jay Graepel, Ph.D.; Wyeth Pharmaceuticals, Collegeville, PA.

Presented at the World Federation for the Society of Biological Society, Sydney, Australia, Feb 9–13, 2004.

235E. Short-term treatment of depressed and anxious primary care patients with multiple, unexplained somatic symptoms using venlafaxine XR. *Jeff Musgnung, MT*[1], Kurt Kroenke, M.D.[2], Isma Benattia, Ph.D.[1], Jay Graepel, Ph.D.[1]; (1)Wyeth Pharmaceuticals, Collegeville, PA; (2)Indiana University School of Medicine, Indianapolis, IN.

Presented at the Annual Meeting of the European College of Neuropsychopharmacology, Stockholm, Sweden, October 9–13, 2004.

236E. Impact of new technology payments for drotrecogin-α (activated): the Mercury study. Liesl M Cooper, Ph.D.[1], Walter Linde-Zwirble, .[2], *Judi Jacobi, Pharm.D., FCCP, BC*[3]; (1)Eli Lilly and Company, Indianapolis, IN; (2)Health Process Management (HPM), Doylestown, PA; (3)Methodist Hospital/Clarian Health, Indianapolis, IN.

Published in Crit Care Med 2003:31(12 Suppl):A119.

237. Impact of glycoprotein use on clinical and economic outcomes in PCI stented patients in academic health centers. *Mandy E. Grant, Pharm.D._Candidate*[1], Michael J. Oinonen, Pharm.D.[2], Joseph P. Cummings, Ph.D.[2], Karl A. Matuszewski, M.S., Pharm.D.[2], David S. Marks, M.D.[3]; (1)Midwestern University, Chicago College of Pharmacy, Downers Grove, IL; (2)University HealthSystem Consortium, Oak Brook, IL; (3)Medical College of Wisconsin, Milwaukee, WI.

PURPOSE: Acute complications of percutaneous coronary intervention (PCI) are mitigated with the use of IIb-IIIa glycoprotein (GP) inhibitors. The advent of drug eluting stents (DES) for prevention of long-term complications (restenosis) has placed increased cost pressures on health centers. The impact of DES on IIb-IIIa has not been described.
METHODS: GP use within bare metal stent (516&517) and DES (526&527) DRGs was queried from the University HealthSystem Consortium (UHC) Clinical Database-Pharmacy for Q2–Q4, 2003. Patient length of stay (LOS), mortality rates, total hospital and pharmacy costs were studied.
RESULTS: GP were used in 8,023 of 12,600 PCI procedures. Eptifibatide was used most frequently (64% of cases). Absolute GP use dropped 7% over Q2–Q4, while DES use increased 35%. DRGs 526 and 516, acute myocardial infarction (AMI) patients, had the highest GP use in all 3 quarters. When GPs were added to therapy, total hospital costs increased approximately $2,000 for DRGs 516, 517, and 526 and $4,000 for DRG 527. GP use was associated with decreased mortality in patients with AMI, notably DRG 516 (1.5% with GP vs. 2.9% without). LOS was not altered by the use of GP for any DRG.
CONCLUSIONS: Increased use of DES has demonstrated minimal impact on use of IIb-IIIa GP inhibitors in 2003. Increasd use was seen in higher risk patients (AMI), consistent with the demonstrated benefits of the agents. GP are associated with decreased mortality. The cost impact of DES may be reduced with the appropriate use of GP in patients selected for high-risk features.

238. The impact of comorbidities and methylphenidate formulation on ADHD outcomes. Maureen J Lage, Ph.D.[1], *Jason E Kemner, M.P.H.*[2]; (1)HealthMetrics Outcomes Research, LLC, Groton, CT; (2)McNeil Consumer and Specialty Pharmaceuticals, Fort Washington, PA.

PURPOSE: Examine how co-morbidities and methylphenidate (M.P.H.) formulation impact treatment patterns and use of emergency room (ER) services in children and adolescents with attention-deficit/hyperactivity disorder (ADHD).
METHODS: Patients from a large claims database age 6–18 diagnosed with ADHD who receive either OROS® M.P.H. (Concerta®; N=4,295) or three-times-daily IR M.P.H. (TID M.P.H.) (N=884) are included in the analyses. Analyses of covariances examine differences in treatment patterns. Multivariate analyses examine the impact of co-morbidities and medication delivery on ER services use.
RESULTS: Individuals who initiate therapy with OROS M.P.H. are significantly less likely to have a 15 or 30 day therapy gap (85% vs. 99%, p<0.0001; 76% vs. 98%, p<0.0001, respectively) or switch ADHD medication (27% vs. 72%, p<0.0001) compared to TID M.P.H.. Diagnosis of oppositional defiance disorder (ODD) is associated with a greater number of visits to the ER (coefficient=0.32, p=0.0316) while the use of OROS M.P.H. compared to TID M.P.H. is associated with significantly less use of ER services.

CONCLUSIONS: In children and adolescents with ADHD a co-morbid diagnosis of ODD is associated with a greater number of ER visits. Use of OROS M.P.H. is associated with better treatment patterns and less use of ER services compared to TID M.P.H.

239E. Cost-effectiveness of intravenous immunoglobulin manufactured from chromatography-caprylate vs. solvent-detergent methods in persons with primary immunodeficiency disease. *Parthiv, J Mahadevia, M.D., M.P.H.*[1], John Strell, Pharm.D.[2], Dan Kunaprayoon, B.S., BA[1], Erwin Gelfand, M.D.[3]; (1)MEDTAP International, Bethesda, M.D.; (2)Bayer HealthCare, Biological Products Division, Research Triangle Park, NC; (3)National Jewish Medical and Research Center, Denver, CO.

Published in Value in Health 2004;7(3):354.

240E. Effects of esomeprazole and placebo on relief of moderate to severe nighttime heartburn, sleep disturbance, and sleep quality in patients with GERD: a multicenter, randomized, controlled trial. David Johnson, M.D.[1], *Albert Roach, Pharm.D.*[2], Barry Traxler, B.S.[3], Joseph A. Crawley, M.S.[3], Kurt Brown, M.D.[3]; (1)Eastern Virginia School of Medicine, Norfolk, VA; (2)AstraZeneca LP - GI/Respiratory, Franklin, TN; (3)AstraZeneca LP, Wilmington, DE.

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241. Estimating the cost burden of insomnia in elderly and non-elderly adults. *Ronald J. Ozminkowski, Ph.D.*[1], Sara Wang, Ph.D.[1], Lucinda Orsini, D.P.M., M.P.H.[1], Kendyl Schaefer, M.Sc.[2], Andrea J. Anderson, Pharm.D.[2], Nadine Barry, B.S.N.[2], Erin L. Albert, R.Ph., M.B.A.[2]; (1)Thomson Medstat, Ann Arbor, MI; (2)Sepracor Inc., Marlborough, MA.

PURPOSE: To assess the cost burden of insomnia in elderly and non-elderly adults.
METHODS: Cost burden was estimated using MarketScan medical claims data (elderly sample included claims for patients ≥ 65 years in private-sector health plans; non-elderly sample included claims for patients 18–64 years in private-sector health plans). Insomnia patients were identified with ICD-9-CM diagnosis codes or by insomnia medication use (zolpidem, zaleplon, temazepam, miscellaneous benzodiazepines, and trazodone). Insomnia patients were compared with a matched set of patients without insomnia (elderly: n=41,502 vs. n=41,511; non-elderly n=86,472 vs. n=86,475) using propensity score analyses, allowing comparison of costs associated primarily with insomnia. Direct costs (inpatient, outpatient, pharmaceutical) were compared for the 6-month period prior to insomnia treatment initiation. Indirect costs related to absenteeism, short-term disability, and workers compensation were compared for non-elderly patients with available data (insomnia n=6525, matched n=6178).
RESULTS: Overall, the 6-month direct costs for insomnia patients were $2,789 (95% CI: $2,619–$2,959; p<0.01) and $2,110 (95% CI: $2,005–$2,216, p≤0.01) higher per person than matched controls respectively for elderly and non-elderly patients. Indirect expenditures were $939 (95% CI: $705–$1,173, p≤0.01) higher for non-elderly insomnia patients compared with the matched controls.
CONCLUSIONS: Based on 6-months of medical claims data, both elderly and non-elderly patients with insomnia have significantly higher direct costs than patients without insomnia, even after using propensity scoring to control for concomitant illness, demographics, and plan type. Non-elderly insomniacs additionally have higher indirect medical costs.

242. Potential medical cost reduction due to decreases in A_{1c} resulting from pharmacist diabetes education and medication recommendations in a community setting. *Shana Gunderson, Pharm.D.*[1], Kwan Y Lee, Ph.D.., M.S.[1], Alyssa H Duvel, Pharm.D.[1], Daniel F Luce, RPh, M.B.A.[2]; (1)Walgreens Health Initiatives, Deerfield, IL; (2)Walgreens Co., Deerfield, IL.

PURPOSE: Research indicates that decreases in A1C-levels from 9% to 8% reduce healthcare cost differentials by $1,101 per diabetic and $1,597 per hypertensive-diabetic over a 3-year period. To combat diabetes and its healthcare costs, a pharmacist-driven community-based diabetes-care program was implemented. Outcomes from this program are presented.
METHODS: Referred type-2 diabetic patients scheduled one to three visits, based on clinical parameters, with specially-trained pharmacists and received education, glucose-meter-training and onsite laboratory testing. Data including demographics, laboratory, medical, and medication recommendations were collected. Differential cost and annual medical inflation rate were literature based. Program effectiveness was evaluated using random coefficient models for continuous and GEE for binary outcomes.
RESULTS: 1,795 patients were seen at first visit, 827 (46%) second, and 389 (22%) completed third visits. Of those completing 3 visits, 369 (95%) continued receiving monitoring of A1C-levels. 80% of patients (297 of 369) received pharmacist education alone and had a significantly reduced average A1C from 7.37% to 7.08% (p<0.0001) from visit one to three. 20% of patients (72 of 369) received pharmacist diabetes education and medication recommendations and had reduced average A1C levels, 8.95% to 7.98% (p<0.0001) from visit one to three. Of the 72 patients, 47% were hypertensive-diabetics (systolic-blood-pressure >140 or diastolic-blood-pressure > 90). Among 35 hypertensive-diabetics and 37 non-hypertensive-diabetics, potential per-patient medical cost reductions based on A1C-level reduction, averaged $1,308 ($94,147), over a 3-year period.
CONCLUSIONS: Pharmacist diabetes education and recommendations significantly decreased A1C-levels in type-2 diabetics resulting in potential healthcare costs reductions of $1,308 per-patient, over three years.

243. A cost analytic model to determine the least costly inpatient erythropoiesis stimulating therapy (EST) regimen. *Samir Mody, Pharm.D., M.B.A.*[1], Sue Watson, Pharm.D.[1], John Fastenau, M.P.H.[1], Adam Decter, M.B.A., MA[2], Jennifer Little, B.A.[2], Mei-Sheng Duh, M.P.H., Sc.D.[2]; (1)Ortho Biotech Clinical Affairs, LLC, Bridgewater, NJ; (2)Analysis Group, Inc, Boston, MA.

PURPOSE: To develop a cost analytic model comparing inpatient costs for ESTs across the nephrology, oncology, and critical care settings.
METHODS: This model assessed pharmacy and nursing costs for the following dosing regimens: epoetin alfa (EPO) TIW (nephrology 3,333U; oncology and critical care 10,000U), EPO QW (nephrology 10,000U; oncology and critical care 40,000U), and darbepoetin alfa (DARB) QW (nephrology 30µg; oncology and critical care 150µg). Pharmacy costs included wholesale acquisition, dispensing and transporting costs; nursing costs included administration time costs. Average length of stay (LOS) for each setting was derived from the 2001 National Hospital Discharge Survey (nephrology 10.1; oncology: 8.6; critical care: 9.2). For total inpatient costs, a weighted average was calculated across settings. All costs were reported in 2003 dollars, with dosing starting on Day 3 of hospitalization.
RESULTS: EPO TIW was the least costly regimen across each setting (Table 1). Sensitivity analyses conducted for changes in LOS and nursing time did not significantly affect the results. Lowering DARB QW dose to 100µg in the oncology and critical care settings still resulted in higher costs compared to EPO TIW.
Break-even analyses for all inpatients suggested that the cost of DARB would have to be reduced by 58% to equal EPO TIW costs.
CONCLUSIONS: EPO TIW was found to be the least costly EST regimen for inpatients.

Table 1: EST regimen costs

Admission Type	EPO TIW	EPO QW	DARB QW
Nephrology	$181	$239	$256
Oncology	$358	$453	$607
Critical Care	$478	$907	$1213
Total	$380	$687	$899

244E. Cost-effectiveness of nesiritide versus dobutmaine in patients with acutely decompensated heart failure. *Tobias Gerhard, B.S.*[1], Issam Zineh, Pharm.D.[2], Abraham G. Hartzema, MSPH, Ph.D.[1], Almut G. Winterstein, Ph.D.[1]; (1)Department of Pharmacy Health Care Administration, University of Florida, Gainesville, FL; (2)Department of Pharmacy Practice, University of Florida, Gainesville, FL.

Presented at the 20th International Conference on Pharmacoepidemiology and Therapeutic Risk Management of the International Society for Pharmacoepidemiology, Bordeaux, France, August 22–25, 2004.

245. A pharmacist's impact on medication safety through automation. *Anisa Mock, Pharm.D.*, Janelle M Berg, Pharm.D., BCPS, Fernando J Zaldivar, RPh; Mercy Hospital, Miami, FL.

PURPOSE: Data from the Institute of Medicine's 1999 report concluded that medication errors are responsible for about 7,000 deaths, at a cost of up to $136 billion dollars annually to the health care system. A novel approach to enhancing medication safety includes Pyxis MedStation software ALERxT and Clinical Data Categories (CDCs). These programs are site-specific and designed to provide last minute warnings and/or documentation upon removal of target medications. The primary objective of this study is to evaluate the impact of these software enhancements, on medication safety.
METHODS: A medication safety subcommittee identified high-risk medications and potentially dangerous situations where alerts would prevent medication errors. Rules triggering a warning and required response were built and tested silently in pilot units to gather baseline data. Nursing personnel also received education in the "test" environment prior to implementation.
RESULTS: In non-profiled areas like the Emergency Room the activated Alerts prevented 23 potential medication errors. In the profiled areas or pilot units, alerts were expected only if the medication was removed on override. Additionally, a pain scale CDC was implemented in two pilot units. During a 10 day observation period it was found that all pain scores were documented in the Pyxis Medstation as required; however, only 43% were documented in the medical record.
CONCLUSIONS: Alert and CDC implementation was successful. These enhancements prevented nursing personnel from carrying out medication errors. In non-profiled areas it is now routine practice to bring the medical record to the Medstation at time of removal.

245A. Cost-efficacy analysis of peginterferon-α2b plus ribavirin compared to peginterferon-α2a plus ribavirin for treatment of chronic hepatitis C.

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PURPOSE: To compare cost-efficacy of combination ribavirin (RBV) plus pegylated interferon alfa-2b (Peg-2b) or pegylated interferon alfa-2a (Peg-2a) treatment in hypothetical cohorts of 100 hepatitis C (HCV) patients, using current patient management algorithms. Randomized phase III trials comparing both Pegs to standard interferon have yielded comparable sustained viral responses (SVR), however clinical use of reported 12 week early viral response (EVR) to discontinue eventual nonresponders may affect overall cost-efficacy (Manns, 2001; Fried, 2002; Davis 2003).
METHODS: A decision analysis model was constructed to compare Peg-2b+RBV and Peg-2a+RBV per approved label doses. An additional analysis was done using Peg-2b+RBV(>10.6mg/kg/d). Base-case assumed average patient weight of 82kg. EVR, a predictor of SVR, was assessed at week-12 for genotype 1 patients with non-responders discontinuing therapy. Genotype 2/3 patients were assumed to be treated for 24 weeks. Product pricing was based on AWP, June 2004.
RESULTS: Peg-2b+RBV resulted in lower overall cohort treatment costs than Peg-2a+RBV. Results are shown below. Evaluating EVR leads to fewer patient treatment weeks and lower cost per SVR for patients treated with Peg-2b+RBV as compared to Peg-2a+RBV.

Cohort Costs for 100 Hepatitis C Patients

Regimen	EVR	Cohort Cost	Patients with SVR	Cost/SVR
pIFN-alpha2b + RBV 800	0.71	$1,956,508	53.80	$36,368
pIFN-alpha2b + RBV > 10.6	0.74	$2,130,667	59.66	$35,716
pIFN-alpha2a + RBV	0.81	$2,321,372	54.13	$42,887

CONCLUSIONS: These results suggest a cost-benefit to treating HCV patients with Peg-2b+RBV because fewer patients are treated beyond week-12 when achieving treatment success is unlikely.

246E. A comprehensive pooled anaylsis of remission data in depressed patients: venlafaxine versus SSRIs (COMPARE). Charles Nemeroff, M.D., Ph.D.[1], *Richard Entsuah, Ph.D.*[2], Mark Demitrack, M.D.[2], Isma Benattia, M.D.[2], Michael Thase, M.D.[3]; (1)Emory University School of Medicine, Atlanta, GA; (2)Wyeth Research, Collegeville, PA; (3)University of Pittsburgh Medical Center, Pittsburgh, PA.

Presented at the Annual Meeting of the American Psychiatric Association, San Francisco, CA, May 17–22, 2003.

Pharmacoepidemiology

247. Use of metformin in type 2 diabetic patients with heart failure or kidney disease. *Jenifer Wogen, M.S.*[1], Paula Jones, M.S.[1], Edward Banfe, M.B.A.[2]; (1)Novartis Pharmaceuticals Corporation, East Hanover, NJ; (2)Consumer Health Sciences, Princeton, NJ.

PURPOSE: While metformin is often used in the treatment of type 2 diabetes (T2DM), it is contraindicated in patients receiving drug therapy for heart failure (HF) and in kidney disease (KD). This study examined metformin use in T2DM in a US-representative population sample.
METHODS: The National Health and Wellness Survey is a survey of 36,452 adults, conducted in June 2003. Patient self-reported characteristics (age, gender, BMI, medication use, and prior diagnosis of T2DM, HF, and KD) were obtained, using stratified sampling to represent the US population based on age, gender, race/ethnicity, and census region.
RESULTS: 9.74% of respondents reported having type 2 diabetes; 3.69% of T2DM patients reported having KD and 8.65% had HF. Characteristics were similar for patients with KD (mean age=57.8, 49% female, mean BMI=33.8) and without KD (mean age=58.1, 51% female, mean BMI=33.6), except for duration of T2DM (mean=13.2 vs 7.8 years, p<.001). Patients with T2DM and HF were older (mean age=63.1 vs 57.6, p<.001) and more likely to be male (59.5% vs 48.2%, p=.01), had longer diabetes duration (mean=10.3 vs 7.8 years, p<.001) and slightly higher BMI (mean=34.7 vs 33.4, p=.005) than those without HF. Among patients treated with an oral diabetic medication, 23% of KD patients and 49% of HF patients reported using metformin.
CONCLUSIONS: T2DM patients with KD or HF frequently used metformin, suggesting that metformin may often be prescribed inappropriately. Novel therapeutic choices with fewer restrictions may play an important role in the management of T2DM in patients with co-morbidities.

248. Anxiety disorders in the United States 1990–2001: trend in complaint, diagnosis, use of pharmacotherapy, and diagnosis of comorbid depression. *David A. Sclar, B.Pharm., Ph.D.*[1], Thea R. Moore, Pharm.D., BCPP[2], Linda M. Robison, MSPH[1], Tracy L. Skaer, B.Pharm., Pharm.D.[1]; (1)Washington State University, Pullman, WA; (2)Florida A & M University, Tampa, FL.

PURPOSE: To discern the trend in the prevalence and population-adjusted rate of U.S. office-based physician visits documenting a diagnosis of anxiety among patients 18 years of age or older.
METHODS: Data from the National Ambulatory Medical Care Survey for the years 1990-2001, were used for this analysis. Anxiety was defined as ICD-9-CM codes 300.00–300.02. Subcategories included: (1) anxiety, unspecified type; (2) panic disorder; and (3) generalized anxiety disorder (GAD). Office visits resulting in a diagnosis of anxiety were partitioned into six, two-year time intervals for trend analysis.
RESULTS: The annualized mean number of office-based visits documenting a diagnosis of anxiety escalated 70.2%, from 5,739,390 in 1990–91, to 9,765,694 in 2000–01. Nearly half of patients presented with complaint of anxiety as a reason for requesting an office visit, and 42.9% were prescribed an antianxiety medication. A concomitant diagnosis of depression increased from 7.1% to 19.8%. The population-adjusted rate of anxiety increased 1.5–fold, rising from 30.8 office visits per 1,000 U.S. population in 1990–91, to 46.2 per 1,000 in 2000–01. There was a 1.2-fold increase in anxiety of unspecified type, from 23.2 to 27.9 per 1,000; a 2.5-fold increase in panic disorder, from 4.5 to 11.4 per 1,000; and GAD more than doubled, from 3.3 to 7.4 per 1,000.
CONCLUSIONS: Further research is needed to examine whether growth in the rate of anxiety is a result of better recognition of the disorder by physicians, increased awareness by patients, or real growth of anxiety disorders over time.

249. Geographic variation in the prescription of stimulants for attention deficit hyperactivity disorder by U.S. physicians. *Larry W. Segars, Pharm.D., BCPS*, David W. Barnett, Ph.D., M.P.H., Antonio Rene, Ph.D., M.P.H., Kristine Lykens, M.P.A., Ph.D.; University of North Texas Health Science Center-School of Public Health, Fort Worth, TX.

PURPOSE: To determine the potential geographic variation in stimulant prescriptions for the treatment of ADHD by U.S. physicians from the 2001 NAMCS dataset.
METHODS: The study utilized the 2001 multi-stage National Ambulatory Medical Care Survey (NAMCS). U.S. office visits associated with ADHD were identified using DMS-IV diagnosis codes. Stimulant treatment was captured by use of the FDA drug classification code. The dependent variable studied was use of a stimulant to treat ADHD with the independent variables assessed including region of country, age group, sex, ethnicity, race, physician specialty and payment type.
RESULTS: The 2001 NAMCS randomly sampled a weighted national estimate of 880,486,669 physician office visits in the U.S. A weighted estimate of 4,219,759 office visits associated with ADHD were sampled. Compared to psychiatrists, pediatricians were 66% less likely to have treated a patient with ADHD managed by a stimulant medication (OR=0.339; *p*0.048; 95% CI 0.116–0.991). Compared to patients living in the Midwest region of the U.S., those living in the Northeast, South and West were 76% (OR=0.242; *p*=0.014; 95% CI 0.080–0.734), 78% (OR=0.219; *p*=0.007; 95% CI 0.075–0.642), and 90% (OR=0.103; *p*=0.019; 95% CI 0.016–0.670), respectively, less likely to be treated with a stimulant medication.
CONCLUSIONS: Regional differences existed in the use of stimulant medication for treatment of ADHD, with patients living in the Midwest region of the U.S. having the greatest odds of having their ADHD treated with a stimulant medication. In addition, psychiatrists were more likely to treat a patient with ADHD on a stimulant medication.

250E. Aberrant drug-related behaviors in opioid clinical trials. Mary-Ann Zalman, Ph.D., E. Douglas Kramer, M.D., *Robert D. Colucci, Pharm.D.*, Curtis Wright IV, M.D., M.P.H.; Purdue Pharma L.P., Stamford, CT.

Presented at the 66th Annual Scientific Meeting of the College on Problems of Drug Dependence, San Juan, Puerto Rico, June 12–17, 2004.

251E. Antidepressant trends among children and adolescents diagnosed with depression: 1990–2001. Tracy L. Skaer, B.Pharm., Pharm.D., Linda M. Robison, MSPH, *David A. Sclar, B.Pharm., Ph.D.*; Washington State University, Pullman, WA.

Presented at the 44th Annual Meeting of the New Clinical Drug Evaluation Unit, Phoenix, AZ, June 1–4, 2004.

252. Duration of physician visit and management of drug therapy. *Agnes Lo, Pharm.D.*, Kathryn M Ryder, M.D., Ronald I Shorr, M.D.; University of Tennessee Health Science Center, Memphis, TN.

PURPOSE: To determine if the duration of physician visit in ambulatory care setting is influenced by patient age, number and therapeutic class of medications, and co-morbid illness.
METHODS: A cross-sectional study of visits to primary care physicians among adults age > 45 was conducted using 2002 National Ambulatory Medical Care Survey data. Primary endpoint is the time patient spent with physician at each visit. Covariates included for analysis were demographics, insurance, previous visits, major reason for visits, number and therapeutic class of medications, and co-morbid illness. Point estimates were obtained using univariate and multivariate linear regression.
RESULTS: Of 28,738 visits in the dataset, 3089 were included for analysis. The mean time spent with physician was 17.9±8.2 minutes. Elderly patients (age >75) were prescribed more medications than patients age 45–64 and age 65–74, p<0.001. Elderly patients were also receiving more medications that require specific monitoring (warfarin, digoxin, ACE inhibitors, diuretics, and

levothyroxine), p<0.001. Cardiovascular and cerebral vascular diseases were more common in elderly patients than in other groups, p<0.001. Despite these differences, there were no differences in either unadjusted or adjusted duration of physician visit among the groups.

	Time spent with physician			
Age group	45–64	65–74	>75	p value
Unadjusted(mins)	17.82	18.13	18.25	0.2027
Adjusted (mins)	18.07	18.03	18.29	0.5093

CONCLUSIONS: Although elderly patients are at higher risk for drug-related problems than younger patients, the duration of physician visit were similar across the age groups. These findings indicate that there is a need for pharmacist monitor drug therapy in the ambulatory setting.

253. Analysis of potential myopathic drug intereactions between simvastatin and amiodarone, verapamil, niacin or gemfibrozil. *Craig D. Williams, Pharm.D.*[1], Jim Fuller, R.Ph.[1], Jamie Lebeter, Pharm.D.[2]; (1)Purdue University School of Pharmacy, Indianapolis, IN; (2)Hendricks Community Hospital, Indianapolis, IN.

PURPOSE: To screen a large outpatient population for high-risk drug combinations with simvastatin and identify any incidence of myopathy or rhabdomyolysis.
METHODS: Electronic pharmacy and medical record databases for a large, inner-city hospital were screened. The database was queried for all patients prescribed simvastatin 10mg or higher, and any dose of niacin, gemfibrozil, verapamil or amiodarone between October 1, 2001 and October 1, 2002. Electronic medical records were then screened for any elevation of CPK in patients who were on a combination above the simvastatin dosage recommended by the manufacturer.
RESULTS: A total of 19,443 prescriptions for simvastatin were identified in 5,169 patients. 336 patients were on an interacting medication at a higher than recommended dose of simvastatin. Amiodarone and verapamil accounted for 38 and 151 patients respectively while niacin and gemfibrozil accounted for 41 and 108 patients. Five CPK elevations above 10x the upper limit of normal were identified. Four were ruled out as drug induced (two acute MI, one post-trauma, one cocaine intoxication). One patient on verapamil was ruled a possible drug-induced myopathy and did have her simvastatin stopped. However, she was re-initiated on the combination 3 months later and has not had any recurrence of symptoms after more than a year of combined therapy.
CONCLUSIONS: While certain drugs should be used cautiously when combined with higher doses of simvastatin due to the risk of myopathy, we were unable to identify a significant risk from four of these drugs when combined with simvastatin in our health care system.

Pharmacogenomics

254. SNP discovery using denaturing HPLC for the *CACNA1C* gene. *Amber L. Beitelshees, Pharm.D.*, Taimour Y. Langaee, Ph.D., Julie A. Johnson, Pharm.D.; Department of Pharmacy Practice, University of Florida, Gainesville, FL.

PURPOSE: Calcium antagonists are widely prescribed cardiovascular drugs. However, variability in the gene encoding the calcium antagonists' target protein, *CACNA1C*, has not been systematically characterized to date. We undertook a SNP discovery effort to characterize polymorphisms in *CACNA1C* using 20 Native Americans, 20 African Americans, and 20 Caucasians.
METHODS: Using Coriell Cell Repository DNA, we amplified exons and intron/exon junctions of *CACNA1C* using polymerase chain reaction (PCR). We pooled PCR products from the 60 individuals with a reference PCR sample and performed denaturing high performance liquid chromatography (DHPLC) using partially denaturing conditions to screen for variations. We then used direct DNA sequencing to further analyze samples containing heteroduplexes on DHPLC and characterize the nature and exact location of the polymorphisms.
RESULTS: After completing mutation discovery on 22 exons, we have found a total of 18 polymorphisms in *CACNA1C*. Twelve of the polymorphisms are located in intronic regions, just proximal or distal to an exon. Of these 12, ten are single nucleotide polymorphisms (SNPs) and two are insertion/deletions. Six of the 18 polymorphisms are located in exons. One of these is a non-synonymous and 5 are synonymous SNPs. Ten of the polymorphisms (55.5%) are new polymorphisms not found in NCBI's SNP database, dbSNP. Allele frequencies range from less than 1% to 40%.
CONCLUSIONS: The *CACNA1C* gene contains frequently occurring polymorphisms that may play a role in interpatient variability in response to calcium antagonists. Future clinical association studies will be needed to determine the relationship between an individual's genotype and clinical phenotype.

255. Vitamin K epoxide reductase gene polymorphisms rare in warfarin-treated population. *Katherine L. Gaston, B.S.*[1], Christina L. Aquilante, Pharm.D.[2], Taimour Y. Langaee, Ph.D.[1], Larry M. Lopez, Pharm.D.[3], Julie A. Johnson, Pharm.D.[1]; (1)Department of Pharmacy Practice, University of Florida, Gainesville, FL; (2)Department of Clinical Pharmacy, University of Colorado School of Pharmacy, Denver, CO; (3)University of Florida, Gainesville, FL.

PURPOSE: There is wide interpatient variability in sensitivity to warfarin and there is interest in understanding the genetic basis for this variability. Vitamin K epoxide reductase is the therapeutic target of the anticoagulant warfarin. Four single nucleotide polymorphisms (SNPs) within the vitamin K epoxide reductase gene, *VKORC1*, have recently been described in individuals requiring high doses of warfarin (greater than 60 mg/week). We sought to determine whether these SNPs occur, and influence warfarin sensitivity, in a large population of patients receiving stable warfarin therapy.
METHODS: Genetic samples were obtained from 350 patients who were within goal INR range and had stable weekly maintenance doses of warfarin over 3 consecutive clinic visits. We determined genotypes of the four SNPs using polymerase chain reaction (PCR) followed by Pyrosequencing. Allele frequencies were determined using gene counting.
RESULTS: Three hundred fifty patients receiving chronic, stable warfarin therapy were included in the analysis. All 350 patients were genotyped at SNP 1 (G558T) and SNP 2 (T607C), and none carried a variant allele associated with decreased warfarin sensitivity. In addition, 200 patients were genotyped at SNP 3 (A1780G) and SNP 4 (T3860G), and again, none carried a variant allele.
CONCLUSIONS: The four recently described SNPs in *VKORC1* were not present in our large population of patients on chronic warfarin therapy. Our data suggest that these polymorphisms may represent rare mutations rather than SNPs and therefore may not be useful in describing interpatient variability in response to warfarin within the general population.

256. Frequency of P2Y12 haplotype and GPIIb/IIIa genotype in African American and Caucasian populations. *George A. Davis, Pharm.D.*, Jeremy D. Flynn, Pharm.D., Elaina M. Carmichael, B.S., Wendell S. Akers, Pharm.D., Ph.D.; University of Kentucky, Department of Pharmacy Practice and Science, Lexington, KY.

BACKGROUND: The adenosine diphosphate (ADP) P2Y12 and glycoprotein (GP) IIb/IIIa receptors play a pivotal role in platelet aggregation. However, inter-individual differences in ADP-induced platelet aggregation have been associated with haplotypes of the P2Y12 receptor gene (H1 and H2) in Caucasian males. Several polymorphisms of the GP IIb/IIIa receptor have been identified and a common point mutation (PLA2) may be a risk factor for acute coronary syndromes and antiplatelet resistance.
PURPOSE: To identify the frequency of P2Y12 haplotype and GPIIb/IIIa genotype in African American and Caucasian population.
METHODS: In 200 subjects, DNA was analyzed using the polymerase chain reaction (PCR)-restriction fragment length polymorphism (RFLP) protocol. The PCR products were digested with RsaI, MSPI, and NciI restriction enzymes. The substitution of cytosine for thymidine at position 1565 in exon 2 of the GP IIIa gene was analyzed to determine the PLA2 polymorphism. Complete linkage disequilibrium between 4 known single nucleotide polymorphisms (SNP) led to use of the T744C SNP for assessing the P2Y12 H2 haplotype. Frequencies of polymorphisms between populations were analyzed using χ^2.
RESULTS: The frequencies for the P2Y12 haplotype H2 were 18% in Caucasians and 15% in African-Americans. Frequencies for the GPIIb/IIIa genotypes PLA1 and PLA2 were 90% and 10% in both populations, respectively. Frequencies of all polymorphisms were in Hardy-Weinberg equilibrium and no ethnic differences were observed.
CONCLUSIONS: The frequencies of P2Y12 and GPIIb/IIIa receptor polymorphisms can now be used to define the population size needed to evaluate their potential risk in atherothrombosis and clinical response to antiplatelet agents.

257. A global view of thiopurine methyltransferase pharmacogenetics. *Mona K. Patel, B.S.*, Derek J. Van Booven, B.S., Howard L. McLeod, Pharm.D.; Washington University School of Medicine, St. Louis, MO.

PURPOSE: Thiopurine methyltransferase (TPMT) catalyses the S-methylation of 6-thiopurine drugs including 6- mercaptopurine, azathioprine, and 6-thioguanine commonly used in leukemia, immunosuppression after organ transplantation, rheumatoid arthritis, and autoimmune diseases. TPMT enzyme activity is controlled by genetic polymorphisms that contribute to differences in toxicity, metabolism, and clinical efficacy of thiopurine drugs among individuals of various ethnic backgrounds. This study documents frequency of variant TPMT alleles in patient populations from seventeen countries, in order to better plan toxicity avoidance programs around the world.
METHODS: Textmining of PubMed identified journal articles that detailed variant allele frequencies of the TPMT gene, including TPMT*2, TPMT*3A, and TPMT*3C in 5,392 healthy, adult subjects from seventeen different countries on five continents.
RESULTS: There was a great range in the frequency of variant alleles (1% to 10.6%). The geographic area with highest variant allele frequency was

subsaharan African, while the lowest frequencies were observed in Asia. The TPMT*3C allele was the most commonly observed variant in both African and Asian populations, while TPMT*3A was most commonly observed in Europe, North America, and South America.
CONCLUSIONS: Significant geographic variation in TPMT genotype exists. This has significant implications for toxicity avoidance, use in public health initiatives, and will help the planning of cost effectiveness studies.

258. Defining the opportunity for pharmacogenetic intervention in primary care. *Gloria S. Rizkallah, Pharm.D.*[1], Terry L. Seaton, Pharm.D.[1], Abigail M. Woodland, Pharm.D.[1], Howard L. McLeod, Pharm.D.[2]; (1)St. Louis College of Pharmacy, St. Louis, MO; (2)Washington University School of Medicine, St. Louis, MO.

PURPOSE: This was a cohort study to determine the frequency of use of medications under pharmacogenetic influence, including sixteen ADR-associated medications, in the primary care setting.
METHODS: Consecutive patients over 3 months were asked to answer a verbal survey of demographics and medication use during the past 12 months (later verified by chart review). The survery specifically identified 16 drugs known to commonly cause ADRs and undergo metabolism by polymorphic enzymes (previously published). The primary outcome was the frequency of medication use.
RESULTS: Overall, 28.6% of patients took at least one of the ADR-associated medications. Neither gender nor race appeared to influence the frequency of use of these medications (p=0.5 and p=0.08, respectively). Patients taking ≥1 of the drugs were older (p<0.001). More patients seen for a chronic visit took ≥1 of the ADR-associated drugs than patients seen for an acute visit (35.8% vs. 18.5%, p<0.001). Overall, patients reported using medications from 7 commonly prescribed drug classess in the primary care setting, all of which contain agents metabolizing, transporting or targeting genes with known genetic polymorphism.
CONCLUSIONS: The findings indicate that at least 1 in 4 primary care patients take at least one medication that commonly causes adverse drug reactions due to genetic variability in drug metabolism. This represents a minimum, as many other medications are putatively influenced by genetic polymorphism. These findings indicate that there is a role for pharmacogenomics in primary care.

259E. Availability of pharmacogenomics-based prescribing information in drug package inserts for currently approved drugs. *Issam Zineh, Pharm.D.*[1], Tobias Gerhard, B.S.[2], Christina L. Aquilante, Pharm.D.[3], Amber L. Beitelshees, Pharm.D.[1], B. Nhi Beasley, Pharm.D.[4], Abraham G. Hartzema, MSPH, Ph.D.[2]; (1)Department of Pharmacy Practice, University of Florida, Gainesville, FL; (2)Department of Pharmacy Health Care Administration, University of Florida, Gainesville, FL; (3)Department of Clinical Pharmacy, University of Colorado School of Pharmacy, Denver, CO; (4)U.S. Food and Drug Administration, Rockville, M.D.

Presented at the 20th International Conference on Pharmacoepidemiology & Therapeutic Risk Management of the International Society for Pharmacoepidemiology, Bordeaux, France August 22–25, 2004.

260. Verified predominance of slow acetylator phenotype for *N*-acetyltransferase (NAT-2) in a Hmong population residing in Minnesota. *Robert J. Straka, Pharm.D.*[1], R. Todd Burkhardt, Pharm.D.[1], Nicholas P. Lang, M.D.[2], Kelly Z. Hadsall, Pharm.D.[3], Ter Vang, Pharm.D.[1], Michael Y Tsai, Ph.D.[1]; (1)University of Minnesota, Minneapolis, MN; (2)Central Arkansas Veterans Healthcare System, Little Rock, AR; (3)North Memorial Hospital, Robbinsdale, MN.

PURPOSE: Hmong refuges from Laos, have a high prevalence of tuberculosis and select cancers. Slow acetylation (SA) by NAT-2 has been associated with increased risk of hepatoxicity and peripheral neuropathy from isoniazid therapy, and select cancers. Given that previous work (Straka J. Clin Pharmacol 1996) indicated a phenotypic predominance of slow acetylators (74.5%) in Hmong relative to that predicted in other Asian groups, such as Thai (36%) or Koreans (9.6%), this study sought to independently confirm or refute this unexpected observation of slow acetylator metabolism phenotype.
METHODS: Unrelated male and female Hmong between 18 and 65 years of age residing in Minneapolis-St. Paul consented to participate in this study then ingested a 12oz can of Coca-Cola® prior to collecting urine for 8 hours. Urinary molar ratios (MR) of the caffeine metabolites (AFMU/1X) were measured by HPLC to identify SA (MR<0.6) or rapid acetylator (RA) (MR>=0.6) status.
RESULTS: Forty-eight SA (90.4%) and 5 RA (9.6%) subjects were identified among 53 analyzable samples provided by 60 participants (27 male, 33 female, mean (±sd) age 30±10 years). This 90.4% slow acetylator prevalence from this study exceeds the 74.5% SA noted in 98 subjects from our previous (1996) study (p<0.02 by χ^2 test).
CONCLUSIONS: This study confirms the predominance of slow acetylators within the Minneapolis-St. Paul Hmong community.
INTERPRETATION: Based on this confirmation, genotypic analysis in the same population is planned in order to understand the genetic mechanism for this unusual phenotypic pattern of acetylation.

Pharmacokinetics/Pharmacodynamics/ Pharmacometrics/Drug Metabolism/ Drug Delivery

261. Twenty-four hour tolbutamide plasma concentration as a phenotypic measure of CYP2C9 activity in humans. *Craig R. Lee, Pharm.D.*[1], John A. Pieper, Pharm.D., FCCP, BCPS[2], Roy L. Hawke, Pharm.D., Ph.D.[1], Alan L. Hinderliter, M.D.[1], Joyce A. Blaisdell, B.S.[3], Joyce A. Goldstein, Ph.D.[3]; (1)UNC-Chapel Hill, Chapel Hill, NC; (2)University of New Mexico, Albuquerque, NM; (3)National Institute of Environmental Health Sciences, RTP, NC.

PURPOSE: To determine if 24-hour tolbutamide plasma concentrations (TOL_{24}) significantly correlate with other validated phenotypic measures of CYP2C9 activity in humans.
METHODS: Sixteen healthy volunteers with *CYP2C9*1/*1* (n=5), **1/*2* (n=5), **1/*3* (n=5), and **2/*2* (n=1) genotypes received a single oral tolbutamide 500-mg dose, with plasma and urine samples collected over 24 hours. Tolbutamide, 4-hydroxytolbutamide (4-OH) and carboxytolbutamide (COOH) concentrations were determined by high performance liquid chromatography. Calculated phenotypic measures included: tolbutamide area under the plasma concentration-time curve ($AUC_{0-\bullet}$), oral clearance (CL_o), formation clearance to 4-OH + COOH (CL_{form}), and the cumulative urinary amount of 4-OH + COOH excreted from 0–12 hours ($A_{e,4+C,0-12}$). Correlations between phenotypic parameters were completed by orthogonal regression. Statistical comparison of TOL_{24} across genotype was completed by analysis of variance and the post-hoc Tukey test.
RESULTS: TOL_{24} demonstrated a statistically significant correlation with CL_{form} (r=0.87, p<0.001), which was slightly stronger than observed between $A_{e,4+C,0-12}$ and CL_{form} (r=0.84, p<0.001), previously identified as the best urinary CYP2C9 phenotypic measure. Significant correlations between TOL_{24} and both $AUC_{0-\infty}$ (r=0.98, p<0.001) and CL_o (r=0.96, p<0.001) were also observed. Moreover, a significant association between *CYP2C9* genotype and TOL_{24} was present (r^2=0.80, p<0.001), with statistically significant differences between *CYP2C9*1/*1*, **1/*2*, and **1/*3* individuals (mean±SD: 5.9±1.0 vs. 12.0±4.3 vs. 17.7±1.5 µg/ml, p<0.05 between each group), respectively.
CONCLUSIONS: TOL_{24} strongly correlated with CL_{form}, CL_o, and $AUC_{0-\infty}$, and significantly differentiated among individuals of diverse *CYP2C9* genotype. TOL_{24} is an easily obtainable phenotypic measure of CYP2C9 activity with potential clinical utility. Future study in larger populations is warranted.

262. Dynamic effects of interferon-beta (IFN-β) on multiple sclerosis patients differing in anti-IFN-β neutralizing antibody status. *Roseane M. Santos-DeSavoy, B.S., M.S.*[1], Bianca Weinstock-Guttman, M.D.[2], Murali Ramanathan, Ph.D.[1]; (1)Univerty at Buffalo, Amherst, NY; (2)Jacobs Neurological Institute, Buffalo, NY.

IFN-β is an immunomodulatory drug widely used for the treatment of relapsing-remitting form of multiple sclerosis (RR-MS). However, only 30% of M.S. patients respond well to IFN-β therapy. The clinical relevance of neutralizing antibodies (NAB), which can cause partial responsiveness, is not well established.
PURPOSE: The objective was to determine whether the dynamics of gene expression induced by IFN-β differ in the presence or absence of NABs. Ten RR-MS patients (6 F, 4 M, 45–57 years) with known previous history of NAB status (four were previously NAB positive, five were NAB negative and one was persistently positive) were enrolled.
METHODS: Blood samples were collected at 0, 4, 8, 24 and 168 hours after the first intra-muscular dose of 30 mg of INF-β1a. Total RNA from mononuclear cells was prepared (TRI Reagent method) and reverse transcribed into cDNA. The mRNA levels of 8 genes were measured (Beta-actin, beta-2-microglobulin, STAT1, Mx1, Mx2, TRAIL, IL-8, MMP9) using real-time PCR with Taqman probes.
RESULTS: The results show that early rather than later measurements are more sensitive to NAB status with maximum effect occurring at 4 hours. NAB positive patients did not show any gene expression responses but patients who were previously NAB positive recover their responses; however, there is a trend toward lower values in these patients compared to NAB negative patients, notably for STAT1, TRAIL and Mx1.
CONCLUSIONS: These findings highlight the usefulness of the gene expression profiling to delineate response differences between individual MS patients for the clinically relevant NAB problem.

263E. Pharmacokinetics of enoxaparin in multiple trauma patients. *Curtis E Haas, Pharm.D., BCPS*, Jamie L Nelsen, Pharm.D., Krishnan Raghavendran, M.D., Lydia Lin, Pharm.D., Qing Ma, Ph.D., Alan Forrest, Pharm.D.; Univerisity at Buffalo, Buffalo, NY.

Presented at the 63rd Annual Meeting of the American Association for Surgery of Trauma, Maui, HI, September 29–October 2, 2004.

264. Estimation of creatinine clearance in moderate to severe liver impairment. David E. Nix, Pharm.D.[1], Paul Nakazato, M.D.[2], Jeffrey F. Barletta, Pharm.D.[3], Kathryn R. Matthias, B.A.[1], Todd S. Krueger, Pharm.D.[4],

Brian L. Erstad, Pharm.D.[1]; (1)University of Arizona College of Pharmacy, Tucson, AZ; (2)Paul Nakazato, M.D., PC, Tucson, AZ; (3)Spectrum Health, Grand Rapids, MI; (4)University of Missouri - Kansas City, Kansas City, MO.

PURPOSE: To develop an equation to predict creatinine clearance (CLcr) in adults with moderate to severe hepatic impairment, and to determine the reliability of serum and urine assays for creatinine in this population.
METHODS: Two sequential 24 h urine collections and three serum samples were collected for determination of creatinine excretion and CLcr. Creatinine in both matrixes was determined by automated chemistry (clinical laboratory) and HPLC. Predictive covariates were evaluated using step-wise multiple regression and NONMEM.
RESULTS: A total of 27 evaluable patients completed the study. Mean age was 49 in males and 53 in females, and mean weight was 76 and 69 kg, respectively. The mean bilirubin was 6.9 mg/dl, albumin was 2.3 g/dl and INR was 2.0. Estimated creatinine excretion was = 282 + ABW◊11.1–314 (if female) mg per 24 h. Mean measured CLcr was 82 ml/min in males and 61 ml/min in females. Using NONMEM for model building, CLcr could be estimated using the following equations: Male CLcr = 4.69/(sCr x (ABW/70)) and Female CLcr = 4.69 x 0.658/sCr. Other more complex candidate models were also developed. Serum creatinine was over-predicted at low concentrations and under-predicted at higher concentrations using the Jaffe method (routine clinical assay). Urine creatinine concentration tends toward over-prediction at lower creatinine concentrations.
CONCLUSIONS: Creatinine excretion and clearance were associated with weight in males but not in females. The new estimation equations provide much less bias than the Cockcroft-Gault equation. Creatinine concentrations determined by clinical autoanalyzer may not be reliable.

265E. Evaluation of precipitated withdrawal in opioid-dependent volunteers given hydrocodone and naltrexone. Donald Jasinski, M.D.[1], *Robert D. Colucci, Pharm.D.*[2], Robert F. Kaiko, Ph.D.[2], Curtis Wright IV, M.D., M.P.H.[2], Christopher D. Breder, M.D., Ph.D.[2], John C. Messina Jr., Pharm.D.[2]; (1)Johns Hopkins Bayview Medical Center, Baltimore, M.D.; (2)Purdue Pharma L.P., Stamford, CT.

Presented at the 66th Annual Scientific Meeting of the College on Problems of Drug Dependence, San Juan, Puerto Rico, June 12–17, 2004.

266E. Pharmacodynamics of antimicrobials against Gram-negative bacteria in pediatric patients: a report from the OPTAMA Program. *Jennifer M. Ellis, Pharm.D.*[1], Joseph L. Kuti, Pharm.D.[2], David P. Nicolau, Pharm.D.[2]; (1)University of Connecticut School of Pharmacy, Storrs, CT; (2)Center for Anti-Infective Research and Development, Hartford Hospital, Hartford, CT.

Presented at the Annual Meeting of the Investigational Disease Society of America, Boston, MA, September 30–October 3, 2004.

267E. Utilization of cyclosporine C2 monitoring in stable Asian transplant patients. *LanChi L. Bui, Pharm.D.*, Tung T. Huynh, Pharm.D., Sean Cao, M.D.; University of California, Irvine Medical Center, Orange, CA.

Presented at the 20th International Congress of the Transplantation Society, Vienna, Austria, September 5–10, 2004.

268. HPLC assay of fluconazole and its application to patients with early septic shock. Mahasen A Radwan, Ph, D[1], *Nouf M Aloudah, M.S.*[2]; (1)King Saud University, Riyadh, Saudi Arabia; (2)King Saud University, Riyadh, AL, Saudi Arabia.

PURPOSE: This work describes a simple and rapid HPLC method for determination of fluconazole in plasma samples in patient suffering from early septic shock.
METHODS: The separation was done using HPLC system with UV absorbance detector. The mobile phase consisted of acetonitrile (20%) in 0.05M ammonium acetate containing 0.1% triethylamine; acetic acid was used to adjust the pH to 7 before the addition of acetonitrile. Sample run time was 11.5 min. Metoclpramide was used as the assay internal standard (IS).Using the chromatographic conditions described, fluconazole and metoclopramide were well resolved with mean retention times of 6.3 and 8.8 min, respectively. Linear response (r>0.995) was observed over the range of 0.5 to 15 µg/ml of fluconazole.
RESULTS: There was no significant difference ($p<0.05$) between inter and intra day studies for fluconazole. The mean relative standard deviation (RSD %) of the results of within day precision and accuracy of the drug were 7.6, the results confirmed the reproducibility of the assay method.The applicability of the assay was demonstrated in measuring fluconazole pharmacokinetics in human plasma after intravenous infusion of fluconazole to patient with early septic shock. The elimination half life was 12.3 ±9.03h after single dose and 41.3 ± 19.99h after repeated doses.
CONCLUSIONS: This work describes a simple and rapid HPLC method for determination of fluconazole in plasma samples with enough sensitivity to monitor some patient suffering from early septic shock.

269E. Compartmental analysis of amprenavir pharmacokinetics including secondary peaks. *Olanrewaju O. Okusanya, Pharm.D.*[1], Alan Forrest, Pharm.D.[1], Michael F Para, M.D.[2], Elizabeth Adams, M.D.[3], Kelvin E. Yarasheski, Ph.D.[4], Sue Rosenkranz, Ph.D.[5], Richard C. Reichman, M.D.[6], Gene D. Morse, Pharm.D.[1]; (1)University at Buffalo, Buffalo, NY; (2)Ohio State University, Columbus, OH; (3)NIH, Bethesda, M.D.; (4)Washington University School of Medicine, St. Louis, MO; (5)Harvard University, Boston, MA; (6)University of Rochester, Rochester, NY.

Presented at the 8th World Congress on Clinical Pharmacology and Therapeutics, Brisbane, Australia, August 1–6, 2004.

270E. Development of a pharmacokinetic/pharmacodynamic model to characterize the in vitro activity and dose-response relationships of daptomycin and linezolid using subpopulation analysis. Patrick F. Smith, Pharm.D., *Sanela Bilic, Pharm.D., M.B.A.*, Brent M. Booker, Pharm.D., A. Forrest, Pharm.D.; University at Buffalo, School of Pharmacy and Pharmaceutical Sciences, Amherst, NY.

Presented at the 14th European Conference of Clinical Infectious Disease, Prague, Czech Republic, May 1–4, 2004.

271E. Optimal sampling strategies (OSS) for sparse PK evaluation of multi-drug anti-HIV regimens. *Qing Ma, Ph.D.*[1], Alan Forrest, Pharm.D.[1], Olanrewaju O. Okusanya, Pharm.D.[1], Sue Rosenkranz, Ph.D.[2], Michael F. Para, M.D.[3], Elizabeth Adams, M.D.[4], Kevin E. Yarasheski, Ph.D.[5], Richard C. Reichman, M.D.[6], Gene D. Morse, Pharm.D.[1]; (1)University at Buffalo, Buffalo, NY; (2)Harvard University, Boston, MA; (3)Ohio State University, Columbus, OH; (4)NIH, Bethesda, M.D.; (5)Washington University School of Medicine, St. Louis, MO; (6)University of Rochester, Rochester, NY.

Presented at the 8th World Congress on Clinical Pharmacology and Therapeutics, Brisbane, Australia, August 1–6, 2004.

272E. Variability in efavirenz concentrations predicts virologic outcome in HIV-infected children. *Richard C. Brundage, Pharm.D., Ph.D.*[1], Florence H. Yong, M.S.[2], Terence Fenton, Ph.D.[3], Stephen A. Spector, M.D.[4], Stuart E. Starr, M.D.[5], Courtney V. Fletcher, Pharm.D., Ph.D.[6]; (1)University of Minnesota, Minneapolis, MN; (2)Genzyme Corporation, Cambridge, MA; (3)Harvard School of Public Health, Boston, MA; (4)University of California, San Diego, San Diego, CA; (5)University of Pennsylvania, Philadelphia, PA; (6)University of Colorado, Denver, CO.

Presented at the 7th Conference on Retroviruses and Opportunistic Infections, San Francisco, CA, January 30, 2000.

273. Removal of non-discrete MIC values: impact on Monte Carlo (MC) analysis. Roger L. White, Pharm.D.[1], *Kiran K. Ubhi, Pharm.D.*[1], Lawrence Friedrich, Pharm.D.[2]; (1)Medical University of South Carolina, Charleston, SC; (2)Bristol-Myers Squibb, Charleston, SC.

PURPOSE: MIC datasets often contain non-discrete (≤ or > an MIC) values. Previous studies found bias in antibiotic use-susceptibility relationships when non-discrete values were removed ("censored"); however, no MC analysis studies have been done. We assessed deletion of non-discrete MIC values on MC target attainment (TA) rates.
METHODS: MICs of ciprofloxacin (C), levofloxacin (L) and gatifloxacin (G) for 2,382 isolates [114 A. baumannii (AB), 100 E. aerogenes (EA), 300 E. cloacae (EC), 643 K. pneumoniae (KP), 870 P. aeruginosa (PA), 240 S. marcescens (SM), 115 S. maltophilia (Smal) were determined. Simulations of AUC distributions using our institution's patient CrCl range for IV C400 mg q8–12h, L500–750 mg q24h, G400 mg q24h were performed. TA rates (at AUC/MIC≥100) were assessed for the full and deleted MIC populations.
RESULTS: Non-discrete MICs (% of isolates) were: AB(65%), EA(80%), EC(79%), KP(72%), PA(24%), SM(12%), Smal(18%). TA with the full MIC range was: EA (0.85–0.92), EC(0.84–0.90), KP(0.81–0.87), SM(0.72–0.90), AB(0.25–0.41), PA(0.13–0.56), and Smal(0.02–0.42). Deletion of non-discrete MICs lowered TA by 16–51% for EA, EC, and KP, however, TA increased for AB and PA by 8–55%. SM and Smal were unaffected.
CONCLUSIONS: Non-discrete MIC values can have a major impact on the outcome of MC analysis. The impact depends on the number of removed values, the proportion at each end of the MIC distribution, drug AUCs, and target AUC/MICs. Removal of these values, especially if they occur in a critical range with resultant AUC/MICs near a desired target, may severely bias TA rates.

274E. Population pharmacokinetics of troxacitabine. *Carlton K.K. Lee, Pharm.D., M.P.H.*[1], Francis Giles, M.D.[2], Malcolm J. Moore, M.D.[3], Ed Chu, M.D.[4], Manuel Hidalgo, M.D.[5], Edmund Capparelli, Pharm.D.[6], Jacques Jolivet, M.D.[7], Sharyn D. Baker, Pharm.D.[5]; (1)Department of Pediatrics, Johns Hopkins University & Department of Pharmacy, The Johns Hopkins Hospital, Baltimore, M.D.; (2)The University of Texas M.D. Anderson Cancer Center, Houston, TX; (3)Princess Margaret Hospital, Toronto, ON, Canada; (4)Yale Cancer Center, VA Connecticut Healthcare System, West Haven, CT; (5)The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, M.D.; (6)Pediatric Pharmacology Research Unit, University of California at San Diego, La Jolla, CA; (7)Shire Pharmaceuticals, Laval, QC, Canada.

PURPOSE: Troxacitabine (TROX) is a L-cytidine analogue anticancer agent currently in phase II/III trials. The study's objective is to develop & validate a population pharmacokinetic (PPK) model for TROX.
METHODS: Plasma samples from 111 cancer patients receiving IV doses of 0.12–12.5 mg/m2 were used to develop the PPK model with NONMEM. About 13 samples per patient were obtained from the 1st dose. 2 covariate groups (I: BSA, SEX, AGE, SCR; II: WT, HT, SEX, AGE, SCR) & PK parameters were evaluated by linear multiple regression. The 2 final PPK models were validated by internal & external methods.
RESULTS: TROX PPK was characterized by a 3-compartment model, exponential interpatient variability (IPV) error model, combination residual error model, & FOCE INTER estimator method. Clearance was influenced by BSA (27% decrease IPV) or WT (20% decrease IPV). Central compartmental volume was influenced by BSA (12% decrease IPV). Model validations reveal both final models accurate in predicting plasma TROX concentrations with improved PK parameter predictions with the addition of covariates.
CONCLUSIONS: Covariate modeling supports the use of BSA in current dosing strategies for TROX.
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275. Oral and IV oxymorphone clinical pharmacokinetics (PK) compared to those of oral oxycodone pharmacokinetics. *Vijay Vashi, Ph.D.*[1], Terry Nichols, M.Sc.[2], Gill Mundin, BSc(Hons)[2], Tammy McIver, M.Sc.[2], Kevin Smith, Ph.D.[2]; (1)Purdue Pharma LP, Stamford, CT; (2)Napp Pharmaceuticals Research Limited, Cambridge, United Kingdom.

PURPOSE: A study was designed to investigate the PK characteristics of oral and i.v. administered oxymorphone. The oxymorphone PK data were then compared and contrasted with oxycodone data from previous studies.
METHODS: Fourteen healthy male subjects participated in a 4-part, single-dose crossover study. Subjects were randomized to receive 0.6 mg oxymorphone i.v., or 3 mg, 6 mg and 9 mg oxymorphone oral solution. Blood sampling was conducted up to 72-hours following administration, and each treatment was separated by a 7-day washout period.
RESULTS: Following oral administration, plasma oxymorphone concentrations were typically low (less than 1 ng/ml) and it was only possible to determine areas under the plasma concentration-time curve (AUC) over a limited period. Mean absolute bioavailabilities of 3.8, 4.9 and 7.2% were associated with the 3, 6 and 9 mg oral doses, respectively. The oral oxymorphone treatments were also associated with a high degree of inter-subject variability; coefficients of variation (CV) of 77%, 75% and 55% following the 3, 6 and 9 mg oral doses. These very low absolute bioavailabilities of oxymorphone contrasts markedly with those of oxycodone, where mean estimates of 46–87% have been reported. Consequently, oxycodone is associated with a low degree of inter-subject variability. Based on a review of 5 studies a mean CV of 34% is associated with the AUC.
CONCLUSIONS: The more consistent pharmacokinetic profile of oxycodone compared to oxymorphone, (higher oral bioavailability and much lower inter-subject variability), may allow for a greater consistency in analgesia when titrating individual patients to optimum pain control.

276E. A novel approach to "humanize" plasma drug concentration profiles for small animal models. *Alan Forrest, Pharm.D.*[1], Olanrewaju O. Okusanya, Pharm.D.[1], Dennis Girard, Ph.D.[2], Brent M. Booker, Pharm.D.[1], Sujata M. Bhavnani, Pharm.D.[3], Paul G. Ambrose, Pharm.D.[3]; (1)SUNY-Buffalo School of Pharmacy and Pharmaceutical Sciences, State University of New York at Buffalo, Amherst, NY; (2)Pfizer Global Research & Development - Groton Laboratories, Groton, CT; (3)Cognigen Corp., Buffalo, NY.

Presented at the 8th World Congress on Clinical Pharmacology and Therapeutics, Brisbane, Australia, August 1–6, 2004.

277. A pharmacokinetic (PK) model for nelfinavir (NFV) and M8 when coadministered with amprenavir (APV) and efavirenz (EFV). *A. I. Chen, Pharm.D.*[1], A. Forrest, Pharm.D.[2], R. DiCenzo, Pharm.D.[1], S. Rosenkranz, Ph.D.[3], M.F. Para, M.D.[4], K.E. Yarasheski, Ph.D.[5], R.C. Reichman, M.D.[6], G.D. Morse, Pharm.D.[1]; (1)SUNY-Buffalo School of Pharmacy, Buffalo, NY; (2)University at Buffalo, School of Pharmacy and Pharmaceutical Sciences, Amherst, NY; (3)Harvard University, Boston, MA; (4)Ohio State University, Columbus, OH; (5)Washington University School of Medicine, St. Louis, MO; (6)University of Rochester, Rochester, NY.

PURPOSE: The purpose of this analysis is to model the PK of NFV & its metabolite, M8, in the presence of APV & EFV
METHODS: In A5043, 14 HIV-seronegative subjects received EFV 600mg po qDx21D, APV 600mg po BIDx11D & NFV 1250mg po BIDx7D. Plasma was obtained (10 samples in 12 h), assayed for NFV & M8 (LCMSMS) & fit by PK models, using weighted nonlinear regression (ADAPT II). Model discrimination was by Akaike's Information Criterion.
RESULTS: The NFV data were best fit by a linear 2 compartment model with 1st order absorption following a fitted lag time; M8 was fit by a linear 1 compartment model with 1st order formation (ClNM8). Mean (CV%) fitted values, for NFV, included total distribution volume (Vss), clearance (Clt), distributional ($aT_{1/2}$, h) & terminal half-lives (bT1/2, h) &, for M8, included distribution volume (VdM8) & clearance (CltM8). Volumes are in L, clearances in L/h (all conditioned on NFV bioavailability); CLNM8, VdM8 & CltM8 are also conditioned on fraction of NFV metabolized to M8:

Vss	Clt	$aT_{1/2}$	$bT_{1/2}$	CLNM8	VdM8	CLtM8
406(16)	43.7(13)	1.34(42)	46.5(47)	6.58(37)	24.3(121)	36.0(32)

Fits were good but M8 troughs tended to be overestimated & peaks were underestimated.
CONCLUSIONS: NFV PK is well-described by this model; M8 may require a model with saturable elimination. The long bT1/2 appears to be drug re-distributing from the peripheral compartment. This model may allow a more appropriate analysis of NFV/M8 disposition, especially when combined with intracellular data, in future studies.

278. Evaluation of ketorolac transdermal systems using rats. *Hyesun Gwak, Pharm.D., Ph.D.*, Youngah Cho, M.S.; College of Pharmacy, Chosun University, Gwangju, South Korea.

PURPOSE: To determine pharmacokinetic profiles of formulated ketorolac transdermal systems and compare with those of oral administration.
METHODS: Male Sprague-Dawley rats weighing 280–320 g were divided into three groups, comprising 6 rats each. Ketorolac tromethamine was administered by oral (2487 μg/kg), transdermal delivery system (TDS) 1 (2101 μg/kg) and TDS 2 (2392 μg/kg) administration. Diethylene glycol monoethyl ether (DGME)-propylene glycol monolaurate (PGML) and DGME-propylene glycol monocaprylate (PGMC) at the ratio of 4 : 6 were employed as a penetration enhancer for TDS 1 and TDS 2, respectively. Serum samples (0.1 ml) were collected from the femoral artery cannula before and 0.25, 0.5, 1, 2, 4, 6, 8, 12, and 24 hr after drug administration and analyzed by HPLC.
RESULTS: Lower C_{max} and prolonged T_{max} of ketorolac were observed with transdermal administration; C_{max} and T_{max} by oral, TDS 1 and TDS 2 administration were 4182.6 ng/ml and 0.25 hr, 2524.9 ng/ml and 2.0 hr and 1733.7 ng/ml and 3.3 hr, respectively. The AUC values obtained by TDS 1 (14721 ng•hr/ml) and TDS 2 (14797 ng•hr/ml) were comparable with oral administration (15704 ng•hr/ml) whereas half-life by TDS administration increased from 3.6 to 6.7 hr, compared to oral administration.
CONCLUSIONS: Ketorolac TDS using DGME-PGMC or DGME-PGML at the ratio of 4 : 6 as a penetration enhancer showed comparable AUC, prolonged half-life and Tmax and decreased C_{max} compared to oral delivery.

Pharmacy Administration

279. Field based medical liaison job satisfaction. Cathleen M. Sass, M.B.A., Pharm.D.[1], *Erin L. Albert, RPh, M.B.A.*[2]; (1)Procter & Gamble Pharmaceuticals, Cincinnati, OH; (2)Sepracor, Indianpolis, IN.

PURPOSE: The field based Medical Liaison (ML) is well established within the pharmaceutical industry. However, not much attention has been focused on the level of job satisfaction associated with this role.
METHODS: A 29 question survey on job satisfaction was developed. It was posted on a web-based survey host site for 4 months in 2004 and received 130 responses.
RESULTS: The majority of MLs have a pharmacy degree (77%). MLs are generally satisfied with their current position (85%). Higher satisfaction was reported when fewer therapeutic areas are covered. Job satisfaction did not correlate with salary. The male respondents (51%) received higher salaries. Intellectual challenge was rated as the most important component of the job (56%). Both genders ranked working for a company that will develop me as the next important component (21%), closely followed by flexible scheduling for women. The most common elements of the position that respondents are least happy with were: compensation/bonus (38%) and unclear direction from company on future options (22%). Not surprisingly, those that ranked their satisfaction level as very or somewhat dissatisfied are more likely to be seeking other employment.
CONCLUSIONS: Salary is not the most important factor when considering job satisfaction for MLs. Intellectual challenge and professional development are critical components. Managers must identify which factors the individual values and address those issues to increase job satisfaction and retention.

280. Impact of the Medicare Prescription Drug, Improvement, and Modernization Act (MMA) of 2003 in low-income patients receiving pharmaceutical company assistance for medications. *Dawn E. Havrda, Pharm.D.*[1], Estee Graves, Pharm.D. candidate[1], William Bender, M.D.[2], Beth A. Omundsen, M.D.[2]; (1)Bernard J. Dunn School of Pharmacy, Shenandoah University, Winchester, VA; (2)Amherst Family Practice, Winchester, VA.

PURPOSE: To evaluate the effect of MMA2003 drug discount cards(DDC) and prescription drug benefit(PDB) in low-income patients receiving pharmaceutical company assistance(PCA) for medication, and to compare projected benefits of MMA to PCA.
METHODS: Medicare patients obtaining 1+ medications (oral/inhaled) through PCA within 6months were included. Information obtained included: household size, total yearly income, medication/dosage. Cash prices obtained

through www.drugstore.com; eligibility/details of DDC and PDB obtained from MMA; discounts for DDC obtained from www.medicare.gov. Paired *t*-tests and Mann-Whitney test were used for continuous and categorical data, respectively.
RESULTS: 137 patients met eligibility. 79.4% qualified for $600credit with DDC; 85.4% for low-income benefits with PDB. Mean number of medications taken was 5.3±2.4 with 3.1±1.8 from PCA. With PCA, total yearly cost of medications was $778.01±931.35 compared to estimated cash cost of $3443.74±1903.39 (p<0.001). Use of PCA resulted in significantly greater yearly savings (76.2%±23.2) versus DDC (25.9%±20.7, p<0.0001) compared to cash costs for all patients. $600credit with DDC would last 3.2±2.6 months for eligible patients and still resulted in yearly costs of $2629.22±1743.93. Patients with total yearly income meeting federal poverty level (FPL)<135% had more savings with PDB (94.2%±2.3, p<0.0001) compared to PCA; patients with FPL>135% incomes had less cost-savings with PDB (39.0%±18.8, p<0.0001) compared to PCA.
CONCLUSIONS: PCA will result in less yearly drug costs for low-income patients compared to DDC including those eligible for $600credit. Low-income patients meeting FPL<135% income will benefit from the PDB, however patients with greater incomes may benefit more from PCA versus PDB.

281. Evaluating a pharmacy-managed medication assistance program in a university hospital setting. *Matthew Strum, Pharm.D., CDE*, Brittany N. Harris, Pharm.D., candidate, Donna S. West, Ph.D.; University of Arkansas for Medical Sciences, Little Rock, AR.

PURPOSE: The purpose of this evaluation was to determine the economic impact of a pharmacy-managed medication assistance program (MAP) in a University hospital setting. The MAP utilizes pharmaceutical manufacturer assistance programs to obtain medications for qualifying patients.
METHODS: The MAP database and the outpatient pharmacy prescription database were used to examine utilization and cost data for patients who received medications through the program during calendar year 2003. Data collected included the following: total number of patients, total number of prescriptions, total service fees collected, and total costs of drugs dispensed through MAP. These data were assessed to determine the expenses avoided by the hospital. Conservative calculations were used to estimate hospital days saved by providing medications for home use (e.g., Lovenox, IV antibiotics). Descriptive statistics are reported.
RESULTS: During 2003, the UAMS outpatient pharmacy filled 42,930 prescriptions for 2458 patients on the MAP. $182,000 in administration fees were collected. Based on actual drug cost to the outpatient pharmacy, the total expense avoided by utilizing MAP was $958,323, saving patients over $1.2 million on prescriptions during the year. Over 1500 patient hospital days were saved through the Lovenox program, and an additional 1200 days were saved by sending patients home on IV antibiotics.
CONCLUSIONS: The MAP has been able to provide prescription medications to an indigent population at little cost while saving the outpatient pharmacy almost $1,000,000 in pharmaceutical costs. Further investigation is needed to determine the clinical impact of the MAP.

Psychiatry

282E. Effect of ziprasidone initial dosing on discontinuation in schizophrenia. *Amie T. Joyce, M.P.H.*[1], Daniel A. Ollendorf, M.P.H.[1], David J. Harrison, Ph.D.[2]; (1)Pharmetrics, Inc, Watertown, MA; (2)Pfizer Inc, New York, NY.

Presented at the 24th Congress of the Collegium Internationale Neuro-Psychopharmacologicum, Paris, France, June 20–24, 2004.

283. Differential rates of clinical trial discontinuation as a measure of treatment effectiveness among antipsychotic medications. *Bruce J Kinon, M.D.*, Hong Liu-Seifert, Ph.D.; Eli Lilly and Company, Indianapolis, IN.

PURPOSE: Antipsychotic treatment discontinuation may be used to measure overall treatment effectiveness. Few studies systematically assess early treatment discontinuation differences among antipsychotics. We investigate olanzapine discontinuation compared to other atypical antipsychotics.
METHODS: A post hoc, pooled analysis of 4 randomized, double-blind clinical trials of 24–28 week duration included 822 olanzapine-treated and 805 risperidone-, quetiapine-, or ziprasidone-treated patients. Discontinuation rate difference was assessed using Fisher's exact test comparing olanzapine to the other atypicals combined. Kaplan-Meier estimators for probability of staying in treatment were obtained for both groups and treatment difference investigated by the log-rank test.
RESULTS: Olanzapine-treated patients were significantly more likely to complete treatment (53.9% vs. 39.3%, p<0.001) and stayed in treatment longer (19.1 vs. 16.1 weeks, p<0.0001) than other atypical-treated patients. Treatment difference was primarily driven by differential discontinuation rates due to poor response/symptom worsening (olanzapine 14.23% vs. other 24.60%, p<0.0001). There was no difference in discontinuation due to medication intolerability or other reasons.
CONCLUSIONS: The predominant reason for difference in early discontinuation between olanzapine and other antipsychotics was significantly higher dropouts due to poor response/symptom worsening with the other antipsychotics. Early treatment discontinuation may be an important gauge of relative treatment effectiveness among antipsychotics.

284. Outpatient care for bipolar disorder in the United States, 1997–2001. David L. Van Brunt, Ph.D., Michael D. Stensland, Ph.D., *Woodie M. Zachry, Pharm.D.*; Eli Lilly and Company, Indianapolis, IN.

PURPOSE: To describe the burden of care for bipolar disorder in outpatient medical practice in the United States.
METHODS: Data for 5 years (1997–2001) of the National Ambulatory Medical Care Survey (NAMCS) and National Hospital Ambulatory Medical Care Survey (NHAMCS) were pooled for analysis and weighted to provide unbiased national estimates. Summary statistics were computed to examine visit rates, payer source, major reason for visit, and provider specialty.
RESULTS: There were an estimated 19.4 million visits with a recorded bipolar diagnosis, representing 0.39% of all outpatient visits for the period. The majority of bipolar visits were to psychiatrists (82.3%), with bipolar visits constituting 10.7% of all visits to psychiatrists. 14.2% of bipolar visits were to primary care specialists. The most common major reason for a bipolar visit was routine follow-up for a chronic problem (64.4%), followed by flare-up for a chronic problem (17.2%). This was in contrast to the general population where the most common reason for visit was an acute problem (35.6%), followed by routine follow-up for chronic problems (28.2%). The primary payment source for bipolar visits was private insurance (41.2% vs. 53.2% in the general population), but with more visits reported as "self-paid" (18.2% vs. 7.2%). Medicare/Medicaid rates were similar (29.7% vs. 29.8%).
CONCLUSIONS: Visits for bipolar disorder take up less than 1% of health care visits overall, but comprise over 10% of visits to psychiatrists. Visits for bipolar disorder are more frequently self-paid than healthcare visits in general.

285. Atypical antipsychotic treatment in Alzheimer's disease: effect on cognition. *Joshua Caballero, Pharm.D.*[1], Michael Hitchcock, B.S.[1], Douglas Scharre, M.D.[2], David Beversdorf, M.D.[2], Milap C Nahata, Pharm.D., FCCP[3]; (1)The Ohio State University, College of Pharmacy, Columbus, OH; (2)The Ohio State University, Department of Neurology, Columbus, OH; (3)The Ohio State University College of Pharmacy, Columbus, OH.

PURPOSE: Approximately 60% of the 4 million Americans with Alzheimer's disease (AD) may develop psychotic features. Studies suggest cognition declines faster in patients with AD and psychosis than those without psychotic features. Atypical antipsychotics are often used to treat psychosis, but the effects on cognition are uncertain. Therefore, the objective of the study was to evaluate the effect of these agents on cognition.
METHODS: Data for a minimum of nine months were retrospectively collected from patients with AD receiving cholinesterase (ChE) inhibitors. Demographic information included age, gender, medication regimens, and Mini Mental State Exam scores (MMSE). A minimum sample of 96 patients was calculated to provide sufficient power. Data were analyzed to compare patients with AD taking atypical antipsychotics and those not receiving antipsychotic therapy using chi square and analysis of covariance (p<0.05).
RESULTS: One hundred patients (72% female) of 274 were studied. Thirty four patients were prescribed an atypical antipsychotic. Quetiapine (n=24) was the most commonly prescribed antipsychotic (mean dose 71 mg/d). The baseline mean MMSE score was 13.90 ±1.09 and a mean annual rate of cognitive decline 2.37 ±0.46 in patients receiving atypical antipsychotics versus 17.23 ±0.84 (p=0.026) and 2.26 ±0.40 (p=NS) in those without psychosis.
CONCLUSIONS: The baseline mean MMSE score was lower in patients with psychosis, consistent with previous findings of increased risk of psychosis with AD progression. Unlike some studies, annual cognitive decline was similar in patients receiving antipsychotics versus those without psychosis, suggesting no adverse impact of atypical antipsychotic therapy on cognition.

286. Greater improvement and response rates with OROS® methylphenidate compared with atomoxetine in children with attention-deficit/hyperactivity disorder. *Jason E. Kemner, M.P.H.*, H. Lynn Starr, M.D., Christa G. Hooper-Wood, Pharm.D., Patrick E. Ciccone, M.D.; McNeil Consumer and Specialty Pharmaceuticals, Fort Washington, PA.

PURPOSE: To compare the efficacy and safety of OROS® methylphenidate (MPH) (CONCERTA®) and atomoxetine (Strattera®) in children with attention-deficit/hyperactivity disorder (ADHD).
METHODS: Children (N=1,323) ages 6–12 with ADHD were randomized (2:1) in a prospective, open-label, 3-week study of OROS M.P.H. and atomoxetine. Subjects were newly diagnosed or were suboptimally managed on previous ADHD treatments and had an ADHD-Rating Scale (ADHD-RS) score ≥24 and a Clinical Global Impressions-Severity of Illness score ≥4. Dosing was based on investigators' clinical judgment in accordance with each product's labeling. Investigators rated treatment response using the ADHD-RS and the Clinical Global Impressions-Improvement of Illness (CGI-I). Parents evaluated treatments using a daily diary.
RESULTS: OROS M.P.H. produced significantly greater improvement in

investigator-evaluated ADHD-RS scores compared with atomoxetine at all 3 weekly evaluations ($P<0.0001$). Response rates (percent of subjects with ≥30% reduction from baseline ADHD-RS score) at each week were significantly greater for OROS M.P.H. compared with atomoxetine (76.1% vs 63.0%, respectively, by Week 3; $P<0.0001$). Remission rates (percent of subjects with ≥50% reduction from baseline ADHD-RS score) at each week were also greater for OROS M.P.H. versus atomoxetine (56.8% vs 40.7% by Week 3; $P<0.0001$). Investigator CGI-I ratings and parental diary scores were consistent with these findings. The incidences of adverse events were similar in both treatment groups.
CONCLUSIONS: Children with ADHD demonstrated significantly greater symptom improvement with OROS M.P.H. versus atomoxetine at all 3 weeks with similar rates of adverse events. Response rates and parental diary ratings were also greater with OROS M.P.H.

287E. Adherence/agitation improvement with orally-disintegrating olanzapine in schizophrenics. *John Houston, M.D.*, Angela Hill, Pharm.D., Hong Liu-Seifert, Ph.D., Bruce Kinon, M.D.; Eli Lilly and Company, Indianapolis, IN.

Presented at the 157th Annual Meeting of the American Psychiatric Association, New York, NY, May 1–6, 2004.

288. Evolution of mood stabilizer utilization among patients with bipolar disorder in a managed care Medicaid program. *Jeff J. Guo, B.Pharm., Ph.D.*[1], Paul E. Keck Jr., M.D.[2], Hong Li, Ph.D.[3], Raymond Jang, Ph.D.[1], Williams Carson, M.D.[4]; (1)University of Cincinnati College of Pharmacy, cincinnati, OH; (2)University of Cincinnati College of Medicine and Cincinnati Veterans Affairs Medical Center, Cincinnati, OH; (3)Bristol-Myers Squibb Company PRI, Wallingford, CT; (4)Otsuka America Pharmaceutical, Inc., Princeton, NJ.

PURPOSE: Drug utilization of mood stabilizers is evolving to new agents from different classes. Atypical antipsychotics olanzapine, risperidone, and quetiapine were approved for bipolar in 3/2000, 12/2003, and 1/2004, respectively. The study objectives are to identify the evolution of mood stabilizer utilization, and to measure use of atypical antipsychotics before and after FDA approved indication.
METHODS: Using a multi-state managed care Medicaid claims database from 1/1/1998 to 12/31/2002, a total of 13,471 patients (age<65) who had at least 3-months continuous enrollment and at least one bipolar diagnosis were selected for this study. A time-series trend analysis was used to measure the drug utilization patterns.
RESULTS: Of 13,471 patients, 64% were female, average age was 29.4 years (SD=13.8). Percentages of mood stabilizer utilization changed from 1998 to 2002: 10% to 6% for lithium, 9% to 20% for atypical antipsychotics, 25% unchanged for other anticonvulsants, 12% to 13% for typical antipsychotics, and 47% to 35% for antidepressants. Consequently, the percentage of bipolar-related prescription costs changed from 1998 to 2002: 21% to 42% for atypical antipsychotics, 50% to 28% for antidepressants, unchanged for lithium (3%), anticonvulsants (23%), and typical antipsychotics (4%). Atypical antipsychotics were used off-label for bipolar treatment. After olanzapine received FDA approval in March 2000, both cost and utilization of atypical antipsychotics increased at about 10–40% annual rates.
CONCLUSIONS: Use of atypical antipsychotics as new mood stabilizers for bipolar disorder has increased while the use of lithium has decreased overtime.

289. Clinical characteristics and medication regimens of patients treated for schizophrenia with conventional depot antipsychotics. *Lizheng Shi, Ph.D.*[1], Haya Ascher-Svanum, Ph.D.[1], Baojin Zhu, Ph.D.[1], Qin Jiang, M.S.[1], Douglas Faries, Ph.D.[1], Scott Andersen, M.S.[1], David McDonnell, M.D.[1], Steve Marder, M.D.[2]; (1)Eli Lilly and Company, Indianapolis, IN; (2)UCLA, Veteran Affairs Great Los Angeles Healthcare System, Los Angeles, CA.

PURPOSE: To assess clinical characteristics and medication regimens of schizophrenia patients treated in usual care with conventional depot antipsychotics (depots) as compared to patients treated with oral antipsychotics.
METHODS: Analyses included 2,186 participants in the U.S. Schizophrenia Care and Assessment Program (SCAP), a 3-year prospective naturalistic observational study of schizophrenia patients (7/1997–9/2003). Participants were recruited from a broad geographical area, and represented large systems of care. Enrollment characteristics were assessed using multiple sources including patients' medical records, a validated self-report health questionnaire, and various standard psychiatric clinician-rated scales.
RESULTS: Compared to patients receiving only oral antipsychotics during the 3-year study (N=1,617), participants treated with any depot (N=569) were significantly more likely to be younger, male, less educated, and with Medicare/Medicaid coverage (all $p<0.01$). Depot recipients were more frequently hospitalized for psychiatric purposes in the year prior to enrollment (44.3% vs. 35.4%, $p<0.001$), arrested (11.8% vs. 5.0%, $p<0.001$), used alcohol or illicit drugs (39.3% vs. 23.7%, $p<0.001$), scored poorer on a global measure of functioning (GAF, $p<0.001$), and exhibited higher psychopathology levels, particularly positive psychotic symptoms, hostility/excitement, and cognitive disorganization (all $p<0.01$). During the 1-year post initiation, depot-treated patients were on the drug for a mean of 331 days (median: 365 days) and frequently augmented with oral antipsychotics (68.3%) (mean: 164 days; median: 144 days).
CONCLUSIONS: Schizophrenia patients treated with depots appear to be distinctively different from those treated with only oral antipsychotics. Findings suggest that current depot utilization is largely restricted to a specific subpopulation of schizophrenic patients.

290. Prescribing practices associated with antipsychotic use in Texas Medicaid youths. *M. Lynn Crismon, Pharm.D.*[1], Nick C. Patel, Pharm.D., Ph.D.[1], Kimberly E. Hoagwood, Ph.D.[2], Michael T. Johnsrud, Ph.D.[1], Karen L. Rascati, Ph.D.[1], James P. Wilson, Pharm.D., Ph.D.[1]; (1)The University of Texas at Austin, Austin, TX; (2)Columbia University, New York, NY.

PURPOSE: To examine current trends of antipsychotic prescribing in children and adolescents enrolled in Texas Medicaid.
METHODS: Antipsychotic prevalence was defined as the number of individuals under the age of 20 years with at least 1 prescription claim for an antipsychotic agent, regardless of subclass, per 1,000 enrolled children and adolescents. Time trends in antipsychotic prevalence were assessed. Physician specialty and psychiatric diagnoses associated with antipsychotic prescribing were also evaluated.
RESULTS: From 1996 to 2001, the prevalence of total antipsychotic use increased, as an additional 9.2 youths per 1,000 enrollees received an antipsychotic prescription. The prevalence of typical antipsychotic use decreased (-3.1), while the prevalence of atypical antipsychotics dramatically increased (+12.4). Psychiatrists accounted for 74.9% of all antipsychotic prescriptions over the 6-year period, and primary care physicians accounted for 11.0%. The number of antipsychotic prescriptions from psychiatrists (+244%) and primary care physicians (+69.4%) increased, attributed to atypical antipsychotics. Disruptive behavioral disorders accounted for the highest percentage of diagnoses associated with antipsychotic treatment, followed by depressive disorders. Approximately 3% did not have a psychiatric or behavioral diagnosis.
CONCLUSIONS: The appropriateness of atypical antipsychotic use should be evaluated as limited data supporting safety and efficacy are available in children and adolescents.

291E. Immediate switching of antidepressant therapy: results from a clinical trial of duloxetine. Madelaine Wohlreich, M.D.[1], Craig Mallinckrodt, Ph.D.[1], *Megan Jones, Pharm.D.*[1], John Watkin, Ph.D.[1], Michael Wilson, Ph.D.[2], John Greist, M.D.[3], Pedro Delgado, M.D.[4], Mauricio Fava, M.D.[5]; (1)Eli Lilly and Company, Indianapolis, IN; (2)Butler University, Indianapolis, IN; (3)Healthcare Technology Systems, Madison, WI; (4)Case Western Reserve University, Cleveland, OH; (5)Massachusetts General Hospital, Boston, MA.

Presented at the 24th Congress of the Collegium Internationale Neuro-Psychopharmacologicum, Paris, France, June 20–24, 2004.

292E. Extended-release carbamazepine for treatment of manic and mixed symptoms. Richard H. Weisler, M.D.[1], Paul E. Keck Jr., M.D.[2], AC Swann, M.D.[3], AJ Cutler, M.D.[4], Terrance A. Ketter, M.D.[5], *Steven D. Valliere, Pharm.D., M.S.*[6]; (1)Duke University and the University of North Carolina, Raleigh and Chapel Hill, NC; (2)University of Cincinnati College of Medicine and Cincinnati Veterans Affairs Medical Center, Cincinnati, OH; (3)The University of Texas-Houston Medical School, Houston, TX; (4)University of South Florida, Winter Park, FL; (5)Stanford University School of Medicine, Stanford, CA; (6)Shire, Medical Science Liaison/Medical Information Services, Newport, KY.

Presented at the 157th Annual Meeting of the American Psychiatric Association, New York, NY, May 1–6, 2004.

293E. Treatment of manic and mixed patients with extended-release carbamazepine. Richard H. Weisler, M.D.[1], Terrance A. Ketter, M.D.[2], AH Kalali, M.D.[3], *Chris Paap, Pharm.D.*[4]; (1)Duke University and the University of North Carolina, Raleigh and Chapel Hill, NC; (2)Stanford University School of Medicine, Stanford, CA; (3)Quintiles CNS Therapeutics and University of California, San Diego and Irvine, CA; (4)Shire, National Medical Science Liaison Manager/Medical Information, Newport, KY.

Presented at the 157th Annual Meeting of the American Psychiatric Association, New York, NY, May 1–6, 2004.

294E. Course of weight and metabolic benefits 1 year after switching to ziprasidone. *Antony Loebel, M.D.*[1], Peter J. Weiden, M.D.[2], David G. Daniel, M.D.[3], Stephen Murray, M.D., Ph.D.[1], Ruoyong Yang, Ph.D.[1], Harold Lebovitz, M.D.[2]; (1)Pfizer Inc, New York, NY; (2)SUNY Downstate Medical Center, Brooklyn, NY; (3)Bioniche Development, Inc, McLean, VA.

Presented at the 157th Annual Meeting of the American Psychiatric Association, New York, NY, May 1–6, 2004.

295E. A longitudinal study of atypical antipsychotic prescribing patterns in the Iowa Medicaid population. *Ryan M. Carnahan, Pharm.D., M.S.*[1], Brian C. Lund, Pharm.D., M.S.[2], Paul J. Perry, Ph.D.[3], Elizabeth A. Chrischilles, Ph.D.[4], Michael A. Flaum, M.D.[5]; (1)University of Oklahoma College of Pharmacy, Tulsa, OK; (2)Laureate Psychiatric Research Center, Tulsa, OK; (3)University

of Iowa Colleges of Pharmacy and Medicine, Iowa City, IA; (4)University of Iowa College of Public Health, Iowa City, IA; (5)University of Iowa Roy J. and Lucille A. Carver College of Medicine, Iowa City, IA.

Presented at the 2004 Clinical and Administrative Pharmacy Research Day of the University of Iowa, College of Pharmacy, Iowa City, IA, April 27, 2004.

296. Four studies of eszopiclone in non-elderly and elderly patients with chronic insomnia. *Russell P. Rosenberg, Ph.D.*[1], Robert Rubens, M.D., M.B.A.[2], John Niewoehner, Pharm.D.[2]; (1)Northside Hospital Sleep Medicine Institute, Atlanta, GA; (2)Sepracor Inc., Marlborough, MA.

PURPOSE: Insomnia affects about 36% of adults and prevalence increases with age. Eszopiclone is a non-benzodiazepine under development to rapidly induce and maintain sleep in patients with insomnia. Data from four studies were analyzed to determine if results were similar in elderly and nonelderly patients with primary insomnia.
METHODS: Data are from randomized, double-blind, placebo-controlled studies of eszopiclone: two 2-week studies of eszopiclone 2 mg in elderly patients (polysomnographic and subjective study: n=264; subjective study: n=159), and two non-elderly studies utilizing eszopiclone 3 mg (6-week polysomnographic and subjective study: n=204; 6-month subjective study: n=788). Each evaluated sleep onset, duration, and maintenance (wake time after sleep onset-WASO).
RESULTS: In all 4 studies, eszopiclone significantly improved patient reports of sleep (onset, $p<0.01$; WASO, $p<0.05$; total sleep time, $p<0.01$) compared with placebo over the relevant study period in elderly and non-elderly patients. In the two studies with polysomnographic data, eszopiclone significantly improved objective measures of sleep onset, total sleep time, and WASO in both populations ($p<0.05$). For most next day measures, eszopiclone patients reported improvements ($p<0.05$) relative to placebo.
CONCLUSIONS: In these four studies, eszopiclone provided consistent improvements in patient-reported and polysomnographic measures of sleep and patient ratings of daytime functioning in non-elderly and elderly patients with primary insomnia.

297E. Efficacy of duloxetine treatment: analysis of pooled data from six placebo-and SSRI-controlled clinical trials. Ralph Swindle Jr., Ph.D.[1], Craig Mallinckrodt, Ph.D.[1], Yili Lu, Ph.D.[1], John Watkin, DPhil[1], *Kimberly Sterling, Pharm.D.*[1], Michael Detke, M.D.[1], Jerrold Rosenbaum, M.D.[2]; (1)Eli Lilly and Company, Indianapolis, IN; (2)Massachusetts General Hospital, Boston, MA.

Presented at the 157th Annual Meeting of the American Psychiatric Association, New York, NY, May 1–5, 2004.

298. Maintenance treatment for bipolar depression using olanzapine or olanzapine/fluoxetine combination. *Scott Andersen, M.S.*[1], Sara Corya, M.D.[1], Holland Detke, Ph.D.[1], Richard Risser, M.S.[1], Mauricio Tohen, M.D.[1], Terrance Ketter, M.D.[2], Joseph Calabrese, M.D.[3]; (1)Eli Lilly and Company, Indianapolis, IN; (2)Stanford University, Stanford, CA; (3)Case Western Reserve University; University Hospitals of Cleveland, Cleveland, OH.

PURPOSE: Olanzapine/fluoxetine combination (OFC) has shown efficacy in treating bipolar depression. Present analyses examined 6-month maintenance data for subjects who achieved remission of depressive symptoms following acute treatment.
METHODS: 379 subjects with bipolar depression completed 8-weeks of randomized, double-blind treatment using olanzapine (OLZ, n=179), placebo (n=145), or OFC (n=55). Of these, 192 were in remission (MADRS ≤ 12) upon entering open-label treatment, at which time they were switched from their acute-phase treatment to 5–20mg/day open-label OLZ. After 1 week on OLZ, subjects could be switched to OFC as needed. Primary efficacy measure was the Montgomery-Åsberg Depression Rating Scale (MADRS). Manic symptoms were monitored using the Young Mania Rating Scale (YMRS). Time to relapse (MADRS >15) was estimated using Kaplan-Meier survival analysis.
RESULTS: Of the 192 remitters, 120 (62.5%) remained free from relapse over the 6-month open-label period. For the 72 subjects (37.5%) who relapsed, median time to relapse was 194 days. Mean MADRS total score at open-label endpoint was 7.93 (SD 9.24, n=192) using a last-observation-carried-forward (LOCF) methodology.
CONCLUSIONS: This study suggests that OLZ and OFC may represent treatment options in the long-term management of bipolar depression. Further studies are necessary to replicate these findings using appropriate controls and double-blind methodology.

299E. Analog classroom study of amphetamine extended-release and atomoxetine in youth with attention deficit hyperactivity disorder. Sharon B. Wigal, Ph.D.[1], James J. McGough, M.D.[2], James T. McCracken, M.D.[2], Joseph Biederman, M.D.[3], Thomas J. Spencer, M.D.[3], Kelly L. Posner, Ph.D.[4], Scott H. Kollins, Ph.D.[5], Tanya M. Clark, B.S.[6], David A. Mays, Pharm.D., M.B.A.[6], Simon J. Tulloch, M.D.[6], M. Alex Michaels, M.D.[6], *Sherry L. Andes, Pharm.D., BSPharm*[7]; (1)Child Development Center, University of California Irvine, Irvine, CA; (2)David Geffen School of Medicine at UCLA, Los Angeles, CA; (3)Harvard University and Massachusetts General Hospital, Boston, MA; (4)Columbia University Medical Center, New York, NY; (5)Duke University Medical School, Durham, NC; (6)Shire Pharmaceutical Development Inc., Rockville, M.D.; (7)Shire, Medical Information Services, Newport, KY.

Presented at the 157th Annual Meeting of the American Psychiatric Association, New York, NY, May 4, 2004.

300E. Dose-response efficacy of mixed amphetamine salts extended-release in adults with attention deficit hyperactivity disorder. Stephen V. Faraone, Ph.D.[1], Joseph Biederman, M.D.[2], Thomas J. Spencer, M.D.[2], Timothy E. Wilens, M.D.[2], Richard H. Weisler, M.D.[3], Stephanie C. Read, M.S.[4], Yuxin Zhang, Ph.D.[4], Simon J. Tulloch, M.D.[4], *David A. Mays, Pharm.D., M.B.A.*[5]; (1)Massachusetts General Hospital, Harvard Medical School, and Harvard School of Public Health, Boston, MA; (2)Massachusetts General Hospital and Harvard Medical School, Boston, MA; (3)Duke University Medical School and University of North Carolina College of Medicine, Durham and Chapel Hill, NC; (4)Shire Pharmaceutical Development, Inc., Rockville, M.D.; (5)Shire, Medical Information Services, Newport, KY.

Presented at the 157th Annual Meeting of the American Psychiatric Association, New York, NY, May 4, 2004.

301E. A cohort analysis of measured growth parameters in children with attention deficit hyperactivity disorder receiving mixed amphetamine salts (MAS XR) for 24 months. Thomas J. Spencer, M.D.[1], Stephen V. Faraone, Ph.D.[2], Jill A. Morgan, Pharm.D., BCPS[3], M. Alex Michaels, M.D.[4], *David A. Mays, Pharm.D., M.B.A.*[5]; (1)Harvard University and Massachusetts General Hospital, Boston, MA; (2)Pediatric Psychopharmacology Unit, Child Psychiatry Service, Massachusetts General Hospital, Boston, MA; (3)University of Maryland School of Pharmacy, Baltimore, M.D.; (4)Shire Pharmaceutical Development Inc., Rockville, M.D.; (5)Shire, Medical Information Services, Newport, KY.

Presented at the 44th Annual Meeting of the Clinical Drug Evaluation Unit, Phoenix, AZ, June 3, 2004.

302E. Safety and efficacy of mixed amphetamine salts extended-release in children and adolescents with oppositional defiant disorder (ODD). Thomas J. Spencer, M.D.[1], Joseph Biederman, M.D.[1], Howard B. Abikoff, Ph.D.[2], Steven R. Pliszka, M.D.[3], Samuel W. Boellner, M.D.[4], Frank A. Lopez, M.D.[5], Stephanie C. Read, M.S.[6], Simon J. Tulloch, M.D.[7], *Steven D. Valliere, Pharm.D., M.S.*[8]; (1)Harvard University and Massachusetts General Hospital, Boston, MA; (2)New York University School of Medicine, New York, NY; (3)University of Texas Health Science Center at San Antonio, San Antonio, TX; (4)Clinical Study Centers, Little Rock, AR; (5)Children's Development Center, Maitland, FL; (6)Shire Pharmaceutical Development, Inc., Rockville, M.D.; (7)Shire Pharmaceutical Development Inc., Rockville, M.D.; (8)Shire, Medical Science Liaison/Medical Information Services, Newport, KY.

Presented at the 157th Annual Meeting of the American Psychiatric Association, New York, NY, May 4, 2004.

303. Research experience gained during ACCP CNS PRN minisabbatical. *Thea R Moore, Pharm.D., BCPP*[1], David A. Sclar, B.Pharm., Ph.D.[2]; (1)Florida A&M University/Lakeland Regional Medical Center, Lakeland, FL; (2)Washington State University, Pullman, WA.

PURPOSE: To obtain analytical skills requisite to conducting both retrospective and prospective inquiries in mental health services research
METHODS: Researcher spent three weeks with faculty and staff at the mentoring institution in order to:
1. Gain an in-depth knowledge of biostatistics, epidemiologic methods, and the Statistical Analysis System [SAS], with a focus on mental health services research.
2. Develop a research protocol, and conduct retrospective analyses of patient's access, use, and outcomes with central nervous system pharmacotherapy using data from the U.S. National Ambulatory Medical Care Survey; the U.S. Health Care Utilization Project; the U.S. National Health Interview Survey.
3. Review study protocols and participate in prospective evaluations of mental health interventions [pharmacotherapy; pharmaceutical services]
RESULTS: Investigator became familiar with a number of biostatistical principles and developed ability to utilize SAS to analyze data sets. Investigator collaborated with faculty and staff at the mentoring institution on research that resulted in a poster presented at a national psychiatry meeting.
CONCLUSIONS: Participation in the ACCP CNS PRN Minisabbatical allowed a junior faculty member to work with a mentor and develop and hone skills and understanding of pharmacoeconomic and pharmacoepidemiological principles. The junior faculty member was able to gain valuable experience in research methodology that can be applied in future endeavors.

304. Twelve months of nightly eszopiclone treatment in patients with chronic insomnia: assessment of long-term efficacy and safety. *Thomas Roth, Ph.D.*[1], Andrew Krystal, M.D., M.S.[2], James K. Walsh, Ph.D.[3], Thomas C. Wessel, M.D.[4], Tim A. Roehrs, Ph.D.[1], Judy Caron, Ph.D.[4], David Amato, Ph.D.[4], Susan M. Skolly, Pharm.D.[4]; (1)Henry Ford Hospital Sleep Disorders Center, Detroit, MI; (2)Duke University Medical Center, Durham, NC; (3)Sleep Medicine and Research Center, St. Luke's Hospital, Chesterfield, MO; (4)Sepracor Inc., Marlborough, MA.

PURPOSE: There are few controlled studies of long-term insomnia therapy. In a pivotal six-month placebo-controlled study, eszopiclone demonstrated efficacy in improving measures of sleep and patient-reported daytime function. To evaluate continued effectiveness and safety, a 6-month open-label extension study in actual practice was conducted; results presented here.
METHODS: Following the 6-month, double-blind phase, 471 patients (111 placebo, 360 eszopiclone) entered the extension and received open-label eszopiclone 3 mg nightly (months 7–12). Endpoints were patient reported measures of sleep efficacy (onset, maintenance, duration, quality) and daytime parameters (alertness, physical well-being, and ability to function [concentrate]), captured weekly using an interactive voice response system. Data from double-blind treatment month 6 was used as "baseline" for this analysis.
RESULTS: Patients previously treated with placebo reported immediate and significant improvements in sleep and daytime functioning (all p values <0.0005 versus baseline). Patients who previously received eszopiclone continued to improve (eg, p< 0.02 for total sleep time for months 7–12). These improvements in reports of sleep and daytime function were sustained for the entire 6-month extension period. At the end of the extension, 86/111 patients (77%) had received eszopiclone for 6 months, and 296/360 patients (82%), for 12 months. There were no significant withdrawal adverse events upon discontinuation; eszopiclone was well-tolerated for up to 12 months of nightly use.
CONCLUSIONS: In this study, patients with chronic primary insomnia who were treated with eszopiclone reported sustained improvement in measures of sleep efficacy and next day functioning over 12 months of therapy.

305E. Safety of intramuscular olanzapine in comorbidly ill, acutely agitated patients with dementia. *Vicki P Hoffmann, Pharm.D.*, John Houston, M.D., Christopher Kaiser, Ph.D., Jonna Ahl, Ph.D., Paula Trzepacz, M.D.; Eli Lilly and Company, Indianapolis, IN.

Presented at the 7th Annual Meeting of the College of Psychiatric and Neurologic Pharmacists, Chicago, IL, April 23, 2004.

306E. Use of anticonvulsant drugs in bipolar disorder: results of a 2003 survey. AJ Cutler, M.D.[1], *Sherry L. Andes, Pharm.D., BSPharm*[2]; (1)University of South Florida, Winter Park, FL; (2)Shire, Medical Information Services, Newport, KY.

Presented at the 157th Annual Meeting of the American Psychiatric Association, New York, NY, May 1–6, 2004.

307. The use of eszopiclone in the treatment of sleep maintenance insomnia: a subset analysis of efficacy by baseline wake time after sleep onset (WASO). *Andrew Krystal, M.D., M.S.*[1], James Roach, M.D.[2], Judy Caron, Ph.D.[2], Robert Rubens, M.D., M.B.A.[2], Andrea J. Anderson, Pharm.D.[2]; (1)Duke University Medical Center, Durham, NC; (2)Sepracor Inc., Marlborough, MA.

PURPOSE: A number of recent hypnotic trials have required baseline WASO as a stringent entry criterion. In a pivotal six-month study of the drug, eszopiclone was shown to rapidly induce and maintain sleep and demonstrated statistically significant improvements in all measures of sleep (sleep latency, total sleep time, WASO) vs. placebo for up to 6 months. As WASO was not an initial entry criterion of this study, this subset analyses was done to determine whether WASO, as a selection criterion, would have affected study outcome.
METHODS: In the parent study, patients meeting DSM-IV criteria for primary insomnia were entered into a 6-month, randomized, double-blind, placebo-controlled, multi-center study to evaluate the efficacy of eszopiclone 3 mg. For the present analysis, patients from the parent study were grouped by baseline WASO into Low-WASO (≤ 30min; n=190) and High-WASO (>30min; n=319).
RESULTS: Over 6-months, statistically significant differences from placebo were noted in WASO in the Low- (p=0.0035) and High-WASO groups (p=0.0055). The magnitude of WASO reduction was directly related to the amount of baseline WASO impairment (p<0.001).
CONCLUSIONS: Had the original study required a WASO entry criterion of >30 min approximately 40% of subjects would have been excluded from the pivotal study. Based on this analysis, eszopiclone 3 mg was effective in reducing WASO regardless of WASO severity at baseline.

308. Racial disparity in depot antipsychotic prescribing patterns. *Russell M. Blaylock, M.S., Pharm.D.*, Carol Tsao, M.D., Patty Guedet, M.D., Angela Paniagua, Pharm.D.; Zablocki VA Medical Center, Milwaukee, WI.

PURPOSE: This project was undertaken to determine if predictors of medication non-compliance could account for racial disparities in depot antipsychotic prescribing reported in previous research. The relationship between race, homelessness, and substance abuse co-morbidity and the prescription of depot antipsychotics was investigated.
METHODS: The study was a multi-center, retrospective chart review with blinded data collection. The subjects were schizophrenic and schizoaffective disorder patients. Homelessness and substance abuse co-morbidity were used as surrogate markers to predict a patient's potential for medication non-compliance.
RESULTS: 1. A total of 1316 black, non-hispanic and 1944 white, non-hispanic patients were included in the study.
2. A total of 164 black, non-hispanic and 42 white non-hispanic patients were homeless (X2 = 140, P<0.0001).
3. A total of 495 black, non-hispanic and 401 white non-hispanic patients had a substance-abuse co-morbidity (X2 = 114, p<0.0001).
4. A total of 78 black, non-hispanic and 141 white, non-hispanic patients were prescribed a depot antipsychotic (X2 = 2.20,P=0.1378 NS).
5. Logistic Regression revealed a significant interaction effect between homelessness, substance abuse co-morbidity, and race (X2 = 6.69, p<0.01).
CONCLUSIONS: 1. Homelessness and substance abuse co-morbidity are better predictors of depot antipsychotic prescribing than race. 2. Black, non-hispanic schizophrenic patients are more likely to be prescribed a depot antipsychotic than White, non-hispanic patients with the same risk factors for non-compliance.

Pulmonary

309E. Relationship between asthma severity and endogenous cortisol excretion. *Hengameh H Raissy, Pharm.D.*, Susan Scott, M.D., H. William Kelly, Pharm.D.; University of New Mexico, School of Medicine, Albuquerque, NM.

Presented at the International Conference of the American Thoracic Society, Orlando, FL, May 21–26, 2004.

310. Community perception of smoking and its relationship to erectile dysfunction. *Sunny A. Linnebur, Pharm.D.*; University of Colorado School of Pharmacy, Denver, CO.

PURPOSE: Tobacco use in the U.S. continues to be a significant health concern. Most anti-tobacco education and advertising efforts focus on warnings of lung cancer and heart disease. Although smoking is a known risk factor for erectile dysfunction (ED), it is unknown if men are aware of this or if this knowledge may effect their decision to stop smoking. The purpose of this study was to investigate community knowledge of the relationship between ED, smoking, and smoking cessation.
METHODS: Male smokers aged ≥18 years were surveyed at a local health fair. Data collected included: age range, race, smoking history, smoking cessation history, knowledge of smoking as a cause of ED, and likelihood of future smoking cessation.
RESULTS: Sixty-two surveys were completed. The majority of subjects was Caucasian and between 41–60 years old. Smoking status was evenly distributed between 6–10, 11–20, and 21–30 cigarettes smoked per day. Thirty-five percent had attempted to quit smoking 1–2 times and 27% had attempted more than 5 times. The majority (55%) stated they were aware that smoking cigarettes/cigars increases ED risk. Forty-one percent stated this knowledge had no effect and they would continue to smoke, 39% stated they were somewhat more likely to stop smoking and 20% stated they were much more likely to stop smoking.
CONCLUSIONS: Over one-half of surveyed men were aware that smoking increases ED risk; 59% indicated this knowledge would positively impact their decision to stop smoking. Education efforts for tobacco cessation in men may be effective if focused around ED.

311. Evaluation of systemic corticosteroid use in the management of acute COPD exacerbations. *Sheryl F. Vondracek, Pharm.D.*, Linh Tran, Pharm.D.; University of Colorado Health Science Center, School of Pharmacy, Denver, CO.

PURPOSE: The Global Initiative for Chronic Obstructive Lung Disease Guideline recommends 30–40 mg oral prednisolone daily for 10–14 days for acute exacerbations of chronic obstructive pulmonary disease (AECOPD). The purpose of this descriptive study was to evaluate systemic corticosteroid use for the management of AECOPD.
METHODS: Retrospective chart review of patients >/= 45 years of age admitted to the University of Colorado Hospital with an ICD-9 Code #491.21 for AECOPD from 7/02–12/03 who received systemic corticosteroids.
RESULTS: There were 145 qualifying admissions. Average patient age was 65 ± 11 years, 52% were men, 67% were Caucasian and 17% were African American. The average length of stay (LOS) was 4.2 ± 3.6 days. An ICU stay occurred in 48% of admissions. Intravenous steroids were started in 56% of patients and 74% received high dose steroids (>80 mg prednisone equivalent [PE]/day). Average steroid use during hospitalization was 755 ± 969 mg PE (average/day = 189.5 ± 166.7 mg PE). Patients who initially received intravenous steroids had a longer LOS compared to patients who received oral steroids (5.1 ± 4.3 days vs. 3.0 ± 2.2 days; P<0.05). There was no statistically significant difference in LOS or 30-day relapse rate between patients who received a high dose vs. low dose regimen and were admitted to the ICU or medical ward. Eighty percent of patients were discharged on a tapered steroid regimen.
CONCLUSIONS: Despite recommendations for lower oral doses, the majority of patients are receiving high intravenous doses of systemic steroids for AECOPD.

312E. Reduced COPD exacerbations and associated health care utilization with once-daily tiotropium in the VA medical system. Steven Kesten, M.D.[1], Kathryn Rice, M.D.[2], Claudia Cote, M.D.[3], Daniel Paulson, M.D.[4], J. Allen Cooper, M.D.[5], Lawrence Korducki, M.S.[1], *Cara Cassino, M.D.*[1], Dennis E. Niewoehner, M.D.[2]; (1)Boehringer Ingelheim, Ridgefield, CT; (2)Veterans Affairs Medical Center, Minneapolis, MN; (3)Veterans Affairs Medical Center, Bay Pines, FL; (4)Hunter Holmes McGuire Medical Center, Richmond, VA; (5)Veterans Affairs Medical Center, Birmingham, AL.

Published in Am J Respir Crit Care Med 2004;169(7):A207.

313E. Improved daytime spirometric efficacy of tiotropium compared with salmeterol in COPD patients. *Cara Cassino, M.D.*[1], Dick Briggs Jr., M.D.[2], Henry Covelli, M.D.[3], Robert Lapidus, M.D.[4], Sudipta Bhattacharya, M.S.[1], Steven Kesten, M.D.[1]; (1)Boehringer Ingelheim, Ridgefield, CT; (2)University of Alabama at Birmingham, Birmingham, AL; (3)Pulmonary Consultants of North Idaho, Couer d'Alene, ID; (4)Rocky Mountain Center for Clinical Research, Wheat Ridge, CO.

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314E. Inspiratory flow through dry-powder inhalers (DPI) in asthmatic children 2 to 12 years old. *Hengameh H Raissy, Pharm.D.*[1], Deborah McNutt, Pharm.D.[2], Michael Monske, Pharm.D.[2], Patricia Marshik, Pharm.D.[2], H. William Kelly, Pharm.D.[1]; (1)University of New Mexico, School of Medicine, Albuquerque, NM; (2)University of New Mexico, College of Pharmacy, Albuquerque, NM.

Presented at the International Conference of the American Thoracic Society, Orlando, FL, May 21–26, 2004.

Substance Abuse/Toxicology

315. Nonclinical safety and immunogenicity evaluation of repeated subcutaneous administration of rhThrombin. *Jane K. Heffernan, B.S.*[1], Margaret Wills, M.S.[2], Rafael A. Ponce, Ph.D.[1], Erika E. Giste, B.S.[1], John P. Volpone, B.S.[1], Nancy J. Jenkins, B.S.[1], Linda A. Zuckerman, Ph.D.[1], Mark C. Rogge, Ph.D.[1]; (1)ZymoGenetics Inc., Seattle, WA; (2)Charles River Laboratories, Sparks, NV.

PURPOSE: Recombinant human thrombin (rhThrombin) is being developed for use in a variety of surgical settings as an adjunct to hemostasis. Current thrombin products carry pathogen transmission risks, and in some patients are immunogenic, leading to autoantibody formation. Subsequent bleeding disorders can occur. A study was conducted in cynomolgus monkeys to assess the safety and immunogenicity from exposure to rhThrombin.
METHODS: Three male and three female cynomolgus monkeys each were assigned to one of three treatment groups (rhThrombin [1000 U/mL], bovine thrombin [1000 U/mL], or vehicle). Animals were treated subcutaneously once weekly for four weeks, then observed for an additional two weeks. Data collected included clinical observations, body weight, clinical pathology measurements, and anatomical pathology findings. A three-tiered ELISA testing approach was used to detect antibodies specific to rhThrombin or to production impurities in rhThrombin- and vehicle-treated animals.
RESULTS: No treatment-related adverse effects were found on review of the clinical and anatomical pathology results. Specific anti-rhThrombin antibodies were not detected in study animals. One of six rhThrombin-treated monkeys had low circulating levels of specific antibodies to host cell proteins at two of nine non-consecutive timepoints.
CONCLUSIONS: Results from this study demonstrated that rhThrombin was well tolerated upon repeated subcutaneous dosing of cynomolgus monkeys. Animals did not develop specific anti-rhThrombin antibodies, but did develop occasional, low levels of antibodies to a host cell protein.

Transplant/Immunology

316. Limited sampling strategy for estimation of mycophenolic acid (MPA) area under the curve (AUC) in hematopoietic cell transplant (HCT) patients. *Juki W. Ng, Pharm.D.*[1], John Rogosheske, Pharm.D.[2], Pamala Jacobson, Pharm.D.[1]; (1)Department of Experimental and Clinical Pharmacology, College of Pharmacy, University of Minnesota, Minneapolis, MN; (2)Department of Pharmacy, Fairview University Medical Center, Minneapolis, MN.

PURPOSE: The purpose of this project was to develop a limited sampling model for the simultaneous estimation of total and unbound MPA AUC. Previously, we demonstrated that subjects with low AUCs were at greater risk of developing graft versus host disease.
METHODS: Intensive pharmacokinetic steady-state sampling was performed between days 3-7 posttransplant in 73 adult subjects while receiving mycophenolate mofetil 1gm q12H PO or IV. Total and unbound MPA plasma concentrations were measured, and true AUC_{0-12} determined. Stepwise regression analysis was performed in the first 34 subjects to build IV and PO models of total and unbound AUC. The predictive performance of these models was tested in the remaining 39 subjects.
RESULTS: The best models for estimation of total and unbound AUCs are below. Trough concentrations were poorly correlated with AUC (r^2<0.34).

PO MPA (n=22)	AUC_{0-12} Models	r_2
total AUC_{0-12}	= 4.43 + 2.76 *C_{0hr} + 0.51 *C_{1hr} + 1.97 *C_{2hr} + 4.27 *C_{6hr}	0.85
unbound AUC_{0-12}	= 63.92 + 2.01 *C_{0hr} + 0.67 *C_{1hr} + 2.05 *C_{2hr} + 4.26 *C_{6hr}	0.90
IV MPA (n=12)	**AUC_{0-12} Models**	**r_2**
total AUC_{0-12}	= -0.49 + 1.58 *C_{2hr} + 0.41 *C_{4hr} + 13.88 *C_{6hr}	0.99
unbound AUC_{0-12}	= 7.99 + 1.40 *C_{2hr} + 2.47 *C_{4hr} + 9.54 *C_{6hr}	0.99

Eighty-three percent of IV and 70% of oral AUC predictions fell within 20% of the true values. No significant bias of the models was observed.
CONCLUSIONS: MPA AUC can be estimated from 3 or 4 MPA concentrations. Trough concentrations are poorly correlated with AUC_{0-12}.

317. Relationship of cyclosporine levels to rejection on transbronchial biopsies in lung transplant recipients. *Marcus Haug III, B.Sc., M.Sc., Pharm.D.*, Omar Minai, M.D., Connie Jennings,, M.D., Jeffrey Chapman, M.D., Sudish Murthy, M.D., Ph.D., Atul Mehta, M.D., Malcolm DeCamp, M.D.; Cleveland Clinic Foundation, Cleveland, OH.

PURPOSE: Cyclosporine (CSA) levels of > 350 ng/ml (C_{min}) were targeted for preventing lung transplant rejection. We describe the relationship of CSA levels, < C_{min} and > C_{min} on day of acute lung rejection on transbronchial lung biopsy (TBLB) in the first year, first 90 days and day 91 through the first year post transplant.
METHODS: All patients who received CSA, with TBLBs performed were included. We identified all TBLB results performed with CSA levels < Cmin and > Cmin (MFPIA assay). χ^2 testing was utilized (p<0.05).
RESULTS: 149 lung transplants received CSA with TBLBs. In the < 90 days post transplant group, 132 (42.3%) TBLBs were positive for rejection. 62 (19.9%) of the 312 TBLBs were associated with CSA levels less than C_{min}. In the > 90 days to 1 year post transplant group, 52 (21.6%) TBLBs were positive for rejection. 78 (32.4%) of the 241 TBLBs were associated with CSA levels < C_{min}. Less rejection was present on TBLBs in the first year with CSA levels > C_{min} (p=0.0258). TBLBs rejection were also lower at day 91 to 1 year with CSA levels > C_{min} (p<0.0389). TBLBs rejection rate was less for day 91 to 1 year compared to TBLBs in the first 90 days post transplant, when levels were > C_{min} (p<0.0001).
CONCLUSIONS: We conclude that there is greater risk for lung rejection in the first year post transplant if the CSA is less than C_{min}. This effect is most significant in the first 90 days post transplant. CSA levels > 350 ng/ml are important in preventing lung rejection in the first year.

318. Treatment outcomes of recurrent hepatitis C: pegylated interferon in non-responders. *Renee M. Devine, Pharm.D.*, Thomas G. Heffron, M.D., Andrei C. Stieber, M.D., Greg A. Smallwood, Pharm.D.; Emory Healthcare, Atlanta, GA.

PURPOSE: This study documented treatment outcomes of patients with recurrent hepatitis C virus (HCV) after orthotopic liver transplantation (OLT) treated with pegylated interferon/ribavirin. It has been proposed that patients previously failing therapy with standard interferon/ribavirin are less likely to respond to pegylated interferon/ribavirin.
METHODS: Single-center, retrospective review of medical records of 38 OLT recipients followed in a pharmacist managed clinic. Patients must demonstrate histological recurrence of HCV and been previously treated with α-interferon/ribavirin. Patients' demographics, biochemical and virologic responses, and other outcomes such as hospitalizations, dropouts, deaths, and adverse events were documented.
RESULTS: Patient's undergoing therapy for recurrent HCV (n=38) were predominantly Caucasian (76%) males (66%) infected with genotype 1 (74%). Mean time to recurrence was 1065.3 ± 891.5 days. Ten (26%) patients have completed therapy. Biochemical response was achieved at 3 months as demonstrated by decrease in ALT (119.3 ± 99.2 vs. 73.2 ± 53.3; p=0.012) Virologic clearance at 3 and 6 months of treatment are 40% (n=12) and 43% (n=13) respectively. Five hospitalizations occurred resulting in thirty-seven days of hospitalization. Eight (21%) patients discontinued therapy due to side effects or progression of HCV. Acute rejection occurred in two (5.3%) patients, both of which were treated and went on to attain viral clearance. Mean cost of treatment including management of adverse effects is $39,000 (AWP). Two (5.3%) patients have died since discontinuing therapy.
CONCLUSIONS: Both biochemical and virologic response can be attained with the use of Pegylated interferon/ribavirin in patients with recurrent HCV previously failing therapy with standard interferon.

319. Comparison of cyclosporine trough levels measured by two different assays. *Jennifer B. Lehneman, Pharm.D.*, Greg A. Smallwood, Pharm.D.; Emory Healthcare, Atlanta, GA.

PURPOSE: Our institution changed cyclosporine assays from the TDX Monoclonal antibody test to a tandem mass spectrometry method which resulted in a noticeable decrease in cyclosporine trough levels being reported. This study was performed to determine the relationship between trough levels

produced by the different tests.
METHODS: Cyclosporine trough levels were performed in parallel using both assays and were collected from kidney, heart, lung and stem cell transplant patients. The levels were plotted (TDX vs. LCMS) to determine the correlation between both assays and the equation for the line of "best fit" was calculated [y = mx + b where Y was the TDX(old method), X was LCMS (new method), M the slope of the line and b was the Y intercept].
RESULTS: A total of 454 trough cyclosporine levels were evaluated. The equation for the line of best fit was y = 1.45 x 37.9 with a Pearson R2 value of 0.95459. Based on patient type line were calculated, the lung transplant population (n = 123), y = 1.5753 x + 53.835 with R2 = 0.945; renal transplant population (n = 61), y = 1.5211 x + 50.96 with R2 = 0.9507; Heart transplant (n = 37) y = 1.6036 x + 47.62 R2 = 0.9177; and stem cell transplant (n = 55) y = 1.4552 x + 47.179 with R2 = 0.9571.
CONCLUSIONS: There was a high degree of correlation between both assay methods. Clinicians need to be educated on this relationship and it's relationship to clinical outcomes.

320. Review of patient outcomes of aspergillus prophylaxis with voriconazole after lung transplantation. *Jennifer B. Lehneman, Pharm.D.*, Gregory A. Smallwood, Pharm.D., Laurie Lesniak, R.N., Bethany Lane, R.N., Seth Force, M.D., E. Clinton Lawrence, M.D.; Emory Healthcare, Atlanta, GA.

PURPOSE: This study was conducted to determine outcomes of lung transplant recipients taking voriconazole for aspergillus prophylaxis.
METHODS: A retrospective review of medical records for all lung transplant recipients prescribed voriconazole for aspergillus prophylaxis from September 2002 through May 2004. Patient demographics, liver function tests (LFTs), duration of therapy, and reason for discontinuation of voriconazole was collected.
RESULTS: All patients receiving voriconazole for aspergillus prophylaxis (N = 37) had an increase in LFTs as demonstrated by ALT at 4 weeks of therapy compared to baseline (106.7 ± 108.8 vs. 28.46 ± 18.3; p=0.018). Discontinuation of therapy due to LFTs occurred in 32.4% (12 /37), 48.6% (18/37) due to financial concerns, 1 patient died on therapy and 16.2% (6/37) were able to continue therapy per protocol. Patients discontinued due to LFTs had higher ALT(198.6 ± 124.5 vs. 49.4 ± 40.7; p=0.008) at 4 weeks into therapy and at time of discontinuation (201.1 ± 120.4 vs. 37.7 ± 23.9; p<0.001). Patients that discontinued drug due to LFTs had an increase in total bilirubin from baseline (0.8 ± 0.48 vs. 2.8 ± 2.7; p=0.012). Duration of therapy was similar for patients discontinued for LFTs vs. other reasons (27.8 vs. 38.9 days; p=0.371). Aspergillus cultures were positive in 8% (3/37) patients after discontinuation of voriconazole.
CONCLUSIONS: All patients receiving voriconazole had elevations in LFTs from baseline with 32.4% requiring discontinuation from therapy. Voriconazole appears to be hepatotoxic to lung transplant recipients.

321. Risk factors affecting the graft and patient survival in kidney transplant recipients. *Jung Mi Oh, Pharm.D.*, Joo Young Kim, M.S.; Graduate School of Clinical Pharmacy, Sookmyung Women's University, Seoul, South Korea.

PURPOSE: To determine the short (1 year of transplant) and long-term (1–5 years of transplantation) risk factors affecting the graft and patient survival in kidney transplantation recipients.
METHODS: Records of 152 patients who received kidney transplantation in 1996 from AMC were followed for 5 years retrospectively.
RESULTS: All patients initiated triple immunosuppressive therapy with cyclosporine, prednisone and azathioprine. One, two, three, four, and five year patient and graft survival rates were 98.7%, 98.0%, 98.0%, 97.3%, 97.3%, and 96.6%, 95.2%, 94.6%, 92.5%, 91.8%, respectively. There were 30 cases of acute rejection (AR) and 6 cases of chronic rejection (CR) within 2.1±3.2 months and 42.1±13.2 months of transplantation, respectively. The risk factors for AR were donor's age older than 30 years (p=0.02) and cardiovascular disease (p=0.05). The risk factors for CR were AR (p=0.0169) and episode of complications within 1 year (p=0.0330). Increasing period of dialysis (p=0.0473), episodes of AR (p<0.0001) and complication (p=0.0317) within 1 year were significant factors for graft loss. Seven grafts were lost from noncompliance during 1–5 year period. The most common cause of the graft loss for both periods was the graft rejection. The graft survival rate was significantly lower in patients with than without rejection episodes (77.4% vs. 90.0%, p=0.002).
CONCLUSIONS: Survival rate of the graft with rejection was significantly lower. The risk factors affecting AR were donor's age older than 30 years and CVD. AR and episode of complications within 1 year were the risk factors for CR and graft loss.

322. Mycophenolate pharmacokinetics in islet cell transplantation. *Kathleen G Green, Pharm.D*[1], Bernard J Hering, M.D.[2], Pamala A Jacobson, Pharm.D[1]; (1)Experimental and Clinical Pharmacology, College of Pharmacy, University of Minnesota, Minneapolis, MN; (2)Diabetes Institute for Immunology and Transplantation, and Department of Surgery, University of Minnesota, Minneapolis, MN.

PURPOSE: Mycophenolate mofetil (MMF) is a desirable immunosuppressant for islet cell transplantation due to its lack of glucose effects. Immunosuppression is an important determinant of graft survival; therefore, we examined MMF disposition in this patient population.
METHODS: We studied eight adults undergoing islet cell transplantation. Subjects received ATG, methylprednisolone, daclizumab, and etanercept peritransplant. Maintenance immunosuppression consisted of MMF (750–1000g BID starting day 24), sirolimus and low-dose tacrolimus. MMF doses were modified in six patients prior to day 60, due to drug intolerance and/or toxicity. Intensive pharmacokinetics were obtained on days 28 and 42, with abbreviated profiles on days 60, 90, 180, 270 and 365.
RESULTS: Total and unbound MPA and total MPAG plasma concentrations were measured with HPLC and analyzed with noncompartmental methods. Early (day 28–42) MPA AUC_{0-12} (mg*h/mL) were higher (65.0) than later (48.4) posttransplant, though not significantly (p>0.1). AUC_{0-6} and AUC_{0-12} were highly variable (CV's 37–40%). Mean dose was 958 and 875 mg on days 28 and 365, respectively. Dose-adjusted AUC exhibited non-linear decline with increasing MMF dose. Median total trough concentrations were 1.16–2.90 µg/mL and highly variable (CV 55.3–58.7%). Percent unbound MPA did not change over time (0.96%, p=0.96). Unbound and total MPA concentrations were highly correlated (r^2=0.94), with a modest correlation between total MPA trough and AUC_{0-6} (r^2=0.48) or AUC_{0-12} (r^2=0.65).
CONCLUSIONS: MPA disposition is highly variable in the first year posttransplant. AUC's were higher early posttransplant. These data suggest that therapeutic drug monitoring will be necessary to maintain consistent exposure.

323E. Racial comparison of T-lymphocyte populations and T-regulatory cell pharmacodynamics during chronic immunosuppression. *Kathryn Gillis, Pharm.D.*, Kiran Dole, Pharm.D., Nicolae Leca, M.D., Samir Yassa, M.D., Rocco Venuto, M.D., Kathleen Tornatore, Pharm, D.; University at Buffalo, Pharmacy Practice, School of Pharmacy, Buffalo, NY

Pending acceptance in American Society of Nephrology 2004.

324. Control of hyperlipidemia in renal transplant patients as defined by the National Cholesterol Education Program (NCEP). *LanChi L. Bui, Pharm.D.*[1], Hai Tran, Pharm.D.[2], Christine J. Leehealey, M.D.[1], Madeleine V. Pahl, M.D.[1]; (1)University of California, Irvine Medical Center, Orange, CA; (2)Cedars Sinai Medical Center, Los Angeles, CA.

PURPOSE: Hyperlipidemia is an important CVD risk factor and is particularly common in renal transplant recipients. The purpose of this study was to determine how well the lipoprotein profiles of kidney transplant recipients are maintained within the target values defined by the 1993 NCEP II guidelines.
METHODS: Medical records fo 257 adult kidney transplant patients with functioning allografts for > 6 mo. were reviewed at UCIMC and Nephrology Associates Clinic in Riverside for demographic information, medications, cardiac risk factors, lipoprotein profile and serum creatine levels. Data were evaluated using odds ratio, a confidence interval of 95% was considered to be statistically significant. Of these, 181 contained complete information.
RESULTS: Treatment goal was met in 70.2% of all patients; 46 patients had incomplete lipid profiles but based on total cholesterol (<200mg/dl) 52.2% met goal of treatment. The remaining 135 patients had complete lipid profiles and 76.3% met the LDL goal. Age (>44 yrs) was the only variable statistically associated with achieving target. Female gender, Asian ethnicity, absence of DM, use of tacrolimus, and higher income bracket were factors that tended to be associated with likelyhood of meeting target levels. HMGCoA inhibitors were used in 50.8%, fibrates in 1.7%, and niacin in 1.1% of all patients. In treated patients, 31.5% failed to meet goal.
CONCLUSIONS: Unlike the general population where 33–50% of hyperlipidemic patients achieved target LDL levels, greater number of transplant recipients were at target LDL levels (76.3%). In addition, 70.1% of all transplant recipients met target levels of total cholesterol.

325. Effect of docetaxel on T-cell activation: a role in immunosuppression? *LanChi L. Bui, Pharm.D.*, David Imagawa, M.D.; University of California, Irvine Medical Center, Orange, CA.

PURPOSE: Docetaxel is a chemotherapy agent which works on microtubules. We hypothesize that disruption of microtubules would prevent the cytoskeletal changes necessary for effective T-cell proliferation and cell differentiation. The objectives of this study are to determine whether docetaxel prevents T-cell proliferation, affects T-cell morphology, and to measure activation of T-cells using intracellular calcium levels.
METHODS: Using performed in vitro proliferation assay using CD4 T-cell line and antigen presenting cell (APC) line restricted to hen egg lysozyme, incubated for 48 hours, quantified with MTT assay. In addition,we performed polarity assay using murine T-cells and measured intracellular calcium at 1-hour and 12-hour pre-incubation with flow cytometry analysis.
RESULTS: Proliferation of lymphocytes was 58% inhibited with smallest dose tested and 85% inhibited with largest dose tested. Number of polarized cells was significantly reduced with docetaxel. Intracellular calcium levels increased at 1-hour incubation when cells were stimulated except at the highest concentration (20mg/L). There was no increase in intracellular

calcium at 12-hour incubation with stimulation except at the smallest dose tested (0.125mg/L)
CONCLUSIONS: Docetaxel inhibited T-cell proliferation. Percent of polarized cells was significantly reduced. Intracellular calcium levels were affected with higher concentration of drug and with longer incubation time.

326. Comparing renal transplant patients' adherence to free cyclosporine and free tacrolimus immunosuppressant therapy. Marie A. Chisholm, Pharm.D.[1], *Herbert E. McGinty, BSPharm*[2], Laura L. Mulloy, DO[3]; (1)University of Georgia College of Pharmacy and Medical College of Georgia School of Medicine, Augusta, GA; (2)University of Georgia College of Pharmacy, Augusta, GA; (3)Medical College of Georgia School of Medicine, Augusta, GA.

PURPOSE: To determine if there is a difference in renal transplant patients' (RTPs) adherence to cyclosporine compared to tacrolimus based immunosuppression therapy when medications are supplied free to the RTPs.
METHODS: Adherence was estimated by comparing tacrolimus or cyclosporine pharmacy refill records to the prescribed regimen for 12-months after transplant. RTPs in the study received their cyclosporine or tacrolimus free from the Medical College of Georgia outpatient pharmacy for their entire first-year after transplantation. Patients' cyclosporine and tacrolimus serum concentrations were used to validate adherence. Kaplan Meier analysis was used to estimate the fraction of RTPs remaining adherent every month and to compare the mean time RTPs were adherent in each group (cyclosporine vs. tacrolimus).
RESULTS: Thirty-three patients were included in the study, 25 (76%) received cyclosporine and 8 received tacrolimus. The mean time to the first non-adherent month was 8 months post-transplant. At 12-months post-transplant, approximately 42% of the patients remained adherent. A greater percentage of the patients who received tacrolimus remained adherent compared to those patients who were taking cyclosporine (63% vs. 33%, $p<0.05$). Approximately 75% of non-adherent patients were found to have subtarget drug concentrations, and only 24% of adherent patients had subtarget levels ($p<0.01$).
CONCLUSIONS: Adherence to immunosuppressant therapy tends to decrease over time, the type of immunosuppressant therapy used affects adherence, and RTPs who are adherent are less associated with subtarget concentrations than those who are non-adherent.

327. Pharmacokinetics of mycophenolate and its glucuronidated metabolites in stable lung transplant recipients. *Mary H. H. Ensom, B.S.(Pharm), Pharm.D.*[1], Lillian S. L. Ting, BSc.(Chem)[2], Nilufar Partovi, BSc(Pharm), Pharm.D.[3], K. Wayne Riggs, BSc(Pharm), Ph.D.[2], Robert D. Levy, M.D., FRCPC[4]; (1)University of British Columbia and Children's & Women's Health Centre of British Columbia, Vancouver, BC, Canada; (2)University of British Columbia, Vancouver, BC, Canada; (3)University of British Columbia and Vancouver General Hospital, Vancouver, BC, Canada; (4)University of British Columbia, St. Paul's Hospital and BC Transplant Society, Vancouver, BC, Canada.

PURPOSE: The purpose of this study was to characterize the pharmacokinetics of mycophenolic acid (MPA) and its glucuronidated metabolites, MPAG (phenolic-glucuronide) and AcMPAG (acyl-glucuronide), in stable lung transplant recipients.
METHODS: Eight patients were entered into this open-label study, following written informed consent. Upon administration of a steady-state morning mycophenolate mofetil (MMF) dose, blood samples were collected at 0, 0.3, 0.6,1,1.5,2,4,6,8,10,and 12 hours post-dose. Total MPA, MPAG, and AcMPAG concentrations were measured by a validated HPLC method with ultraviolet detection and pharmacokinetic parameters analyzed by non-compartmental modeling using WinNonlin 4.1.
RESULTS: Patient characteristics included: 3 males and 5 females, on average 5.2 years post-transplant (range:2.1–9.2yr), mean(±SD) age of 46.9±14.0yr and weight 69.8±22.2kg. Mean albumin concentration was 3.7±0.6g/dL and serum creatinine was 1.3±0.5mg%. All patients also were on prednisone, with 6 on tacrolimus and 2 on cyclosporine. MMF dosage ranged from 1.5 to 3 grams daily (34.2±10.5 mg/kg/day; range:18.3–54.0 mg/kg/day). Mean(±SD) for MPA were: area-under-the-curve [$AUC_{(0-12h)}$] 42.33±19.49 µg*hr/mL; dose-normalized $AUC_{(0-12h)}$ 39.63±20.99µg*hr/mL; maximal concentration (C_{max}) 7.80±3.32µg/mL; time to C_{max} (T_{max}) 2.25±3.15h; and minimum concentration (Cmin) 1.10±0.64µg/mL. AUC ratios of MPAG:MPA and AcMPAG:MPA were 18.68±6.60 and 0.17±0.11, respectively.
CONCLUSIONS: This is the first study to determine the pharmacokinetics of MPA and its glucuronidated metabolites in the lung transplant population. Further studies should focus on determining if genetic variability in UDP-glucuronosyltransferase enzymes can explain the observed wide interpatient variability and on identifying MMF dosing strategies that optimize immunosuppressive efficacy and minimize toxicity in lung allograft recipients.

328E. Pegfilgrastim after high-dose chemotherapy (HDC) and autologous peripheral blood stem cell transplantation (ASCT). *Madan Jagasia, M.D.*, John Greer, M.D., Adetola Kassim, M.D., Shin Mineishi, M.D., David Morgan, M.D., Katherine Ruffner, M.D., Friedrich Schuening, M.D.; Vanderbilt-Ingram Cancer Center, Division of Hematology-Oncology, Department of Internal Medicine, Vanderbilt U Medical Center, Nashville, TN.

Presented at the Annual Meeting of the American Society of Clinical Oncology, New Orleans, LA, June 5–8, 2004.

329E. Pharmacokinetics of mycophenolic acid and clinical outcomes in liver transplant recipients with hepatitis C. *Theodore M. Sievers, Pharm.D.*, Curtis D Holt, Pharm.D., R. Mark Ghobrial, M.D. Ph.D., Lucy Artinian, R.N., Sue V. McDiarmid, M.D., Ronald W. Busuttil, M.D. Ph.D.; Dumont-UCLA Transplant Center, Los Angeles, CA.

Presented at the Annual Meeting of the American Transplant Congress, Boston, MA, May 14–19, 2004.

330E. Cytomegalovirus and drug resistance mutations in liver transplantation. *Greg A. Smallwood, Pharm.D.*; Emory Healthcare, Atlanta, GA.

Presented at the Annual Meeting of the American Transplant Congress, Boston, MA, May 14–19, 2004.

331. Lamivudine resistant hepatitis B following liver transplantation. *Greg A. Smallwood, Pharm.D.*, Kathleen Connor, PA, Carlos Fasola, M.D., Andrei Stieber, M.D., thomas Heffron, M.D.; Emory Healthcare, Atlanta, GA.

PURPOSE: The aim of this review is evaluate outcomes of patients with lamivudine resistant, recurrent hepatitis B following liver transplantation.
METHODS: All hepatitis B surface antigen positive patients received, after liver transplant, hepatitis B immune globulin (HBIG) and titrated to maintain hepatitis B surface antibody (HBSAnti) levels above 500 i.u./ml along with lamivudine. With recurrence of the hepatitis B surface antigen, patients were started on valganciclovir 900mg orally then treatment was converted to adefovir 10mg daily.
RESULTS: Of patients transplanted for hepatitis B(n = 44), 21 (42%) were actively replicating. Only 9 (20.4 %) had recurrence of HBV surface antigen at a mean time to recurrence being 501 (± 281) days. sOf the 9 patients with recurrence, 1 recurred prior to the advent of lamivudine and did not survive. Three patients have been maintained on lamivudine alone without resistance developing (1368 ± 402 days). The last five patients (each replicator) developed resistant recurrence and was begun on valganciclovir 900mg daily prior to switching to adefovir. Patients taking valganciclovir, a reduction in viral load was noted [1,910 pg/ml to 103 pg/ml]. Of the 5 patients, 4 have been maintained on Adefovir with a mean viral load drop of 2 log counts. One patient has been started on peginterferon-α 2a which produced an additional 2 log drop in his viral load.
CONCLUSIONS: Numerous options currently are available for recurrent HBV following liver transplantation which shows tremendous promise. Additional work should be done with peginterferons in combination with adefovir.

332. Impact of gender and race on posttransplant metabolic complications. *Agnes Lo, Pharm.D.*, Lauren Webb, BSc, A. Osama Gaber, M.D.; University of Tennessee Health Science Center, Memphis, TN.

PURPOSE: The purpose of this retrospective study is to determine if gender and race affects the incidence of metabolic complications post renal transplantation.
METHODS: Renal transplant recipients with functioning renal allograft for at least one year posttransplant and a minimal follow-up of 3 years were included. The subjects were divided into four groups: black female (BF), non-black female (NBF), black male (BM), and non-black male (NBM). Metabolic profiles were determined at baseline and at 12 months post-transplant: body mass index (BMI), fasting blood glucose (FBS), triglycerides (TG), total cholesterol (TC), systolic or diastolic blood pressure (SBP or DBP), and immunosuppression.
RESULTS: There were 28 BF, 11 NBF, 36 BM, and 27 NBM. There were no differences in age, transplant characteristics, and immunosuppressive regimens among the groups. Regardless of gender and race, BMI, FBS, TG, and TC significantly increased posttransplant, while SBP and DBP decreased posttransplant. BF had the most significant weight gain posttransplant compared to other groups, $p<0.01$. Majority of BF (68%) also developed metabolic syndrome at 1 year posttransplant compared to 46% NBF, 47% BM, and 33% NBM. Patient and graft survival, acute rejection rates, and incidence of posttransplant diabetes mellitus were similar among the groups. BM had the highest serum creatinine (1.9 mg/dL) compared to other groups (1.2 to 1.4 mg/dL), $p=0.01$.
CONCLUSIONS: BF may be at the highest risk for posttransplant metabolic complications due to the significant weight gain posttransplant. The long-term effects of these metabolic abnormalities on transplant outcomes remained to be determined.

Urology

333E. Efficacy of vardenafil in a broad population of men with ED irrespective of prior sildenafil use: a retrospective analysis of a 2 year investigation. *Gerald Brock, M.D.*[1], Hartmut Porst, M.D.[2], Christian Stief,

M.D., Ph.D.[3], Manfred Beneke, Ph.D.[4], Ernst Ulbrich, M.D.[4], Inigo Saenz de Tejada, M.D.[5]; (1)St. Joseph's Medical Center, Lawson Research Institute, London, ON, Canada; (2)Private Practice, Hamburg, Germany; (3)Hannover Medical School, Hannover, Germany; (4)Bayer Vital GmbH, Leverkusen, Germany; (5)Fundacion para la Investigacion y el Desarollo en Andrologia, Madrid, Spain.

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334E. Long term efficacy of vardenafil provides rapid and consistent satisfaction with erection hardness and sexual experience in men with erectile dysfunction. *Gerald Brock, M.D.*[1], Serge Carrier, M.D.[2], Inigo Saenz de Tejada, M.D.[3], Christian Stief, M.D., Ph.D.[4], Ernst Ulbrich, M.D.[5], Manfred Beneke, Ph.D.[5], Hartmut Porst, M.D.[6]; (1)St. Joseph's Medical Center, Lawson Research Institute, London, ON, Canada; (2)McGill University Health Centre-Royal Victoria Hospital, Montreal, QC, Canada; (3)Fundacion para la Investigacion y el Desarollo en Andrologia, Madrid, Spain; (4)Hannover Medical School, Hannover, Germany; (5)Bayer Vital GmbH, Leverkusen, Germany; (6)Private Practice, Hamburg, Germany.

Published in Journal of Andrology 2004;March/April Suppl:93.

335. Prevalence of depression, falls and fractures, skin infections, urinary tract infections, and vulval vaginitis among patients with overactive bladder. *Theodore Darkow, Pharm.D.*[1], Christina L. Fontes, M.S.[1], Todd E. Williamson, Ph.D.[2], Thomas A. Telly, R.Ph.[2]; (1)Prescription Solutions, Costa Mesa, CA; (2)Yamanouchi Pharma America, Inc., Paramus, NJ.

PURPOSE: This analysis evaluated the clinical impact of overactive bladder (OAB), especially regarding the prevalence of important comorbid conditions, within a managed care population.
METHODS: This was a retrospective analysis using claims data from a managed care organization of approximately 2.7 million lives. OAB patients >18 years old were identified between July and December 2001 and followed for 360 days. A random sample of controls was matched 1:1 on propensity score, which was estimated using patient demographics and diagnosis of osteoporosis, stroke, diabetes, or urethral stricture during a 180-day pre-index period. Medical claims were examined for any diagnosis of the studied comorbidities. Unadjusted prevalence rates for depression, skin infections, and vulval vaginitis were compared between OAB cases and controls using Chi square. Prevalence of falls and fractures, UTIs, and any comorbid condition were compared using logistic regression, adjusting for additional confounders.
RESULTS: A total of 23,112 OAB cases and controls were identified. Mean age was approximately 69 years, and 67.6% were female. Prevalence of all conditions were significantly higher (p<0.0001) for OAB cases than controls: falls and fractures, 25.3% vs. 16.1%; depression, 10.5% vs. 4.9%; UTIs, 28.0% vs. 8.4%; skin infections, 3.9% vs. 2.3%; vulval vaginitis, 4.7% vs. 1.8%. Prevalence of any comorbid condition was also significantly higher for OAB cases (52.1% vs. 27.9%).
CONCLUSIONS: This analysis demonstrates that OAB patients often have additional comorbidities related to their disease. Thus, OAB is an important condition in need of greater focus and better management by clinicians.

336E. Vardenafil 10 mg offers an 88% and 81% probability of successful penetration and maintenance within three attempts. *Wayne J.G. Hellstrom, M.D.*[1], Muammer Kendirci, M.D.[1], Martin Homering, MSPH[2], Marc Thibonnier, M.D.[3]; (1)Tulane University School of Medicine, New Orleans, LA; (2)Bayer AG, Wuppertal, Germany; (3)Bayer Pharmaceuticals Corporation, West Haven, CT.

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Women's Health

337. Comparison of symptom scales for premenstrual symptoms in women taking oral contraceptives. *Andrea L. Coffee, Pharm.D., M.B.A.*, Patricia J. Sulak, M.D., Thomas J. Kuehl, Ph.D.; Scott & White Memorial Hospital and Clinic, Temple, TX.

PURPOSE: This study compared two daily symptom scales used in research to evaluate pharmacotherapy in women with premenstrual symptomatology.
METHODS: Reproductive-age women participating in a prospective oral contraceptive study completed two scoring instruments—a daily menstrual calendar which included a mood score of 0–10 (a composite of anxiety, depression, and irritability) and the Penn State Daily Symptom Report (DSR17) that contained 17 elements with each rated 0–4. Ten elements were behavioral components (DSR10), 7 elements were physical symptoms (DSR7), with one element specifically mood swings (DSRmood).
RESULTS: Daily scores were available from between 1 and 3 consecutive standard 21/7-day cycles for 109 subjects. The mood score was significantly related to DSR17, DSR10, DSR7, DSRmood (p<0.000001) with coefficients of concordance of 0.46, 0.23, 0.09, and 0.29, respectively, and R-squares of 0.38, 0.34, 0.25, and 0.36, respectively. The daily mood score is positively correlated with all 17 elements of the DSR17 (0.26 to 0.58) with greatest correlation to the "mood swing" element. Using multiple regression analysis, all but three elements of the DSR17 were significantly (p<0.05) related to the daily mood score. Daily mood scores and DSR17 also demonstrated the same pattern of increase immediately before and during the 7-day hormone-free interval.
CONCLUSIONS: A simple daily mood score scaled from 0 to 10 is concordant with the more complex 17-element symptom index and demonstrates the same pattern of change during cycles of oral contraceptive use. The simple scoring system represents an advantage for long duration oral contraceptive studies.

338E. A randomized, open-label, cross-over study comparing the effects of transdermal vs. oral estrogen therapy on free testosterone levels in naturally menopausal women. Jan L. Shifren, M.D.[1], Sophie Desindes, M.D.[2], Stephanie Stanworth, M.S.[3], Marilyn McIlwain, B.S.[4], *Norman A. Mazer, M.D., Ph.D.*[3]; (1)Harvard Medical School, Boston, MA; (2)University of Sherbrooke, Sherbrooke, QC, Canada; (3)Watson Laboratories, Inc., Salt Lake City, UT; (4)Watson Laboratories, Inc., Morristown, NJ.

Presented at the 86th Annual Meeting of the Endocrine Society, New Orleans, LA, June 16–19, 2004.

339. Pharmacokinetics of intravenous immunoglobulin (IVIG) before and during pregnancy. *Mary H. H. Ensom, B.S.(Pharm), Pharm.D.*[1], Martha E. Kinnear, BSc(Pharm), student[1], Edwina Houlihan, R.N.[2], Mary D. Stephenson, M.D., M.Sc.[3]; (1)University of British Columbia and Children's & Women's Health Centre of British Columbia, Vancouver, BC, Canada; (2)Children's & Women's Health Centre of British Columbia, Vancouver, BC; (3)University of Chicago, University of British Columbia, and Children's & Women's Health Centre of British Columbia, Vancouver, BC.

PURPOSE: To characterize intravenous immunoglobulin (IVIG) pharmacokinetics in women with recurrent miscarriage.
METHODS: Of 20 enrolled women (9 in an open-label pharmacokinetic study for treatment of antiphospholipid antibody syndrome and 11 in a randomized placebo-controlled trial for idiopathic secondary recurrent miscarriage), 14 received IVIG (GamimuneN 5%) 500–1000mg/kg and 6 placebo over a 2–10h period q4wks pre-pregnancy until up to 18–20 weeks gestation. Serum IgG concentrations were measured by rate nephelometry before and at 0.5h and 1,2,3, and 4 weeks following the 1st dose, and a dose during each of the 1st and 2nd trimesters.
RESULTS: Mean(±SD) age was 34.5±4.4yr(IVIG) and 34.5±4.8yr(placebo). History of spontaneous abortions was 4.5±2.2(IVIG) and 3.5±0.8(placebo). Pharmacokinetic parameters(mean±SD) were:

	IVIG			Placebo(P)		
	C_{max}(g/L)	C_{min}(g/L)	AUC_{0-t} (g*h/L)	C_{max}(g/L)	C_{min}(g/L)	AUC_{0-t} (g*h/L)
Prepregnancy (n=12 IVIG;n=6P)	26.8±4.2	12.5±1.8	11735.3±1800.6	10.1±2.6	8.6±2.6	5768.0±1405.3
1sttrimester (n=9 IVIG;n=3P)	30.8±7.5a	12.6±2.7	11901.7±2546.6	11.4±3.4	9.2±2.6	6846.2±2018.0
2ndtrimester (n=7 IVIG;n=2P)	27.1±4.1a	11.6±2.8	11365.2±1781.9	10.5±0.2	9.4±1.2	6761.2±321.9

Dosages (on mg/kg basis) and AUCs did not differ significantly within the IVIG group between the 3 sampling periods. Roughly-estimated contributions of exogenously-administered IVIG to total AUC_{0-t}[calculated as mean AUC_{0-t}(IVIG group) minus mean AUC_{0-t}(placebo group)] were 5967.3g*h/L (pre-pregnancy), 5055.5g*h/L(1st trimester), and 4604.0g*h/L(2nd trimester).
CONCLUSIONS: Pregnancy did not have a significant effect on exposure to the same mg/kg dosage of exogenously-administered IVIG. The estimated contribution of exogenous IVIG(i.e., ~5200g*h/L) to total AUC_{0-t} was similar to, albeit slightly lower than, that contributed by endogenous IgG(i.e., ~6500g*h/L). These preliminary data warrant further study in larger groups of patients.

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.

340. Pharmacist program to review new antipsychotic orders on hospitalized patients. *Dan Moellentin, Pharm.D.*, Jamie Cronin, Rph, Pharm.D., David Crabtree, M.S., Cpt; Eastern Maine Medical Center, Bangor, ME.

Several hospital regulatory boards recommend pharmacist review of patient's medications where new antipsychotics are ordered for in-patients. Evaluation prior to first dose is not always feasible, and in some cases the delay caused could cause harm to personnel or patients. At EMMC, a computer rule alerts a clinical pharmacist of a new order for typical and atypical antipsychotics. After reviewing the medicine and medical history and pre-hospitalization medication regimen, recommendations are made if drug association is suspected. Using pharmacist documents of evaluated cases over a 6 month period, post-operative patients accounted for 61% of cases. Gases, sedatives, benzodiazepines, and fluid balance were most often identified. Hypotensive

agents (18%)were identified as next leading cause. Drug-drug interactions were uncovered as the 3rd leading cause (12%) most frequently involving CYP2D6, 3A4, 1A1, p-gp, and to a lesser extent phase II reactions. While initial computer checks prevent dosage extremes at the time of order review, some doses may be extreme for individual patients and dosing was likely responsible for delirium in 9% of cases found (for example one patient began having hypnogognic hallucinations with metoclopramide but to normalalized once dose was lowered. In 9% of patients, dosage reduction for age or creatinine clearance resolved the delirium. As a method to determine the need and on-going requirement of anti-psychotics in hospitalized patients, a computer summary of patients receiving target drugs provides clinical pharmacists with a tool for reviewing the patient's medication and medical history for possible reversible drug-induced causes.

341. Drug-drug interaction screening and management process improvement. Kelly M. Smith, Pharm.D., *Sony Tuteja, Pharm.D., BCPS*, Heather H. Cornett, Pharm.D., Julie A. Flynn, Pharm.D., Lucy B. Wells, B.S., Kimberley B. Hite, M.S., Pharm.D.; University of Kentucky, Lexington, KY.

PURPOSE: The high volume of alerts triggered by drug-drug interaction (DDI) screening software may desensitize users to clinically important interactions. A program was undertaken to educate pharmacists about 29 DDIs of the highest clinical importance (as identified by Malone et al), assess drug interaction screening software, and make process improvements in both a hospital and outpatient pharmacy.
METHODS: Current vendor-supplied drug interaction screening software were tested for their ability to detect each of the 29 DDI pairs, with subsequent customization as needed. Monographs were developed for each DDI pair to educate pharmacists about their relevance. A report prompting pharmacists to intervene on target DDIs was also pursued.
RESULTS: The outpatient pharmacy computer system initially failed to capture 1 DDI, as well as those involving combination products. All interactions were captured by the hospital system, yet had differing severity codes (38% contraindicated, 48% severe, 14% moderate). Because the severity codes cannot be readily altered, daily DDI reports are being created for dissemination to hospital pharmacists to prompt interventions, with subsequent documentation in the clinical intervention system. Structured monographs for each DDI pair are disseminated electronically to pharmacy staff and archived on the Drug Information Center website. Additionally, case discussions highlighting the DDIs are presented at weekly staff meetings.
Conclusion: Pharmacy drug interaction screening software were successful in identifying a majority of clinically serious DDIs. Additional efforts, including customizing software, delivering routine educational programs, and providing daily prompts of potential DDIs, were necessary to heighten pharmacists' awareness of serious drug-drug interactions.

342. Effect of internal reporting criteria on suspected adverse drug reactions submitted to MedWatch. *Kelly M. Smith, Pharm.D.*, Amber P. Lawson, Pharm.D., Heather H. Cornett, Pharm.D., Sony Tuteja, Pharm.D., BCPS; University of Kentucky, Lexington, KY.

PURPOSE: To streamline suspected adverse drug reaction (ADR) reports submitted to MedWatch, internal hospital criteria for MedWatch reporting had been utilized. Each month, a drug information specialist or pharmacy resident reviewed each ADR for potential MedWatch submission. This study evaluated the contributions of a hospital's ADR reporting system to MedWatch by (1) determining the frequency of suspected ADRs submitted to MedWatch, and (2) comparing this frequency to those deemed reportable according to both internal and FDA criteria for serious adverse events.
METHODS: Reports submitted during 2003 were retrospectively evaluated by a single investigator for reporting suitability via both internal and MedWatch criteria. Internal criteria included reactions: related to a molecular entity marketed for less than three years; not reported in the package insert; occurring with a greater frequency, or those of greater severity or poor patient outcome, as subjectively deemed by the reviewer.
RESULTS: Utilizing internal criteria, 52 (4.4%) of 1062 ADRs were deemed reportable to MedWatch, yet 32 (3%) were submitted. According to FDA criteria, 353 (33%) serious ADRs were reportable, 6.7% (24) of which were actually submitted. Capture rates varied amongst the individuals serving as reviewers.
Conclusion: A streamlined approach to submitting suspected ADR reports to MedWatch failed to capture a significant number of reportable reactions according to either FDA or internal criteria. The suitability of internal reporting criteria, as well as the use of multiple reviewers, needs to be reconsidered. Criteria prompts will be built into the review system to increase future capture rates.

343. Utilization of fentanyl patient-controlled analgesia in a large academic medical center. *Angela Clark, Pharm.D.*[1], Suzanne A. Nesbit, Pharm.D., BCPS[1], Stuart Grossman, M.D.[2]; (1)The Johns Hopkins Hospital/Department of Pharmacy, Baltimore, M.D.; (2)Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, M.D.

PURPOSE: Fentanyl has also been associated with medication errors, especially when used as patient-controlled administration (PCA). Fentanyl is the only opiate dosed in micrograms (as opposed to milligrams), which may lead to pump-programming errors. Fentanyl was recently classified in the top five drugs involved in medication errors at The Johns Hopkins Hospital from 8/1/2002–1/31/2003.The objectives of the study were to investigate the utilization of fentanyl PCAs by conducting a review use of fentanyl PCA to determine prescribing patterns and related adverse events.
METHODS: Data was collected concurrently by chart review over a three month period from December through February 2003. Patient selection was based on a pharmacy generated report of all patients who were ordered fentanyl PCAs. Pediatric and MICU patients were excluded.
RESULTS: Four hundred patients were started on Fentanyl PCA during this time and a total of 185 patients were studied. Approximately half (49.7%) of the patients were on the GI surgery service. Twenty-six patients (14.1%) had documented allergies to opiates. It was discovered that 74.6% of the preprinted PCA order sheets were not completed properly. Forty percent of patients studied experienced documented adverse drugs reactions.
CONCLUSIONS: Fentanyl was the first-line opioid for PCAs in our surgical patients. Post-operative /acute pain management was the primary indication in 99.5% of the patients. Dosing units were not indicated on 37.7% of the incomplete orders. In response to our findings, the PCA preprinted order sheet have been revised to decrease the potential for medication errors.

344E. Delay in dose titration of lipid-lowering therapy leads to adverse cardiovascular outcomes. *Amy S. Friend, Pharm.D.*[1], Tamara S. Evans, Pharm.D., BCPS[2], Ellen M. Schellhase, Pharm.D.[1], Masoor Kamalesh, M.D.[1]; (1)Richard L. Roudebush VA Medical Center, Indianapolis, IN; (2)Pfizer, Indianapolis, IN.

Presented at the American College of Cardiology Annual Scientific Session, New Orleans, LA, March 10, 2004.

345. Evaluation of cardiac catheterization complications at an academic medical center. *Emily J. Young, Pharm.D.*, Kerry K. Pickworth, Pharm.D.; The Ohio State University Medical Center, Columbus, OH.

PURPOSE: To incorporate pharmacist involvement in a continuous quality improvement initiative regarding evaluation of cardiac catheterization complications. Complications were evaluated in order to 1) determine if complications were associated with therapeutic modalities (adjunctive therapies and fluid administration) and 2) identify areas for improvement in regards to medication administration.
METHODS: A retrospective analysis of cardiac catheterization complications that occurred between July 1, 2003 and December 31, 2003 was conducted. Patient demographics, history of present illness, significant past medical history, catheterization procedure details, type of complication as defined by the American College of Cardiology percutaneous coronary intervention guidelines, pertinent vitals and laboratory data, medication history, and hydration history were collected from computerized patient profiles, pharmacy databases, and patient charts. Descriptive statistics were employed in order to analyze the data.
RESULTS: During the six-month study period, 2152 cardiac catheterizations were performed. Complications occurred in 3.1% of patients. The study population (n=64) consisted of 58% females with a mean age of 64 years. Vascular complications occurred in 2.5% of patients. Of the vascular complications, 48% were associated with drug therapy including heparin (37%), enoxaparin (23%), and warfarin (17%). Renal complications occurred in 0.6% of patients. Lack of fluid administration prior to and following cardiac catheterization was identified in 92% of patients experiencing renal complications.
CONCLUSION: A pharmacist was able to identify that 48% of vascular complications were associated with drug therapy adverse events and 92% of renal complications were associated with lack of fluid administration. Targets for improvement have been identified.

346. Development of a multidisciplinary hemostasis monitoring program for post-cardiac surgery patients. *Jeremy D. Flynn, Pharm.D.*, Wendell S. Akers, Pharm.D., Ph.D.; University of Kentucky, Department of Pharmacy Practice and Science, Lexington, KY.

Background: Bleeding and severe coagulopathy are commonly associated with cardiac surgery and leads to increased morbidity and mortality. Strategies to limit perioperative bleeding include reducing preoperative exposure to antiplatelet agents, tight control of anticoagulation, and the administration of hemostatic agents or blood products. However, determining which patients are at appropriate risk to receive prophylaxis and subsequent treatment is highly variable since no national guidelines have been adopted.
PURPOSE: To establish a multidisciplinary hemostasis monitoring service in order to develop institution-specific treatment algorithms and practice guidelines for the management of perioperative bleeding in patients undergoing cardiothoracic surgery.
METHODS: A multidisciplinary hemostasis monitoring service was organized to prospectively collect patient-specific variables demonstrated in the literature to predict or influence perioperative administration of antifibrinolytics, antiplatelet agents, protamine, vitamin K, and blood products in patients undergoing cardiac surgery. This information was entered

it into an electronic database to coincide with bleeding indices and utilization of hemastatic agents or blood products.
RESULTS: Currently, 84 patients are in the database. The average chest tube output was 1036±89ml and the average change in hematocrit was -4.4±0.1. 58.3% of patients received antifibrinolytics, 32.1% received at least one blood transfusion, and 3.6% went back for reexploration. The most common comorbidities were hypertension (77%), hyperlipidemia (77%), diabetes (31%), CHF (30%), and COPD (23%).
CONCLUSIONS: Information derived from this hemostasis monitoring service provides important data regarding institution-specific risk factors, clinical outcomes, and a platform to monitor new and existing treatment strategies to manage perioperative bleeding.

347. Use of a heart failure questionnaire to establish need for a novel clinic in community pharmacy. *Jean S Cottrell, Pharm, D, CGP*[1], Barbara Rogler, RPh, M.S.[2]; (1)Eckerd Patient CARE Center, Latham, NY; (2)Pfizer, Delmar, NY.

Introduction The American College of Cardiology/American Heart Association (ACC/AHA) guidelines recommend frequent monitoring of heart failure patients and an ACE-Inhibitor for all patients. It is estimated that there is a significant gap between these guidelines and current practice. Community pharmacists are in position to assist with monitoring these patients, however, they frequently lack pertinent information such as diagnoses and medical histories. Objective To assess the level of activity of ambulatory patients using a validated questionnaire for the purpose of establishing the need for a collaborative care heart failure clinic in two community pharmacies. Methods The Minnesota Living with Heart Failure Questionnaire, an ACC/AHA approved level of activity assessment tool, was randomly mailed to 200 patients from 2 community pharmacies. It included a section for the patient to add diagnoses of different types of heart disease as well as a section to provide their name for follow-up from the pharmacist. Patients received a survey if they were currently taking digoxin and a loop diuretic without warfarin. Responses from surveys will be compiled with post-MI data from local hospitals to demonstrate to outpatient clinics the need for intervention. An algorithm will be developed based on the ACC/AHA guidelines, including correspondence with prescribers to provide feedback on patient outcomes and ensure appropriate drug therapy. The following outcomes will be tracked; 1) Medication Adherence, 2) Blood Pressure to JNC VII goal, 3) Weight, 4) Level of Activity via the Minnesota HF Questionnaire, 5) Number of patients prescribed an ACE-Inhibitor.

348. Assessment of the VA Loma Linda Healthcare System Lipid Clinic. *Reza Taheri, Pharm.D.*[1], Kenneth Wong, Pharm.D.[2], Phillip Ng, Pharm.D.[2], George Tran, Pharm.D.[2], Geir Frivold, M.D.[2]; (1)Loma Linda University, 11262 Campus Street, Loma Linda, CA; (2)VA Loma Linda Healthcare System, Loma Linda, CA.

PURPOSE: To assess the success rate of the Lipid Clinic in improving patients' lipid indices.
METHODS: A retrospective analysis of patients enrolled in the clinic was performed. Baseline, before enrollment, and most current lipid indices, Liver Function Tests (LFTs) and drug utilization data were collected. A paired T test was used to evaluate continuous variables and chi squared test for discrete variables.
RESULTS: A total of 104 patients (age 60±8.6, 99% male) had both baseline and follow-up data. Average total cholesterol and LDL-C decreased by 40mg/dL and 32mg/dL respectively (p<0.0001). Over 88% of the patients were already on a lipid-modifying agent before Lipid Clinic enrollment. Number of patients on combination therapy increased from 23 at baseline to 45 after the enrollment in the Clinic (p<0.0001).
TABLE: Cholesterol and LFT Changes

	Baseline Average (SD) mg/dL	Current Average (SD) mg/dL	Change (%) mg/dL	p value
Total Cholesterol	235 (77.7)	195 (57.5)	40 (17)	<0.0001
LDL-C	142 (52.1)	110 (42.1)	32 (22.5)	<0.0001
HDL-C	36 (9.6)	36 (9.0)	0 (0)	1
Trigs	389 (835.5)	285 (538.1)	104 (26.7)	0.287
ALT	41 (20.6)	33 (23.6)	8 (19.5)	<0.0001
AST	25 (12.3)	25 (12.8)	0 (0)	1

CONCLUSIONS: Even though the great majority of patients were already on a lipid-modifying agent before clinic enrollment, a significant drop in both LDL-C and total cholesterol was obtained with diligent and continuous follow-up in the Lipid Clinic. This aggressive approach did not result in increased LFTs or any cases of rhabdomyolysis.

349. Hypertension management in a family medicine residency training program. *Toni L. Ripley, Pharm.D.*, Shaunta Martina, Pharm.D., Donald Harrison, Ph.D.; University of Oklahoma College of Pharmacy, Oklahoma City, OK.

PURPOSE: Documentation of hypertension management in patients in a Family Medicine residency training program was done to evaluate success of achieving therapeutic goals defined in the medical literature and to assess the role for clinical pharmacy services.
METHODS: Medical records of 228 patients within the Family Medicine Center from 11/1/01 to 10/31/02 with a diagnosis of hypertension, diabetes, or renal disease were randomly identified. Results from the patients in the hypertension arm are reported.
RESULTS: 70.6% patients had hypertension. 36.6% of patients were on 1 drug; 37.9% were on 2 drugs; 22.3% were on ≥3 drugs; 3.1% were not treated with drug therapy. Heart rate was assessed in only 0.44% of sample; 15.5% were taking negative chronotropic medicines. Blood pressure goals, defined as < 140/90 and < 130/85, were not met in 56.5% and 83.4% of patients, respectively. Overall, the average blood pressure was 141.6/85.6. Patients were most likely to be controlled on one or two medicines. There were no differences in achieving control between males and females or Caucasian and African American patients. Medication management errors included duplicate therapy, inadequate/absent assessment of electrolytes and renal function, suboptimal assessment of heart rate, suboptimal use of combination anti-hypertensives, and drug interactions.
Conclusion: Current management of hypertension is suboptimal based on Healthy People Goal aiming for 50%. Areas for improvement include lifestyle modifications and drug therapy management. We hypothesize that clinical pharmacists can help improve blood pressure control at this Family Medicine Center. Additional data from evaluation will be reported.

350E. Impact of a clinical pharmacist on costs associated with routine fluconazole prophylaxis in a surgical intensive care unit. *Edward T. Horn, Pharm.D.*, Todd W. Nesbit, Pharm.D., Kenneth M. Shermock, Pharm.D., Vince Bittinger, M.B.A., Todd Dorman, M.D., Pamela Lipsett, M.D.; The Johns Hopkins Hospital, Baltimore, M.D.

Presented at the 33rd Critical Care Congress of the Society for Critical Care Medicine, Orlando, FL, February 25, 2004.

351. Effect of pharmacist-run sedation rounds on clinical outcomes in the medical intensive care unit (MICU). *John Marshall, Pharm.D.*, Christine A Gongleski, Pharm.D.; Boston Medical Center, Boston, MA.

PURPOSE: The use of sedation/analgesia algorithms has demonstrated benefit in the Intensive Care Unit (ICU). One of the most challenging aspects of sedation algorithms is initial and ongoing adherence. We hypothesized that a formal, consistent intervention by pharmacists to promote adherence to the institution's sedation algorithm would decrease the duration of mechanical ventilation and improve overall clinical outcomes.
METHODS: In February 2004, an intervention algorithm was instituted whereby an ICU pharmacist evaluated mechanically ventilated patients receiving continuous sedation and made recommendations based on established institutional sedation guidelines. Demographics, APACHE II scores, duration of mechanical ventilation, and ICU/hospital length of stay were collected. This data was compared to retrospective controls collected before February 2004. Nominal data was evaluated using the Fisher's exact test and continuous data was evaluated using the Student's t test.
RESULTS: Data was collected for 78 control and 57 intervention patients. The groups were well matched in terms of baseline demographics. The mean duration of mechanical ventilation was reduced from 338.4 hours in the controls to 176.5 hours in the intervention patients (P=0.0016). The mean ICU and hospital lengths of stay were significantly reduced in the intervention patients (P=0.0015 and P=0.0012, respectively). The total use of sedating agents trended downward in the intervention patients.
CONCLUSION: The institution of pharmacist-run sedation rounds improved adherence to an existing sedation algorithm and resulted in a significant decrease in the duration of mechanical ventilation in patients receiving continuous sedation.

352. Implementation of a computerized provider order entry system: lessons learned. *Brian Pinto, Pharm.D.*, Sandi Mitchell, M.S., Michael Brown, Pharm.D., M.S., Connie Saltsman, Pharm.D., M.B.A., Annette Rowden, Pharm.D., BCPS, Kimberly Liss, Pharm.D.; The Johns Hopkins Hospital, Baltimore, M.D.

PURPOSE: To describe a unique approach to pharmacy involvement in the implementation of a computerized provider order entry (CPOE)system.
METHODS: The Johns Hopkins Hospital is a 920 bed tertiary teaching facility that in October 2002 set out to implement an institution-wide CPOE system which would replace an existing system active on nine adult medicine units. The goal of the new CPOE system was to provide enhanced clinical functionality for all inpatient and outpatient ordering needs. A steering committee, with active pharmacy involvement, was formed to evaluate, review, and select a vendor. Subsequently, an aggressive timeline was developed to build the application infrastructure needed to deploy the CPOE system. Several design teams, composed of steering committee and healthcare staff, were formed to address development and implementation issues for pharmacy, pathology, nutrition, and radiology services.
RESULTS: In June 2004, the former CPOE system was disabled and the new system was activated for approximately 200 adult medicine beds. Deployment of the system for all other functional units is ongoing. Due to extensive pharmacy involvement, the institution was able to meet an aggressive timeline while providing a high level of clinical medication order

functionality including customized dose range checks and guided orders. Based on user feedback and production reports, the design teams will continue to customize the system to address the needs of critical care, pediatric, and oncology patient populations.
CONCLUSION: Successful implementation of a CPOE system requires extensive collaboration between pharmacy and information systems throughout all phases of the project design and implementation.

353. Development of a rural medication access and service learning program. *Carolyn C. Brackett, Pharm.D, BCPS*, Katherine A. Kelley, Ph.D.; The Ohio State University College of Pharmacy, Columbus, OH.

Service learning is a priority at The Ohio State University College of Pharmacy and an increasing number of faculty are developing service-learning courses for Pharm.D. students in order to expand traditional teaching and learning roles. The University also emphasizes Outreach and Engagement; in keeping with these priorities, we developed a service-learning course designed to establish a medication access program in an underserved, rural community. We obtained a University grant to cover startup costs of the program, and established relations with the county health department, the single local physician, the mayor, and the city council. We also constructed a focus group of local residents who are involved in community activities and solicited their input. All parties agreed that a medication access program is a main concern in the area because of high unemployment and underinsurance. The service-learning student participated in all meetings and negotiations and was instrumental in establishing good relations with the community. The next step of the program will be a year in length and will involve a second service-learning student. We have purchased equipment and will establish the program in conjunction with monthly public health preventative medicine clinics. The service-learning student will help construct and launch the program. The ultimate goal of the program is to recruit and train community-based volunteers to operate the program, thus making it an integral part of the community. The College of Pharmacy will continue to oversee the program, seek ongoing funding for its support, and offer service-learning students a non-traditional Pharm.D. rotation.

354. Pharmacist education in pain and palliative care: a report from the 2003 national pain and palliative care summit. Chri Herndon, Pharm.D.[1], *James B. Ray, Pharm.D.*[2], Phyllis Grauer, Pharm.D.[3], Joseph Dasta, M.S., RPh[4], Christina Smith, Pharm.D., M.B.A.[5], Keith Moore, Pharm.D.[6], Thomas Zaugg, Pharm.D.[7], Vanita Pai, Pharm.D.[4], Deanna Maynard, Pharm.D.[8]; (1)Clinical Affairs, Ortho-McNeil, O'Fallon, IL; (2)Hamot Medical Center, Erie, PA; (3)Palliative Care Consulting Group, Dublin, OH; (4)College of Pharmacy, The Ohio State University, Columbus, OH; (5)Medical Affairs, Janssen Pharmaceutica, Titusville, NJ; (6)Clinical Affairs, Xanodyne, Florence, KY; (7)Dept. of Pharmacy, Upper Valley Medical Center, Troy, OH; (8)Medical Liaison, Purdue Pharma LP, Lexington, KY.

Institutions of pharmacy education have moved slowly to embrace the importance of pain and palliative care education in their didactic and experiential curricula. Despite pharmacists' crucial role in the appropriate interdisciplinary management of pain and associated symptoms, a paucity of structured classes, modules, clerkships, and other postgraduate experiences continue to exist. Recently a National Pain and Palliative Medicine Summit was convened to bring together professionals interested in change in the education, provision, and policy surrounding pain and palliative care in the United States. Representatives from the professions of pharmacy, medicine, and nursing all provided current barriers and opportunities for improved education in the field of pain and palliative care in their respective professions. Pharmacists, and students of pharmacy, have numerous barriers to adequate education in the care of persons in need of pain and palliative medicine. Although recent research suggests a positive trend in the provision of this knowledge, much room for improvement still exists. Unfortunately, recent media attention has focused on several shortcomings in the attitude, skills, and knowledge of pharmacist with respect to pain and palliative care. To address these issues, and strategies for enacting change in the current pharmacy school curricula, pharmacists in two focus sessions identified initiatives necessary to begin a structured approach to changing the ways in which our pharmacists and students of pharmacy are introduced to pain and palliative medicine. These initiatives, identified as crucial by the pharmacy task force at the 2003 Pain and Palliative Care Summit, will be presented.

355. Pharmaceutical care in Kenya: an elective course to prepare students for an international clerkship. *Ellen M. Schellhase, Pharm.D.*, Julie A. Everett, Pharm.D., James Fuller, Pharm.D.; Purdue University, Indianapolis, IN.

BACKGROUND: Purdue University School of Pharmacy (PUSP) was invited to join an existing program established by Indiana University School of Medicine (IUSM), which provides medical care to the Kenyan population. PUSP will provide pharmaceutical care for this initiative. This partnership created an opportunity for the development of an international advanced clerkship rotation in Eldoret, Kenya. In Spring 2004, PUSP offered a two-credit elective course to prepare pharmacy students for this eight-week advance clerkship.
METHODS: The overall instructional format consisted of lecture and small group discussion. Disease states included: HIV/AIDS, opportunistic infections, malaria, malnutrition, typhoid, tuberculosis, and parasitic infection. Cultural activities included instruction in conversational and medical Swahili, reading and reflection on a Kenyan novel, and a guest lecture by medical faculty with practice experience in Kenyan. Student performance was assessed utilizing: written care plans, weekly quizzes, reflection papers, oral presentations, travel preparation assignments, and a formulary management exercise (in a setting with limited resources).
RESULTS/CONCLUSION: Fourteen students were enrolled in the course and will be participating in the advanced clerkship rotation in Eldoret, Kenya. Evaluations of the course were favorable but provided suggestions for improvement including: reassessment of workload and incorporation of additional cultural awareness activities. This elective is a unique opportunity for students to learn about international pharmaceutical care and apply skills previously acquired to an international setting.

356E. The development and implementation of an advanced clerkship site in Eldoret, Kenya. *Ellen M. Schellhase, Pharm.D.*, Julie A. Everett, Pharm.D., Christopher M. Scott, Pharm.D., BCPS, Steven R. Abel, Pharm.D., FASHP; Purdue University, Indianapolis, IN.

Presented at the World Congress of Pharmacy and Pharmaceutical Sciences of the International Pharmaceutical Federation, New Orleans, LA, September 4-9, 2004.

357E. Impact of multidisciplinary diabetic group visits in a physician residency program. *Jonathan D Ference, Pharm.D.*, Kara Levri, M.D., Janice M Setezenfand, R.N., Frank D'Amico, Ph.D., Melissa A Somma, Pharm.D.; University of Pittsburgh Medical Center - St. Margaret, Pittsburgh, PA.

Presented at the Annual Conference of the Society of Teachers of Family Medicine, Toronto, Ontario, Canada, May, 2004.

358E. Pre- and post-rotation assessment of pharmacy student learning: development and implementation. *Jill S. Burkiewicz, Pharm.D.*, Kathleen J. Chavanu, Pharm.D., Tammi J. Garzanelli, RPh, Angelica A. Munoz, Pharm.D., Julie A. Weberski, Pharm.D.; Midwestern University Chicago College of Pharmacy, Downers Grove, IL.

Presented at the Annual Meeting and Seminars of the American Association of Colleges of Pharmacy, Salt Lake City, UT, July 10–14, 2004.

359. Evaluation of drug serum concentration monitoring at a large, tertiary care hospital. *Justine S. Gortney, Pharm.D, BCPS*, Jeannine Thomas, Pharm.D., Mariamma Abraham, Pharm.D., Mitra Dadyan, Pharm.D.; Baylor University Medical Center, Dallas, TX.

PURPOSE: To evaluate the practices of hospital personnel in the ordering process, obtaining samples, and assessing drug serum concentrations (levels).
METHODS: Medical records of 100 patients were prospectively reviewed from 9/03 to 1/04. (Patients monitored by the kinetics service were excluded). A total of 86 levels were evaluated. Fifty nurses were given a written quiz regarding drug level monitoring. Primary endpoints were 1) to determine if the ordering process for drug levels was correct and if blood was being drawn at designated times, and 2) compare results of the manual process with a written quiz from nursing to determine knowledge of staff in regards to drug level monitoring. Secondary endpoints included actions taken in response to drug levels and clinical usefulness of ordered levels.
RESULTS: The ordering and extraction of levels was performed accurately in 89.5% of cases, and no relationship existed between specific drugs and inappropriate blood draws by personnel. Knowledge of nursing staff demonstrated on the quiz correlated well to daily practice. Action was taken by the physicians 80% of the time in response to drug levels, however 41% of the total levels ordered were not clinically appropriate when evaluated by kinetic standards.
CONCLUSIONS: Nursing and laboratory staff are following physician orders for obtaining drug levels. Physicians need additional education regarding ordering drug levels with regards to pharmacokinetic principles of narrow-therapeutic index drugs. Actions to be taken include: participation in training of new medical residents, written article in physician newsletter, and specific education given to individual physician departments.

360. Information literacy training for the 21st century: The Medicines Information Retrieval Project. *Lisa E. Vivero, B.S., Pharm.D.*, Martin C. Henman, B.Pharm., Ph.D., Arlene Healy, MLIS, Niamh Brennan, MLIS; University of Dublin Trinity College, Dublin, Ireland.

PURPOSE: Adequate information literacy skill training is necessary to impart life-long learning and effective professional pharmacy practice. The Medicines information Retrieval Project (MIR) is an ongoing collaborative teaching effort between the School of Pharmacy and the Library. MIR integrates didactic lectures, practical assignments, small group teaching and individual, interactive web-based learning to teach transferable medicines information retrieval and assessment skills throughout the four year pharmacy course.
METHODS: Our approach is a blend of the two schools of training — library skills training for librarians, and traditional medicines information skills

training - and to infuse them with our own ideas for using information sources and manipulating today's information technology rich environment. For this to be successful it was necessary to transform the generalized literacy skills training methods into methods targeted at the individual user's needs.
RESULTS: Challenges observed and the lessons learned are presented: they are, 1) the need for epistemological revision of information literacy training, 2) the ease of access to electronic sources, 3) the increasing variety of information sources and 4) the preferred orientation of many students towards electronic rather than hardcopy sources.
CONCLUSION: Ongoing close collaboration between the School of Pharmacy and the Library is essential for medicines information training. Collaboration has resulted in a clearer understanding of what pharmacy students require from the library and what they can expect from library services, while fostering effective information literacy skills and the confident utilization of information resources within the undergraduate course.

361. Enhancement of an ambulatory care practicum experience using Blackboard® as a course management tool. *Mary A. Halloran, Pharm.D., BCPS*, John R. Walker, Pharm.D.; University of Oklahoma Health Sciences Center, College of Pharmacy, Oklahoma City, OK.

PURPOSE: The development of online courses in higher education has increased dramatically in the last decade, with many pharmacy schools utilizing internet access extensively in traditional and distance environments. Extending this application beyond the classroom presented a unique opportunity to enhance the Ambulatory Care practicum experience through integration of various procedural and educational components of the practicum into a user-friendly, easily accessible, WEB-based course.
METHODS: The password-restricted course was administered through the University of Oklahoma Health Sciences Center using Blackboard® as an application service provider. Using the Blackboard® template, a faculty preceptor and a 4th-year pharmacy student worked on concept development, content posting, and site maintenance. Practicum students enrolled in the course were provided with instructions for access and site navigation prior to beginning the rotation. Procedural responsibilities and interactive sessions requiring utilization of posted materials were conducted throughout the month. Accession of posted materials to complete requirements and prepare for these sessions was assessed.
RESULTS: Feedback from the students indicated a very favorable response to the online course. Students were pleased with the completeness of the material content, ready availability of required course materials, logical flow and ease of use of the site, and ease of access to the website from any location with internet access. Students also appreciated the self-paced learning environment provided by this venue.
CONCLUSIONS: Web-based availability of course materials complemented the practicum experience, improved student access to required content, and facilitated learning and communication between students and faculty outside of the traditional practicum environment.

362E. "Silver Scripts": First-year students develop pharmaceutical care skills through community outreach to underserved seniors. *Melissa A Somma, Pharm.D.*, Meredith L Rose, Pharm.D., Teresa E Donegan, Ph.D., Gary P Stoehr, Pharm.D.; University of PIttsburgh School of Pharmacy, Pittsburgh, PA.

Presented at the Annual Meeting of the American Association of Colleges of Pharmacy, Salt Lake City, UT, July 10–14, 2004.

363. Pharmaceutical Spanish. *R. Lilia Compadre, Ph., D.*[1], Cesar M. Compadre, Ph., D.[2], Eduardo Ochoa, M.D.[3]; (1)College of Pharmacy, University of Arkansas for Medical Sciences & LA CASA Health Network, Little Rock, AR; (2)College of Pharmacy and College of Public Health, UAMS; and LA CASA Health Netwrok, Little Rock, AR; (3)College of Medicine and College of Public Health, UAMS, & LA CASA Health Network, Little Rock, AR.

PURPOSE: Spanish for Pharmacist was a course offered at the College of Pharmacy, University of Arkansas for Medical Sciences to produce pharmacists who possess the skills and knowledge needed to serve their Latino American patients and to improve the pharmaceutical care of this population.
METHODS: The course emphasized pronunciation, because the most common form of communication between pharmacists and patients is oral, and comprised the study of the Latino American language and culture, as well relevant regulations and current ideas about diversity because all these support the delivery of competent pharmaceutical care.
RESULTS: The students enrolled in the course had opportunities to interact with Latino costumers at clinics, community base organizations, and health fairs; and actively contributed in the development of a database containing various scenarios of pharmaceutical encounters and a bilingual list of pharmaceutically related expressions.
CONCLUSIONS: The unprecedented increase of the Latino population in Arkansas and the fact that a substantial majority of Latinos has various degrees of language and cultural barriers to the services available in this country called for the development of an elective course focused in improving the pharmaceutical care of Latinos. This course supports the mission of the college related to provide excellent pharmaceutical education.

364. Outcomes of pharmacy student involvement in refill clinics during an ambulatory clinical experiential training rotation. *Santhi Masilamani, B.S., Pharm, Pharm.D., CDE*[1], Monica Robinson, Pharm.D.[2]; (1)Harris County Hospital District, Houston, TX; (2)TSU, Houston, TX.

PURPOSE: Refill clinics as a starting point in a primary care clinic provides a good foundation for further direct patient care activities for students. A half day session was set up once a week to provide this experience for students.
METHOD: Pharmacy students participated for a half a day each week in refill clinic activities. Each student prepared a SOAP note including last visit date, pertinent vitals, lab parameters, and co-morbidities and placed it in the patient's medical record. Guidelines prepared by their preceptor, the drug information handbook, and micromedex were used to determine necessary monitoring parameters. The preceptor then reviewed the SOAP notes and authorized the refills.
RESULTS: Clinic activities allowed the students to list appropriate criteria without using references by the 3rd week. Various skills such as documentation, communication with providers, time management, data collection, and data analysis were enhanced. Students displayed increased comfort with chart reviews, knowledge of chronic disease monitoring parameters, national guideline goals, compliance tracking, and appropriate follow-ups before getting into direct patient care activities. Students organized data in an effective format for periodic reports and participated in reviewing policies written based on the results. Student participation showed indirect benefits to the clinic such as decreasing wait times for patients, decreased work load for the physicians, a more efficient processes for refill renewals, and improved patient care. Formulary adherence and medication safety were important factors in improving patient care. Abnormal labs, poor patient follow ups, and inappropriate indication alerts alos lead to improved medication safety.

365. Development of an evidence-based internal guideline for emergent rapid-sequence intubation. *Christine K Howe, BSc, BSc, Phm*, Lisa D Burry, BSc Phm, Pharm D, FCCP, Vagia T Campbell, RRCP, RRT, David Dushenski, M.D. CCFP(EM), H Brian Goldman, M.D., MCFP(EM), FACEP, Mary Dawson, RRCP, RRT; Mount Sinai Hospital, Toronto, ON, Canada.

BACKGROUND: During the local SARS outbreak the need for a clear readily accessible rapid sequence intubation (RSI) guideline was identified.
PURPOSE: Our objective was to develop a safe internal guideline that used evidence to direct appropriate use of equipment, techniques and medications related to emergent RSI.
METHODS: An extensive literature search regarding equipment, techniques and medications related to emergent RSI was conducted by 2 respiratory therapists and 2 pharmacists. From the published literature, data was extracted and collated to determine the most appropriate methods for RSI as well as agents for sedation and paralysis.
RESULTS: Based upon the best available evidence, an algorithm was developed and reviewed by other respiratory therapists and pharmacists as well as by physicians from Anesthesia, Critical Care and Emergency departments. The document outlined criteria for use, contraindications and complications, as well as the procedure for performing emergent RSI (including medication selection and dosing). The document was abbreviated into a laminated pocket card with one side outlining the procedure and the other providing a flow-diagram for medication selection and dosing.
CONCLUSIONS: An easy to use evidence-based emergent RSI document can be developed and successfully used through the collaboration of a multi-disciplinary team.

366. Evaluation of outcomes following cardiac resuscitation secondary to ventricular fibrillation or pulseless ventricular tachycardia. *Rhonda D. Cobb, Pharm.D.*, Mary Ann Peberdy, M.D., Patricia Pecora Fulco, Pharm.D.; Virginia Commonwealth University Medical Center, Richmond, VA.

PURPOSE: Ventricular fibrillation (VF) and pulseless ventricular tachycardia (VT) remain the most frequent etiologies of sudden cardiac arrests. Adequate healthcare provider education, advanced cardiac life support (ACLS) experience, and algorithm familiarization are all necessary components to improve cardiac survival outcomes in the hospitalized patient. Cardiac multidisciplinary resuscitation teams within the hospital may enhance patient survival.
METHODS: The objective of this study was to evaluate patient survival in hospitalized cardiac arrests when treated by an emergency cardiac resuscitation team. A retrospective evaluation of all adult cardiac resuscitation events with documented VF/VT from July 1, 2001, until June 30, 2003 was reviewed.
RESULTS: A total of 207 in-hospital resuscitation events were identified during the two-year period. Twenty-one cardiac arrests were documented VF and pulseless VT events. Thirty-three events were excluded secondary to insufficient rhythm documentation. A return of spontaneous circulation (ROSC) occurred in seven patients. Five patients survived to hospital discharge. In the ROSC group, 71% received defibrillations and 60% of these

were optimally sequenced. Epinephrine and amiodarone were administered optimally in 29% and 49% of the ROSC cases, respectively.
CONCLUSION: The results demonstrated a diminished survival in patients with documented VF/VT cardiac arrests. Optimal rhythm documentation, defibrillation timing and adequately administered pharmacotherapy were identified areas of improvement. Based on these data, continued ACLS education is necessary for quality improvement of the cardiac teams' response to VF/VT arrests.

367. The role of the clinical pharmacist in a diabetes disease management model. *Andria K. Hornaday, Pharm.D.*, Teri A. Wooton, Pharm.D., CDE, Suzanne H. Trautman, Pharm.D., CDE, Jeff Patchett, RPh, M.B.A.; NorthEast Medical Center, Concord, NC.

PURPOSE: To assess and improve adherence to therapeutic goals recommended by the American Diabetes Association (ADA) for aspirin and ACE-inhibitor use, A1c, blood pressure and LDL in ambulatory patients with diabetes using pharmacist-directed interventions.
METHODS: Patients with new-onset diabetes or A1c > 8% were identified and referred to the pharmacy program. During routine clinic visits with a pharmacist, patients with opportunities to optimize care were identified and recommendations were made to the referring physician. Data were collected between September 2001 and May 2004. A voluntary patient satisfaction survey was conducted during the third year of the research. The disease management database was queried for assessment of and change in selected indicators and compared to patients enrolled in the pharmacy program.
RESULTS: A total of 614 patients were referred to the pharmacy program. Assessment of indicators increased as follows: A1c 28.81%, LDL 28.7%, SBP 15.03%, DBP 15.03%, aspirin use 29.11%, ACE-inhibitor use 18.61%. Baseline vs. end of study values for enrolled patients achieving ADA goals were as follows: A1c 39.34% vs. 40.72%, LDL 37.91% vs. 42.02%, SBP 51.66% vs. 54.89%, DBP 59.2% vs. 68.08%. Patient satisfaction was high; with 92% of respondents stating the service was beneficial.
CONCLUSION: A pharmacist-based intervention improves adherence to national recommendations for assessment and improves clinical indicators. The majority of patients felt that these services had a positive impact on their diabetic care. These results demonstrate that future opportunities exist for pharmacists to optimize care of diabetic patients.

368. Evaluation of pharmacist impact on providing comprehensive diabetes care recommended by the American Diabetes Association. *Eunice P. Chung, Pharm.D.*[1], Liling Taing, Pharm.D.[2]; (1)Western University of Health Sciences, College of Pharmacy, Pomona, CA; (2)Huntington Memorial Hospital, Pasadena, CA.

PURPOSE: To assess the baseline level of compliance with the American Diabetes Association (ADA) standard of care recommendations and to increase the compliance rate through specific recommendations at a community hospital ambulatory care clinic.
METHOD: A chart review was conducted to assess the baseline compliance rate to 10 selected ADA standard of care recommendations for diabetic patients coming to the medicine clinic between January and March 2004. For noncompliant areas, specific recommendations were made. Data was then reanalyzed to determine the impact of pharmacist interventions in increasing the adherence to the ADA standard of care recommendations.
RESULTS: At baseline, the average compliance rate was 58%, varying from 36% to 81%, pneumococcal vaccination and ACE inhibitor or ARB therapy respectively. Areas identified as most noncompliant were routine A1C and urinalysis monitoring, pneumococcal and flu vaccination, tight blood pressure and lipid control. A total of 231 recommendations were made by the pharmacist, of which 68% were accepted. Pharmacist interventions increased the compliance rate on average 25% for the 8 immediately measurable outcomes. The highest impact was seen in increasing the rate of pneumococcal vaccination and updating A1C and urinalysis data. Results of tighter blood pressure and lipid control recommendations could not be evaluated at the time of the analysis.
CONCLUSION: Diabetes care requires a comprehensive management beyond simple blood sugar control. Our results indicate that there is a significant room for improvement in providing comprehensive care to diabetic patients, and pharmacists can play a vital role in providing this.

369. A multidisciplinary educational program to reduce insulin medication errors. *KarenBeth H. Bohan, Pharm.D., BCPS*[1], Mary Jo Cannon, R.N., M.S.N., WOCN[2], Joan DeRocco-DeLessio, M.S., R.N., CNA[2], Thomas Mecca, B.S., R.Ph.[2], Elizabeth Trzcinski, R.N., B.S.N.[2], Michael L. Adler, M.D., FACE[2]; (1)Nesbitt School of Pharmacy at Wilkes University, Wilkes-Barre, PA; (2)Wyoming Valley Health System, Wilkes-Barre, PA.

PURPOSE: Insulin administration errors were the third most common type of medication misadventure at the Wyoming Valley HealthCare System in 2003. Potential contributing factors include a change in the insulin products on formulary, the availability of new types of insulin, as well as errors involving the use of the abbreviation "U" for "units".
METHODS: A multidisciplinary Insulin Education Task Force was convened and charged to develop a mandatory comprehensive and ongoing educational program for all nurses. The task force included nurses, pharmacists, and a physician. Our chief of endocrinology presented information about insulin administration via a videotape and we offered the program during all nursing shifts at multiple times over a one-month period. Outcomes were assessed using a pre- and post-test. The participants completed a program evaluation that included their opinions about why insulin errors have occurred.
RESULTS: 393 nurses attended the program. A score ≥80% on the pre- and post-tests were achieved by 36% and 81% of nurses respectively. 61% stated that the most important factor contributing to insulin errors was lack of knowledge about the different types of insulin and when to appropriately administer them.
CONCLUSIONS: A knowledge deficit appears to be a factor that contributes to insulin errors. Our program demonstrated that education can improve short-term knowledge. Future plans include a 3-month refresher of these principles and administering the post-test again in 6 months. This program has already been incorporated into the newly hired nurses orientation program and will become part of yearly competencies.

370. Evaluation of the effectiveness of pharmacist-administered diabetes education and management services. *Kelly R. Ragucci, Pharm.D., BCPS, CDE*, Andrea M. Wessell, Pharm.D., BCPS, Stacy M. Prutting, Pharm.D., BCPS, CDE, Joli D. Fermo, Pharm.D., BCPS, CDE, Jennifer N. Mazur, Pharm.D., CDE, Melissa M. Blair, Pharm.D., BCPS, CDE; Medical University of South Carolina, Charleston, SC.

PURPOSE: To evaluate the effectiveness of pharmacist-administered diabetes services on select diabetes performance measures, compare these to the National Committee for Quality Assurance (NCQA) report and identify areas where improvement is warranted.
METHODS: Patients were referred to clinical pharmacists at three university-based primary care clinics for diabetes management services. Glycosylated hemoglobin (A1C), blood pressure (BP), low density lipoprotein (LDL) and aspirin use were compared at baseline and one year after patient enrollment as well as to published NCQA guidelines. Paired-statistical tests were utilized to compare endpoints and cost avoidance comparators were calculated for those patients with a 1% reduction in A1C.
RESULTS: Between April and December 2002, clinical pharmacists enrolled 191 patients. The average A1C at one year was 7.8%, compared to 9.5% at baseline (change -1.7%, $p<0.05$). Overall, 72 patients (38%) experienced a 1% or greater reduction in A1C. The average BP decreased from 141/79 to 135/75 mmHg ($p=0.007$) and average LDL decreased from 114 to 112 mg/dl ($p>0.05$). Aspirin use increased from 34% at baseline to 73% at one year ($p<0.0001$). Except for the lipid profile, all measurements exceeded the NCQA goals for diabetes recognition programs. Based on an estimated savings of $820 for a 1% decrease in A1C, total cost avoidance was calculated as $59,040.
CONCLUSION: The performance of diabetes management services by clinical pharmacists resulted in significant improvements in A1C, BP and aspirin use. Continued efforts in diabetes education should be made to further improve clinical, economic and humanistic outcomes.

371. Impact of a diabetes collaborative care pilot program on patient outcomes. *Nicole M. Stack, Pharm.D.*[1], Kathleen M. Melbourne, Pharm.D., CDOE[2]; (1)Albany College of Pharmacy, Albany, NY; (2)University of Rhode Island, Kingston, RI.

PURPOSE: To examine the impact of the interventions of clinical pharmacists over a six-month period on the clinical and humanistic outcomes of patients with type 2 diabetes compared to standard medical care alone.
METHODS: Outcomes in a group of patients receiving individualized counseling and education from pharmacists with specialized diabetes training in addition to standard medical care (Intervention group, N= 38) were compared to those of patients receiving standard medical care alone (Control group, N= 78). The primary outcomes of the study included changes from baseline in mean A1c and low density lipoprotein cholesterol (LDL-C) levels. Patient satisfaction with care and patient diabetes knowledge in addition to several secondary outcomes including microalbumin, aspirin and ACE inhibitor use, eye exams, vaccinations, and smoking status were also examined.
RESULTS: Mean baseline A1c of the Intervention Group was 8.5% compared to 7.8% in the Control Group ($p= 0.033$). At 3 and 6 months, the mean Intervention Group A1c was 7.1% and 6.6%, respectively while the average Control Group A1c was 7.9% at three months ($p= 0.007$) and at 6 months ($p< 0.0001$). There were no significant differences in LDL-C levels. Certain secondary outcomes showed statistically significant increases in the intervention group at 3 and 6 months.
CONCLUSION: There were clinically and statistically significant reductions in A1c in patients with diabetes who received the diabetes collaborative care intervention. Collaboration efforts between pharmacists and physicians can lead to beneficial effects on the glycemic control and care of patients with type 2 diabetes.

372. Pharmacist impact on clinical outcomes in a diabetes disease management program. *Patrick Kiel, Pharm.D., candidate*, Amie D. McCord,

Pharm.D.; Midwestern University Chicago College of Pharmacy, Downers Grove, IL.

PURPOSE: To evaluate changes in clinical outcomes for patients enrolled in a pharmacist-coordinated diabetes disease management program
METHODS: Medical records of 157 patients enrolled in the diabetes management program between June 2003 through April 2004 were retrospectively reviewed. Data collection included baseline and follow up values for A1c and lipids as well as frequency of adherence to preventive care including annual foot and eye examinations, and daily aspirin therapy.
RESULTS: For patients with both baseline and follow up data, the mean A1c reduction was 1.6% (n=109). For patients with an initial A1c of > 8.5% the mean reduction was 2.6% (n=57). The percentage of patients with A1c < 7% increased from 19% at baseline to 50% at follow-up. The mean LDL reduction observed was 16mg/dl (n=73) and the percent of patients < 100mg/dl increased from 30% at baseline to 56% at follow-up. The frequency of baseline microalbumin screening increased by 20% and the number of patients with annual eye and foot exams increased by 27% and 15%, respectively. The percentage of patients on daily aspirin increased from 42% at baseline to 80% at follow-up.
CONCLUSION: The pharmacist-coordinated diabetes disease management program was effective in improving clinical outcomes for enrolled patients. Significant improvements were observed in HbA1c and LDL values as well as the frequency of adherence to preventive care. Improvement in these areas is known to reduce the risk of microvascular and macrovascular complications associated with diabetes.

373. Pharmacy based activity to reverse and manage disease (PHARMD): the hypertension project. Catherine A. Harrington, Pharm.D., Ph.D.[1], *Jacintha S. Cauffield, Pharm.D., BCPS*[2], Ceressa T. Ward, Pharm.D.[1], Deborah H. Kennedy, Pharm.D., BCPS[1], Paula Anderson-Worts, D.O., M.P.H.[3]; (1)Nova Southeastern University, Palm Beach Gardens, FL; (2)Southwest Washington Medical Center, Vancouver, WA; (3)Nova Southeastern University, Ft. Lauderdale, FL.

PURPOSE: To: 1) increase access to hypertension screening, referral, and follow-up to minority populations, specifically African-Americans; 2) produce individualized cardiac risk assessments based on personal and family history; 3) educate consumers on the warning signs of heart attack and stroke; and 4) determine the effectiveness of a screening program in a community pharmacy.
METHODS: Pharmacist screening was conducted in two pharmacies serving large minority populations. Subjects were recruited by an in-store promotional campaign. Screening included assessment of blood pressure (BP), body mass index (BMI), and cardiac risks. Subjects with elevated BP were invited to return for further assessment of cholesterol and glucose. Recommendations and referral for physician treatment were based upon JNC VII. All subjects received education on cardiac risk management.
RESULTS: In eight months, 569 subjects were seen in 735 encounters. Screening services reached 1.5% of adults within study zip codes. African Americans comprised 50% of subjects screened. The average overall BMI was 29. Stage I BP was present in 30% of the screened population, with an average BP of 151/98. Hypertension was reported by 40% of subjects. Of these, 69% were taking antihypertensive medication and had an average BP of 141/85. The remaining 31% not taking antihypertensive medication had an average BP of 133/86. An additional 9% of subjects without a hypertension diagnosis had BPs averaging 152/96.
CONCLUSIONS: Access to blood pressure screening, referral, and follow-up for minority populations was increased. Diagnosis and treatment of hypertension continues to be suboptimal. Alterations to program execution could enhance its effectiveness.

374E. Assessment of a community pharmacy-based disease-state management program. *Denise Cuellar, RPh, M.B.A.*, Melanie Dodd, RPh, Pharm.D., BCPS; University of New Mexico College of Pharmacy, Albuquerque, NM.

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375. Post-discharge follow-up phone call by a pharmacist and impact on patient care. *Gail M. Burniske, Pharm.D.*, Allison E. Burnett, Pharm.D., Toby Trujillo, Pharm.D., BCPS, Jeffrey Greenwald, M.D.; Boston Medical Center, Boston, MA.

PURPOSE: There is a time between hospital discharge and patient follow-up that has been deemed by many healthcare workers as a "black hole". Continuity of care is of utmost importance, yet there is no effective uniform system in place to ensure this vital continuity. The literature suggests that discharge counseling and care in the post-discharge period is in need of improvement and is an excellent opportunity for intervention by a pharmacist.
METHODS: A prospective, randomized trial using two similar inpatient general medicine firms was conducted to determine if a post-discharge phone call from a pharmacist reduces 30-day readmission rates. The primary endpoint was a comparison of the number of hospital readmissions (any cause) during the 30-day post-discharge period between groups. Secondary outcomes include the number of patients for whom interventions were made pertaining to primary discharge diagnosis, medications and follow-up appointments.
RESULTS: Interim data analysis will be presented. To date, 50 telephone interviews have been completed (goal = 100). Interim data reveals that patients receiving a post-discharge phone call are 23% less likely to be readmitted to the hospital within 30 days (total of emergency room visits and inpatient hospitalizations). The interviewing pharmacist performed interventions on 72% of patients. Types of interventions included calling the physician, patient education and resolving missing prescriptions.
CONCLUSIONS: If this project yields positive results, the pharmacy department will attempt to implement a full-time formal discharge and follow-up service.

376. Physician survey of outpatient clinical pharmacy services. *Melissa M. Blair, Pharm.D., BCPS, CDE*, Joseph Mazur, Pharm.D., BCPS; Medical University of South Carolina, PO Box 250584, Charleston, SC.

PURPOSE: A pharmacy-run Pharmacotherapy Clinic was developed to serve as a referral source for physicians without access to an ambulatory clinical pharmacist. In order to prioritize development and initiation of services, it was felt that knowledge of physician attitudes and previous experience concerning clinical pharmacy services would be beneficial.
METHODS: One hundred and fifty-seven attending physicians were identified as a potential referral base for the Pharmacotherapy Clinic. A seven question anonymous survey was developed and distributed via campus mail to all identified physicians.
RESULTS: Sitxy-one out of 157 surveyed physicians responded (39%), most of whom (82%) had previously worked with a clinical pharmacist. Patient education and device teaching were the most common roles that physicians thought clinical pharmacists should provide (84% and 80% respectively). Initiating drug therapy was the least accepted role of a clinical pharmacist in the prescribing process (23%). Physicians commonly felt that patients would benefit from the Pharmacotherapy Clinic providing anticoagulation (62%), smoking cessation (59%), and financial assistance (51%) services. More specifically, surveyed physicians stated they would most likely refer patients for: anticoagulation (31%), financial assistance (26%), therapeutic drug monitoring (25%), and pain management (25%).
Conclusion: Surveyed physicians had a wide range of opinions concerning the role of clinical pharmacists in the prescribing process, but identified several services that could be beneficial to themselves and their patients. The results of this survey will be used to prioritize development of services in the Pharmacotherapy Clinic.

377. Provision of pharmacotherapy services in a rural nurse practitioner clinic. *Miranda R. Andrus, Pharm.D., BCPS*[1], Deidre B. Clark, Pharm.D.[1], Katherine C. Herndon, Pharm.D., BCPS[2]; (1)Auburn University Harrison School of Pharmacy, Auburn, AL; (2)Pfizer Inc., Birmingham, AL.

PURPOSE: To describe the interventions and services provided by a clinical pharmacist in a medically indigent rural nurse practitioner clinic.
METHODS: A retrospective review of patients referred to a pharmacotherapy clinic in a small nurse practitioner practice was performed. The primary reason for referral, duration of follow-up, educational interventions, clinical interventions (initiation or discontinuation of pharmacotherapy, dosage adjustments, preventative care recommendations), and clinical outcomes were documented.
RESULTS: Nurse practitioners referred 126 patients to the clinic over a 2 Ω year period. Twenty-five patients (19.8%) referred to the clinic failed to keep their initial appointment. The mean age of the patients (53.5% female) with one or more clinic visits was 53 ± 13 years. Medication assistance programs were utilized by 44.6% of patients. The most common reason for patient referral was hyperlipidemia (80.2%), followed by anticoagulation (12.9%). The pharmacist documented 732 clinical interventions during 708 patient visits (mean = 7.0 visits per patient) with a mean follow-up duration of 9.1 months per patient. Initiation of new drug therapy or dosage adjustment accounted for 52.2% of the clinical interventions. Comprehensive educational services were provided to patients at every visit (mean = 5.6 educational interventions per visit). Among patients referred for hyperlipidemia with one or more follow-up visits (n = 70), the mean LDL cholesterol decreased from 140 ± 35 mg/dL to 104 ± 38 mg/dL ($p<0.001$).
CONCLUSION: A pharmacotherapy service in a rural nurse practitioner practice can provide many opportunities for pharmacist intervention and can improve patient outcomes.

378. Improvement in quantity and quality of venous thromboembolism prophylaxis for medically ill patients: impact of a clinical pharmacy education program. *Paul P. Dobesh, Pharm.D.*, Zachary A. Stacy, Pharm.D.; St. Louis College of Pharmacy, St. Louis, MO.

PURPOSE: The American College of Chest Physicians recommends unfractionated heparin or low-molecular-weight heparin for prevention of venous thromboembolism (VTE) in medically ill patients. Despite these recommendations, a previous analysis at our institution revealed a low utilization of VTE prophylaxis. Our objective was to evaluate the effectiveness of a pharmacist education program on improving the quantity and quality of VTE prophylaxis in medially ill patients.

METHODS: An educational program focusing on the importance of VTE prophylaxis in medically ill patients was developed by clinical pharmacists and presented to nurses, pharmacists, and physicians in a 493-bed community teaching hospital. Educational programs (inservices, newsletters, and quality assurance programs on VTE prophylaxis) were conducted between 6/02–6/03. A post-education retrospective chart review was conducted in medically ill patients with discharge dates between 10/03–3/04 (n=250). These post-education data were compared to our initial pre-education analysis, with discharge dates from 1/01–3/02 (n=344). Data collection included patient demographics, VTE risk factors, VTE prophylaxis utilization, and type of prophylaxis.
RESULTS: Patient demographics and primary diagnoses were similar between groups. The mean number of risk factors per patient in the pre-education group was 2.53±0.96 and 2.38±0.88 in the post-education group (p=NS). Pharmacy education increased the utilization of any VTE prophylaxis (43% vs. 57%;p=0.002) and suitable prophylaxis (38% vs. 48%;p=0.025). Optimal prophylaxis, as defined by the published literature, was also improved (11% vs. 44%;p<0.001).
CONCLUSIONS: A hospital wide clinical pharmacy education program can significantly improve the quantity and quality of VTE prophylaxis in medically ill patients in a community teaching hospital.

379. Pediatric human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) infection: the role of a pharmacist in a clinical hospital setting. *Sanju K. Patel, R.Ph.*; Children's Medical Center of Dallas, Dallas, TX.

PURPOSE: The HIV/AIDS epidemic among pediatric patients presents challenging issues of drug therapy. The goals of therapy are: maximum suppression of viral load, preservation of immunologic function, improvement of quality of life, and reduction of HIV related morbidity and mortality. The introduction of highly active antiretroviral therapy (HAART) is vital to achieve these goals. Palatable pediatric formulations are not yet available for many antiretroviral medications. The pharmacist plays an essential role on the medical team to help achieve goals of therapy.
METHODS: Patients ranging in age from birth to age 18 are followed in clinic and evaluated by a nurse, physician, social worker and pharmacist, who then make group decisions after assessment of each patient. The pharmacist monitors drug therapy, ensures patient education and commitment, provides staff education and drug information, and recommends therapy adjustments as necessary. The pharmacist engages in teaching techniques to prepare young children to swallow pill formulations, and recommends alternative methods for liquids that may not be palatable.
RESULTS: The pharmacist provides the most accurate drug information and has the knowledge and tools to recommend appropriate drug therapy. Since there are a limited number of antiretrovirals available, it is crucial that patients adhere to a regimen to avoid drug resistance and therefore achieve goals of therapy.
CONCLUSION: The pharmacist plays a key role in the management of pediatric HIV/AIDS patients on HAART. As each patient has unique circumstances, the patient-pharmacist relationship is important to increase adherence to a medication regimen.

380. The effectiveness of using a worksheet to screen pneumococcal vaccine candidates and increase the rate of vaccination. *Eunice P. Chung, Pharm.D.*[1], Levita K. Hidayat, Pharm.D.[2], Jean M. Pallares, Pharm.D.[2]; (1)Western University of Health Sciences, College of Pharmacy, Pomona, CA; (2)Huntington Memorial Hospital, Pasadena, CA.

PURPOSE: A pneumococcal vaccine screening worksheet was implemented to increase the rate of vaccination at a community hospital ambulatory care clinic. The purpose of this study is to determine the effectiveness of the worksheet in increasing the vaccination rate.
METHODS: The worksheet was used to identify pneumococcal vaccine candidates between August 2003 and March 2004. A retrospective chart review was conducted to assess the number of missed opportunities for vaccination as determined by the number of clinic visits during the one year prior to the date of vaccination. Demographics of all patients screened were also evaluated to streamline future screening process.
RESULTS: A total of 338 patients were screened, of which 232 were determined to be candidates for vaccination. Pneumococcal vaccine was successfully administered to 196/232 (84.5%) patients. The patients who had one or more indications for pneumococcal vaccination had a mean of 7 + 4.9 clinic visits during the 12 months preceding the screening date, during which pneumococcal vaccine was not addressed. Age, 65 or above, and diabetes were the leading indications for vaccination. Majority of patients was first time recipients; only 5% of the patients qualified for a revaccination. Reasons for not administering vaccine despite meeting the criteria were, patient refusal (64%), physician disagreement (17%), logistical slip (11%), and active contraindications (8.3%).
CONCLUSION: Preventive medicine issues such as immunization receive minimal attention during a compact clinic visit. The worksheet served as a useful tool in identifying and vaccinating patients who have been overlooked during many previous visits.

381. An innovative role for the pharmacy technicians in promoting influenza vaccination at Eastern Maine Medical Center. *Shewan Aziz, Phd., Rph*, Marybeth Boudreau, Pharm.D., Libby Karen, R.N., Angela Hollis-Dumas, CPhT, James Raczek, M.D., Jamie Cronin, Pharm.D., David Crabtree, CPhT; Eastern Maine Medical Center, Bangor, ME.

PURPOSE: To show that utilizing decentralized pharmacy technicians is an effective approach to improve the rate of flu immunization at a health system.
METHODS: The pharmacy computer system was programmed to screen for patients at high risk for developing influenza based on CDC criteria. The pharmacy technicians (PT) used the computer-generated reports and triplicate influenza vaccine consent / order forms to interview eligible patients and to screen for allergic reaction to influenza vaccine or eggs and for contraindications, such as pregnancy and Guillain-Barre Syndrome. The PT also handed patients a 2003–2004 CDC copy of influenza vaccine information. Patients then had the option to accept or decline the influenza vaccination through signing the consent/order form. If the patient declined the vaccine the PT left the white copy of the order sheet in the chart, a pink copy was handed to the patient and a yellow copy was sent to the Pharmacy. If the patient accepted the vaccine the white and pink copies posted into the chart and the yellow copy was sent to the Pharmacy. After the vaccine is administered the white and pink copies were signed off and the patient was given the pink sheet with the date.
RESULTS:

Action/Reason	Patient #	
Received Influenza	467	36.7%
Declined/Already Received	535	42.1%
Patient's Decision	203	16.0%
Medical Reason	48	3.8%
Allergy	15	1.2%
Reason Not Given	3	0.2%
Total	1271	100.0%

CONCLUSIONS: The number of high-risk patients immunized from October 2003–February 2004 was 3 times of that recorded for year 2002–2003.

382. Clinical pharmacist optimizing medication therapy limits overall health care spending in a capitated outpatient adult population. *Jeanette L. Altavela, Pharm.D., BCPS*[1], James R. Tobin, M.D., M.S.[2], Matthew K. Jones, B.A.[3], Brian M. Lenker, B.S.[3], Peter G. Zajkowski, M.A.[3]; (1)Greater Rochester Independent Practice Association, Rochester, NY; (2)Consultant, Ashville, NC; (3)GRIPA, Rochester, NY.

PURPOSE: This study is designed to determine whether a clinical pharmacist's recommendations to physicians regarding optimal medication therapy in outpatients ultimately decreases overall health care utilization costs in capitated patients in an internal medicine practice.
METHODS: A prospective, concurrent, controlled study comparing two internal medicine practices. The pharmacist made suggestions to optimize medication therapy in the active practice, and proposed suggestions but did not communicate with the control practice for 12 months. Total health care utilization costs were compared 12 months before and 12 months after the study period for each practice.
RESULTS: There were 127 and 216 adult patients (29–92 years old) in the active and control practice, respectively. The mean total per member per month (PMPM) costs decreased 16% in the active practice (p=0.12) and increased 40% in the control practice (p=<0.001), using a paired *t*-test on the log-transformed data. A subgroup analysis of patients over 65 years old revealed the mean total PMPM increased 30% (p=0.277) in the active practice (N=44) and increased 66% (p=0.001) in the control practice (N=146).
CONCLUSION: A clinical pharmacist can promote optimal medication therapy in outpatients by working with primary care physicians within their office practice. Improving medication therapy can result in limiting total health care utilization costs.

383. Medication cost avoidance and savings associated with pharmacist involvement in an indigent Columbus Neighborhood Health Center (CNHC) system. *Laura E. Hall, Pharm.D., BCPS*, Ruth E. Emptage, Pharm.D., Milap C. Nahata, Pharm.D., FCCP; The Ohio State University College of Pharmacy, Columbus, OH.

PURPOSE: To determine the medication cost avoidance and savings associated with pharmacist activities including formulary management, Pharmacy Benefits Manager (PBM) interaction, and implementation of various programs (Federal 340 B health center pricing program, manufacturer patient assistance programs (MAPs), and Pfizer Sharing the Care (STC) program) for an indigent patient population.
METHODS: Financial and medication use data compiled from PBM and internal pharmacy program reports reviewed quarterly at Pharmacy and Therapeutics Committee meetings were evaluated. Patient population demographics were obtained from CNHC's internal billing and tracking system.
RESULTS: Medication cost avoidance and savings have increased since the initiation of the partnership between CNHC and OSU in 1991. In 2003, the

medication needs of 11,872 uninsured patients were met. Drugs were most frequently used for cardiovascular disease, diabetes, and neurological/psychiatric illnesses. With 63% uninsured, most below federal poverty level, patient co-pay has remained <$10 per monthly prescription. Using a negative formulary with pharmacist managed prior-authorization, retail (non-340 B) cost to CNHC has remained <$26/prescription/month. Generic drug utilization has increased, ranging from 51–72% of prescriptions. For year 2003, the drug cost avoidance/savings of $1.95 million (41.6% 340 B pricing, 35.6% STC program, 22.8% MAPs) were achieved, and the cost of pharmacy services was $130,000. This occurred while maintaining standards of care and staying within the $1.2 million drug budget for 2003.
CONCLUSIONS: Active participation of pharmacists can markedly increase medication cost avoidance and savings for low-income patients, while meeting their medication needs.

384E. Medication error reduction in a pediatric emergency center. *Brenda E. Darling, Pharm.D.*, Paula J. Mialon, Pharm.D.; Children's Medical Center, Dallas, TX.

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385. Planning and implementation of a multimodal medication error tracking, reporting and prevention program. *Tracy Stillwell, Pharm.D.*[1], Carolyn Robbins, B.S. Pharm[1], Ann Riley, Pharm.D.[1], Mabroor Ahmed, B.S.[2], Brenda D. Jamerson, Pharm.D.[2]; (1)Lincoln Community Health Center Pharmacy, Durham, NC; (2)Campbell University Department of Clinical Research, Morrisville, NC.

PURPOSE: Lincoln Community Health Center (LCHC) is a primary care health care facility that served a total of 35,168 patients in 2003: 87% minorities, 82% below the poverty level. Based upon recommendations from the IOM report "To err is human", pharmacy administration began to examine systems and processes in order to prevent medication errors.
METHODS: During 2001, a performance improvement goal was initiated. The activities were: 1) Plan - identified pharmacy resources for the project and identified medication error data; 2) Do- mapped prescription workflow, collected data and categorized as to type, severity and point of detection; 3) Study- analyzed data to determine performance gaps/improvement opportunities and conducted a root cause analysis; 4) Act- implemented education sessions, initiated staff competency training, installed robotic dispensing system, and conducted a failure mode analysis.
RESULTS: There were 7/36,931 medication errors (0.02%) in 4Q 2001 and 2/42,151 medication errors (0.005%) in 4Q2002 that reached the patient. Pharmacy staff processed 6.2% more prescriptions in 2002 compared to 2001 and 25.6% more prescriptions in 2003 compared to 2002. During this time, there was no increase in pharmacist headcount and an increase of 1.5 FTE in technician headcount. Pharmacy staff increased their efficiency by 20% over the years 2001 to 2003.
CONCLUSIONS: Medication errors decreased and pharmacy staff efficiency improved to a meaningful and measurable degree following implementation of performance improvement initiatives. These results suggest that pharmacy led, team-based medication error improvement programs can be successfully planned and implemented in health care facilities similar to LCHC.

386. Ambulatory care pharmacists' role in the care of patients with chronic kidney disease. *Robin E. Bennett, Pharm.D.*[1], Renee M. DeHart, Pharm.D.[2]; (1)Methodist Healthcare, Memphis, TN; (2)Samford University McWhorter School of Pharmacy, Birmingham, AL.

PURPOSE: Between 1992 and 2001, the size of the Medicare population with CKD increased by 53% in diabetics and by 140% in non-diabetics. Pharmacists' involvement in the care of patients with CKD has historically focused on patients with ESRD. The involvement of pharmacists in the care of earlier stages of CKD has yet to be well established. A survey was created for ACCP's ambulatory care PRN pharmacists to address their current role in the care of patients in this population.
METHODS: The survey, cover letter, and stamped addressed return envelope were sent to 1028 potential respondents. Survey questions addressed use of and frequency of monitoring for CKD complications in at risk patients. Other information collected included respondent demographics, participation in nephrology referrals, and familiarity with National Kidney Foundation guidelines. Pharmacists indicating routine provision of care to patients at risk for or with CKD were included in the analyses.
RESULTS: Five hundred and thirty five of the 1028 completed and returned the survey (response rate of 52%). Survey data demonstrated that 85% of respondents routinely monitor for kidney dysfunction in at risk populations. In relation to anemia secondary to CKD, only 24% reported routinely monitoring Hgb/Hct concentrations. In addressing renal osteodystrophy, 16% routinely monitor Ca++/PO4 concentrations and 3.6% routinely monitor intact parathyroid hormone concentrations. Of responding pharmacists, only 39% have recommended patient referral to a nephrologist.
CONCLUSION: Surveyed ambulatory care pharmacists are routinely assessing for kidney dysfunction, but are not incorporating other recommended CKD guidelines into routine practice.

387. Pharmacist managed anemia program in an outpatient hemodialysis population. *Ted Walton, Pharm.D.*, Michael D. Knauss, Pharm.D., Katherine P. Holloway, Pharm.D.; Grady Health System, Atlanta, GA.

Erythropoietin alpha is the standard of care for anemia treatment in stage 5 chronic kidney disease patients. A pharmacist-managed anemia program was developed giving a clinical pharmacist authority to initiate, monitor, and change erythropoietin and iron therapy in the outpatient hemodialysis unit. All erythropoietin doses were administered subcutaneously. Data was collected from May 2002 to May 2004 totalling 228 patients and 1379 patient-months of pharmacist monitoring. Demographic data show the study population to be 67 % male, 88 % African-American and have an average age of 46 +/- 13 years. The most common etiology of renal failure was hypertension (50.4 %), diabetes mellitus (25.4 %) and human immunodeficiency virus (HIV) (10.5 %). The average initial hemoglobin was 9.5 gm/dl and was 11.8 gm/dl at six months. Iron parameters show an initial average ferritin of 187 ng/ml with an iron saturation of 22 %. These parameters improved to a ferritin of 495 ng/ml and iron saturation of 32 % at six months. At six months, 80 % of patients had a hemoglobin > 11 gm/dl compared to the national average of 75 % and 93 % of patients had a hemoglobin > 10 gm/dl. The average erythropoietin dose in the study group was 121 units/kg/week (8,420 units) compared to the national average of 229 units/kg/week (16,000 units). This difference results in an annual cost avoidance of $3,000 per patient. Pharmacist-management of anemia can provide a cost-effective method in the chronic kidney disease population.

388. Implementation and evaluation of rasburicase guidelines for prevention and treatment of tumor lysis syndrome in a large academic medical center. *Amy J. Hatfield, Pharm.D.*, Alix A. Butler, Pharm.D.; The Johns Hopkins Hospital, Baltimore, M.D.

PURPOSE: Limited recommendations exist for the use of rasburicase. FDA-approved labeling recommends 0.15–0.2mg/kg/day for 5 days in pediatric patients receiving chemotherapy at risk for hyperuricemia. This evaluation describes the implementation of rasburicase guidelines and evaluates outcomes following guideline institution.
METHODS: Guidelines were developed from literature review and manufacturer recommended indications. Oncology pharmacy clinical specialists (OPCS) were contacted for each potential use to review required criteria and recommend a single dose rounded down to the closest 1.5mg-vial based upon patient parameters. OPCS followed patients for response and need for subsequent doses.
RESULTS: 16 patients (8 pediatric, 8 adult) have been administered 18 doses of rasburicase since implementation in January 2004. OPCS were contacted for 100% of doses administered and recommendations were accepted. Mean uric acid level on presentation was 13.7 mg/dL (7–24.7 mg/dL) vs. 2mg/dL (<0.2–4.4 mg/dL) post-rasburicase in 14 patients who required one dose. Two patients who required two doses had levels of 9.3 and 10.2 mg/dL after one dose, and both 0.5 mg/dL after the second dose. Total drug acquisition cost for these 16 patients was $24,951 for the dosing strategy based on implemented guidelines vs. $170,753 based on package insert recommendations. Utilization of these guidelines resulted in a potential cost savings of $145,802.
CONCLUSIONS: The implemented guidelines target patients at highest risk for tumor lysis syndrome. Clinical outcomes of normal uric acid levels was achieved in all patients, most with only one dose. Implementation of guidelines with concurrent review and intervention minimizes costs and unnecessary use of rasburicase.

389. Therapeutic interchange of darbepoetin alfa for epoetin alfa for chemotherapy-induced anemia. *Deborah A. Blamble, Pharm.D.*, Kenneth M. Shermock, Pharm.D., Todd W. Nesbit, Pharm.D., Brian Pinto, Pharm.D., John Fetting, M.D.; The Johns Hopkins Hospital, Baltimore, M.D.

PURPOSE: To determine the success of implementation and the economic impact of a therapeutic interchange program of darbepoetin alfa for epoetin alfa for chemotherapy-induced anemia in a large academic medical center.
METHODS: An economic forecast model was developed to determine the impact of increased use of darbepoetin. Based on that model, and an assumption of equal safety and efficacy to epoetin, the interchange program was implemented. The therapeutic interchange began on July 1, 2003, following approval by the Pharmacy and Therapeutics Committee. When the pharmacy receives an order for epoetin, a pharmacist evaluates the patient for eligibility to participate in the interchange. Providers are allowed to write "Do Not Substitute" on orders for epoetin to avoid the therapeutic interchange. An analysis was performed after implementing the program to determine the level of compliance and the economic impact of the interchange program.
RESULTS: The economic forecast model estimated a potential for between $490K and $640K in annual cost savings by instituting a therapeutic interchange program from erythropoietin to darbepoetin. An analysis of three months of data from August 2003 through October 2003 showed that nearly 90% of erythropoeitic growth factor doses dispensed were darbepoetin, compared to 100% epoetin in the previous year. The estimated annual cost savings associated with the program was $560K in FY2004.

CONCLUSION: A therapeutic interchange program of darbepoetin for epoetin was successfully implemented in a large academic medical center. The program resulted in significant economic benefit to the institution that was consistent with forecasted savings.

390. Pharmacy quality assurance tool facilitates clinical trial development at a comprehensive cancer center. *Diana Vamos, Pharm.D.*, Jennifer Nishioka, R.Ph., Michael Kane, R.Ph., Shalu Gupta, Pharm.D., Stacey Hong, Pharm.D., Joseph Aisner, M.D., Susan Goodin, Pharm.D.; Cancer Institute of New Jersey, New Brunswick, NJ.

PURPOSE: Clinical trials offer the best treatment for patients with cancer, yet less than 5 percent of adults and less than 60 percent of children are enrolled on clinical trials. To assess areas for potential trial development we designed a 'non-protocol' form for use at our center. Our goal was to assess deficiencies in our menu of trials and indirectly increase awareness of trials.
METHODS: We captured all chemotherapy orders for ambulatory patients at The Cancer Institute of New Jersey who were not enrolled on a clinical trial. Completion of a 'non-protocol' form was required by the pharmacy with the first set of chemotherapy orders for any regimen new for that patient. The form required completion of one of three areas: trial availability, reason for ineligibility or other reason for not enrolling the patient.
RESULTS: From June 2003 through June 2004, 270 forms were collected which accounts for approximately 70 percent of all new chemotherapy orders. The most prominent opportunities identified for trial development include second line therapies for many tumors and the full data will be presented. Surprisingly, about 10 percent of patients refused protocol therapy despite seeking care at a Comprehensive Cancer Center.
CONCLUSION: The data generated from the implementation of this novel pharmacy service is of strategic importance to the cancer center. It is reviewed quarterly with the tumor-focused groups of the cancer center to identify areas for developing clinical trials. Psychosocial evaluation of the reasons for refusal may also yield important insights for clinical trials education.

391. A retrospective drug use evaluation of epoetin-α and darbepoetin-α within the Cleveland Clinic Health System. *Jodie M Fink, Pharm.D., BCPS*[1], Mandy C Leonard, Pharm.D., BCPS[1], Jennifer Shamp, Pharm.D.[2], Sandra S Axtell, Pharm.D.[3], Marcia J Wyman, Pharm.D.[1], Morton P Goldman, Pharm.D., BCPS[1], David A Kvancz, M.S., FASHP[1]; (1)The Cleveland Clinic Foundation, Cleveland, OH; (2)The Ohio State University, Columbus, OH; (3)Hillcrest Hospital, Mayfield Hts., OH.

PURPOSE: The Cleveland Clinic Health System (CCHS) conducted a retrospective drug use evaluation (DUE) of epoetin alfa (Procrit®, EPO) and darbeopoetin alfa (Aranesp™, DARB) for chemotherapy-induced anemia (CIA). The objective was to trend usage patterns in the ambulatory setting.
METHODS: Data was collected for patients initiated on EPO or DARB for ≥3weeks between July 2002–July 2003. Information collected included demographics, doses, frequency and duration of therapy, hemoglobin (Hgb) and hematocrit (Hct) levels, iron studies, and chemotherapy regimen.
RESULTS: Data from 114 patients were collected (40% male); 55 EPO and 59 DARB patients. Mean baseline Hgb levels were 9.95g/dl and 9.80g/dl in the EPO and DARB patients, respectively. Hgb levels were similar over the course of therapy for both groups. The average duration of therapy was 13.2wks in the EPO group and 13.6wks in the DARB group. Forty-seven patients reached Hgb levels of ≥12g/dl (EPO n=23; DARB n=24). The most frequent doses were EPO 40,000Units weekly and DARB 200µg every other week. The number of patients with transfusions was similar between the groups (EPO n=11; DARB n=7), and had no effect on the average Hgb levels. Only 10.5% of patients had iron studies drawn prior to therapy.
CONCLUSION: Based on these data, EPO and DARB produce similar Hgb levels in patients with CIA within CCHS; 42% and 41% with Hgb ≥12g/dl, respectively. The most common regimens were EPO 40,000Units weekly and DARB 200µg every other week. Recommendations for a therapeutic interchange program and routine iron studies will be forth-coming.

392. Development of a Web-based, computerized and patient-specific pediatric emergency drug card for hospitalized patients. *Michael A. Veltri, Pharm.D.*, Carol Matlin, R.N., M.S., Christoph U. Lehmann, M.D.; The Johns Hopkins Hospital, 600 North Wolfe Street, Baltimore, M.D.

PURPOSE: Due to the large variation in pediatric patient sizes, nearly all medication doses need to be individually calculated based on patient weight or body surface area. This step takes additional time and introduces an opportunity for error. In addition, the chance of a dose-calculation error is magnified during the stress of an arrest or emergency situation. The purpose of this project was to develop a computer-generated pediatric emergency drug card (PEDC) that contains precalculated patient-specific doses, and could be used in code situations throughout a large academic medical center.
METHODS: Content for the PEDC was developed by a multidisciplinary team, including pharmacy, nursing, and physicians. Pediatric advanced life support (PALS) and institution-specific guidelines were used to develop the dose calculation logic.
RESULTS: A user friendly, web-based computer program was successfully developed using Cold Fusion®, that generates patient specific PEDCs. The PEDC content includes precalculated PALS drug doses, continuous infusion medication calculations (concentrations and rates), and defibrillator doses. It is printed upon admission and is used institution-wide for all pediatric patients. It is kept at the ready in all pediatric patient's bedside charts, which accompany patients wherever they are in the institution.
CONCLUSION: Computers are uniquely suited to perform mathematical calculations repeatedly, with 100% accuracy. Utilizing this strength, a web-based computer program that generates a patient specific PEDC can be successfully developed. The use of these computer-generated PEDCs can be incorporated into the care of pediatric patients in a large academic medical center.

393. Pediatric pharmacology research and development center. Richard D Leff, Pharm.D.[1], *Trey Putnam, Ph.D.*[1], Reza Mehvar, Ph.D.[1], George McCracken, M.D.[2], Beverly Rogers, M.D.[3], Hasan Jafri, M.D.[2], John Tourville, Pharm.D.[3], Harvey Jones, M.S.[3]; (1)Texas Tech University Health Sciences Center, Dallas, TX; (2)University of Texas Southwestern Medical Center, Dallas, TX; (3)Children's Medical Center, Dallas, TX.

Preclinical and clinical testing are an essential part of the approval process of the U.S. Food and Drug Administration. We have previously collaborated to support the establishment of a NICHD-sponsored Pediatric Pharmacology Research Unit (PPRU). The PPRU will focus on conducting pediatric clinical trials. We have recently obtained funding and are in the process of establishing an early-stage analytical laboratory to support a broad range of preclinical pediatric drug studies. Capabilities of the PPRU and the Pediatric Pharmacology Research & Development Center (PPRDC) will be synergistic and promises to enhance our knowledge of drug therapy in infants and children. A tandem triple quadrupole mass spectrometer (API 3000ô, Applied Biosystems) will be the core LC-MS/MS system to deliver the desired analytical sensitivity, specificity, and ruggedness for drug development. The specific aims of the PPRDC include support of studies of bioavailability, formulation, drug metabolism, pharmacokinetics/dynamics, etc. in accordance with regulatory guidelines (i.e., GLP). The PPRDC represents a unique collaboration between University of Texas Southwestern Medical Center, Texas Tech University Health Sciences Center, and Children's Medical Center of Dallas. Unique to the collaboration is the capability of both preclinical and clinical studies in infants and children. The collaboration provides an unique training opportunity for health professionals. Pediatric pharmacology fellowships are planned to begin July, 2005.

394. Pharmacy interventions for computerized neonatal parenteral nutrition orders. *Sheila A. Pedigo, Pharm.D.*, Gary R. Gutcher, M.D., Carol Matsy, R.Ph., Erika Delph, R.Ph.; Virginia Commonwealth University Medical Center, Richmond, VA.

PURPOSE: This report documented pharmacy interventions on computerized neonatal parenteral nutrition (PN) orders to identify medication errors and to quantify extraneous dispensing issues.
METHODS: Parenteral nutrition prescriptions were prospectively evaluated by pharmacists for accuracy. Orders were screened for 1) correct patient and weight 2) dosages as standard range 3) and dispensing issues. Four evaluation periods three to five months in duration were performed on nutrient orders after PN computer enhancements. Interventions were considered prescribing errors or dispensing issues and classified as high, moderate, or minimal clinical significance.
RESULTS: A total of 4857 parenteral solutions were evaluated. The control phase indicated high to moderate error rates of 13 and 36 per 100 orders respectively while minimal errors and pharmacy issues were 43 and 8.1 per 100 prescriptions. System changes to the ordering process resulted in error decrement then escalated to 7.6–21.8 per 100 orders for high, moderate errors. Pharmacy dispensing issues increased to 76.9 per 100 orders (NS). The PN high, moderate error rate did not change in the final evaluation period after computer advancements yet minimal errors and pharmacy dispensing issues were three to six times higher. (NS).
CONCLUSION: Pharmacists must continue to evaluate computerized neonatal PN orders to prevent high, moderate medication errors. The pharmacy dispensing issues should be assessed for production and clinical relevance.

395. Pharmacist intervention in rehabilitation unit. *Dan Moellentin, Pharm.D.*, Renee Ford, Pharm.D.; Eastern Maine Medical Center, Bangor, ME.

Rehabilitative Medicine Units have taken on ,higher acuity patients than in the recent past in part due to changes in Skilled Facility acceptance policies of hospital discharged patients who require care or drugs that would surpass insurance reimbursements. Pharmacists that have Internal Medicine training with emphasis on Neurology can play a valuable role in the contemporary Rehabilitation Unit. Patients in one unit were studied for 6 months after a clinical pharmacist was introduced to multidisiplinary rounds and patient care on a 70-bed unit. Unit costs were compared with pharmacy cost-transfer prior to pharmacist installation and after and adjusted for census. There were no significant differences in case mix prior to or post pharmacist implimentatation. Intervention types by volumne were as follows: ADR assessment and prevention, CNS changes, drug-drug interactions, nausea and

vomiting, depression, antibiotic choice and duration, agitation, anticoagulation, diabetes, anemia, HIT management and transition to warfarin, IgG utilization, hemodynamics, pain, and miscellaneous. Quality of patient care and LOS were positively impacted (cost avoidance), impact was also made on drug costs incurred. Drug expenses reduced an average of $145.37 per intervention. Interventions averaged 4 per day 5 days a week. Time expended was 2.3 hours per day. Drugs providing the largest financial impact were 1) IgG 2) erythropoeitin 3) direct-thrombin inhibitors 4) intravenous anti-zeisure medications 5) antibiotics 6) prompt ADR recognition and management, and 6) Interferons. Placement of a clinical pharmacist on a Rehabititation Unit provides significant opportunities to reduce suffering, Length of Stay, and decrease drug expenses.

396E. Impact of a pharmacist on a patient-focused community-based outreach program. *Darshana S. Rathod, Pharm.D.*; Baylor Specialty Health Centers, Dallas, TX.

Presented at the ALCALDE Southwest Leadership Conference, Galveston, TX, May 2002.

397. Assessment of medication therapy management services in a pharmaceutical care asthma clinic. *Leigh Ann Ramsey, Pharm.D., BCPS, CDE*, Lisa M. Murphey, Pharm.D., BCPS, Margaret B. Pitcock, Pharm.D., Carol Hope, Pharm.D.; University of Mississippi Medical Center, Jackson, MS.

PURPOSE: To determine whether medication therapy management by pharmacists decreases emergency care for asthma and improves compliance.
METHODS: Retrospective study of patients followed for 12 months. The enrolled cohort acted as its own historical control. The primary outcome was utilization of Emergency Department (ED) services and hospitalizations for asthma; secondary outcomes evaluated compliance. Data retrieved from disease modules completed at each visit. The study interval constituted one year prior to referral for asthma management (year 1) compared to one year after (year 2).
RESULTS: Thirty-one patients enrolled. In year 1, 14 patients had >2 ED visits for asthma; in year 2, 7 patients had >2 ED visits for asthma. Average ED visits in year 1 was 1.548 compared to 0.645 in year 2. In year 1, 8 patients had 1–3 hospitalizations for asthma; in year 2, 4 patients had 1–3 hospitalizations for asthma. Average hospitalizations in year 1 was 0.354 compared to 0.129 in year 2. On initial visit, 52% patients had compliance score of <50, with 32% of patients scoring >90. On final visit, 38% patients had compliance score of <50, with 55% scoring >90.
CONCLUSION: Preliminary analysis revealed a decrease in utilization and cost of emergency services for asthma after pharmacist intervention. This assessment ratifies the benefit previously observed, a decrease in emergency services; it also demonstrates an increase in patient compliance with pharmacist involvement. Study limitations include estimates of ED and hospitalizations from patient-reported data. These results will support implementation of a prospective evaluation of this service.

398. Outcomes of a pharmacotherapy clinic in a community health center associated with an indigent care urban health system. *Santhi Masilamani, B.S., Pharm, Pharm.D., CDE*; Harris County Hospital District, Houston, TX.

PURPOSE: A pharmacotherapy clinic was established in a primary care providing community health program (CHP) associated with an indigent care health system in Houston, TX.
METHODS: Adult patients identified with high-risk chronic disease parameters were referred to the Clinical Pharmacy Specialist for management until goal. Physician progress notes described reasons for referral and nursing personnel made the appointments at specified time periods. All visits, new and follow-up were set at 20 minute intervals due to lack of scheduling software sophistication. Each visit included medication review, polypharmacy screening, focused physical assessment, medication adjustment, patient education, and refill authorization.
RESULTS: Over 300 patients are actively enrolled in this clinic. Referrals were primarily for diabetes, followed by hypertension, lipid management, asthma, and pain management. Outcomes data was tracked with an access database. One year outcomes for A1C were 2% average reduction for those with a baseline > 9% and 1% average reduction for those with a baseline between 7–9%. Lipid outcomes showed a 14 mg/dl reduction in LDL. 90% of the patients referred for hypertension met BP goals. The other 10% were sent to hypertension specialty clinic for secondary cause evaluation. Asthma and pain management referrals were not sufficient in number for evaluation.
CONCLUSIONS: The pharmacotherapy clinic has been extremely successful with metabolic syndrome referrals added to the referral criteria recently. The clinic has reached maximum capacity. Pharmacy administration has taken steps to expand the program to the remaining ten community health centers.

399. Pharmacist assisted renal medication dosing (PHARMD) trial. *Jennifer L. Mazzola, Pharm.D.*[1], Pritesh J. Gandhi, Pharm.D., BCPS[1], Paul P. Belliveau, Pharm.D.[1], Gary R. Tataronis, M.S.[2], Kabeer Mago, Pharm.D.[3]; (1)Massachusetts College of Pharmacy and Health Sciences, Worcester, MA; (2)Massachusetts College of Pharmacy and Health Sciences, Boston, MA; (3)UMass Memorial Medical Center, Worcester, MA.

PURPOSE: We sought to determine if there were differences in the appropriate dosing of renally-excreted medications between areas of the hospital traditionally followed by a decentralized pharmacist to those areas of the hospital not followed by a decentralized pharmacist.
METHODS: All patients with renal dysfunction (serum creatinine greater than 1.4 mg/dL) were prospectively identified and were included if they were greater than 18 years of age and prescribed a medication requiring renal dose adjustment. Group 1 included patients traditionally followed by a decentralized pharmacist; group 2 consisted of patients not covered by a decentralized pharmacist. The primary endpoint was to compare the incidence of inappropriate medication dosing between the two groups. Cost avoidance and the number of accepted recommendations were secondary endpoints.
RESULTS: There were a total of 240 renally dosed drugs in group 1 versus 245 in group 2. Approximately 1.3% (n=3) of the medications in group 1 were inappropriately dosed compared to 22% (n=53) in group 2 (p=0.001). The estimated cost avoidance associated with these interventions were $4,500 over a three-month period or about $18,000 annually.
CONCLUSION: Active monitoring of and intervention for hospitalized patients with renal dysfunction can decrease the number of inappropriately dosed renally-excreted medications in patients with renal dysfunction. This, in turn, may decrease hospital costs associated with excessive dosing in this population.

400. Development of a focused pharmacotherapy module education program for medical residents and critical care/pulmonary fellows in a medical intensive care unit (MICU). *Joseph E. Mazur, Pharm.D., BCPS*[1], Brian Zeno, M.D.[2], Alice M. Boylan, M.D.[2], John E. Heffner, M.D., FCCP[3]; (1)Medical University of South Carolina, PO Box 250584, Charleston, SC; (2)Medical University of South Carolina - Department of Pulmonary & Critical Care Medicine, PO Box 250630, Charleston, SC; (3)Medical University of South Carolina - Executive Medical Director, PO Box 250332, Charleston, SC.

PURPOSE: The American College of Critical Care Medicine has outlined guidelines for residency training involving clinical pharmacists as part of the healthcare team.We developed for later outcomes testing a modular critical care educational program for MICU housestaff at an academic teaching university hospital to meet these guidelines.
METHODS: The MICU director in collaboration with a clinical pharmacy specialist identified safe medication practice guidelines as a quality improvement initiative. A series of Intranet-based and live case discussions/lectures to housestaff were developed for presentation bi-weekly over a one month time period. Examples of areas covered in the core curriculum comprise: antimicrobial/antifungal management, vasopressors/inotropes in shock states, hypertensive urgencies and emergencies, status epilepticus, and sedative-neuromuscular blockers. Content and formatting were revised based on attendee feedback. To assess medication use competency, residents will be provided pre- and post-test questions before lectures. The lectures will be made available on the hospital Intranet via PowerPoint slide format with case discussions. A satisfaction survey is planned to be distributed after their one month blocks to determine the quality of education provided to them.
RESULTS: To date, 84 PGY 1-6 have attended 12 months of pilot lectures providing feedback to refine the lecture modules. Residents have responded positively, and a final series of PowerPoint slides are being developed.
CONCLUSION: Sufficient evidence-based studies exist to allow the development of short PGY 1-6 resident educational modules, which are well received and attended. Future outcomes studies are needed to determine the effect on knowledge and skills of this program.

401. Implementation of after hours remote pharmacy services within a health system. *Susan Trzop-Haiden, R.Ph.*, Shewan Aziz, Phd., Rph, William Boynton, R.Ph., James Raczek, M.D.; Eastern Maine Medical Center, Bangor, ME.

PURPOSE: Maine hospitals without twenty four-hour pharmacy services need to comply with the JCAHO first dose review requirement and the new State regulation, which requires a pharmacist to review a medication order within 28 hours of initiation. This study describes an innovative and a cost-effective means of providing concurrent order review to these hospitals.
METHODS: Eastern Maine Health System consists of 4 acute care facilities, one critical access hospital, one rehabilitation facility and one psychiatric facility. Eastern Maine Medical Canter (EMMC) is a 425-bed community based teaching hospital and is the only facility providing 24/7 pharmacy services. In 2003, EMMC pharmacy initiated the process of providing remote order verification during weekends and holidays to three out of the four acute care facilities.
RESULTS: EMMC Pharmacists provide drug order review and entry services via facsimile and electronic imaging technology during the hours the client hospital pharmacy is closed. In addition, EMMC pharmacists have access to patient profiles, laboratory data and policies to clarify and clinically intervene on inappropriate medication orders. The pharmacist is also able to provide drug information to nurses and physicians and to alert the hospital pharmacy

staff about patients or issues that required follow up by the hospital pharmacists in the morning.
CONCLUSIONS: The shortage of pharmacists, limited hospital pharmacy budgets, and increasing pharmacists' salaries have made it difficult to comply with the concurrent medication review requirement. This abstract demonstrates that the use of a pharmacist driven remote verification is the most effective and economical option for compliance.

402. Reimbursement for psychiatric services and development of a medication database: two examples of psychiatric clinical pharmacy services at a large outpatient community mental health center. *Christopher M. Gillette, Pharm.D.., BCPP*[1], Joshua A. Bellamy, Pharm.D..[2]; (1)Human Service Center, Peoria, IL; (2)Pfizer Inc., New York, NY.

The Human Service Center (HSC) is a comprehensive Community Mental Health Center located in Peoria, Illinois. A clinical pharmacist was hired and tasked with supporting the multi-disciplinary outpatient clinical treatment teams by providing clinical pharmacy services and administrative duties. Clinical pharmacy services include consulting on pharmacotherapy-related issues with staff and patients and monitoring medication utilization trends. Administrative services include monitoring the procurement and distribution of medications, managing the medication budget, and actively participating in administrative systems development.
Critical elements vital to the success of the clinical pharmacy service include the ability to be reimbursed for these services and the development of a medication database. Clinical pharmacy services provided to consumers with Mental Health conditions were reimbursed by Illinois State Medicaid through the Illinois Department of Human Services, Division of Mental Health. An exemption was granted for the clinical pharmacist to become a Qualified Mental Health Professional (QMHP) based on academic education and experience. As a QMHP, the clinical pharmacist can bill Illinois Medicaid for services including medication monitoring and training. A medication database was created using Microsoft Access® and is updated daily with changes to treatment regimens. These data provide information essential to identify prescribing trends, opportunities to control cost, and improve client care.
This innovative clinical pharmacy practice site serves as a model for community mental health clinics to replicate. Clinical pharmacy services have enabled the clinic to increase utilization of industry-sponsored medication programs, manage drug costs and associated administrative duties while improving client education related to pharmacotherapy.

403. Pharmacist-initiated comprehensive bone health protocol improves the identification, prevention, and treatment of bone disease in an outpatient kidney and pancreas post-transplant clinic. *David J. Taber, Pharm.D., BCPS*[1], Elizabeth Ashcraft, B.S.[2], G. Mark Baillie, Pharm.D., M.H.A.[2], Bart Lawrence, Pharm.D., BCPS[3]; (1)Wingate University School of Pharmacy, Wingate, NC; (2)MUSC, Charleston, SC; (3)Pfizer Global Pharmaceuticals, 175 Beresford Creek St, Charleston, SC.

PURPOSE: The aim of this study was to determine the impact on patient outcomes with the implementation of a pharmacist initiated comprehensive bone health protocol.
METHODS: This was a retrospective chart review which consisted of two groups, patients transplanted up to one-year prior to the implementation of the protocol (group 1), compared with patients transplanted after the protocol implementation with at least 3 months of follow-up (group 2). The protocol was developed to provide a comprehensive set of guidelines on how to diagnose, prevent, treat, and monitor bone disease within the post-transplant population. Pharmacists saw patients prior to providers and used the protocol to guide and support recommendations made to the providers.
RESULTS: A total of 208 patients were included in this study, of which, 132 patients were in group 1 and 76 patients were in group 2. Patients in the two groups were well matched for both demographic features (age, race, gender, height, weight, IBW, BMI, and history of hypertension or hormone replacement), as well as transplant characteristics. Patients in group 2 were more likely to have a post-transplant DEXA scan (74% vs. 54%; p<0.005), more likely to receive appropriate doses of supplemental calcium and vitamin D (68% vs. 45%; p=0.002), and more likely to receive appropriate treatment for bone disease (81% vs. 66%).
CONCLUSIONS: The implementation of a pharmacist initiated comprehensive post-transplant bone health protocol improved the identification, prevention, and treatment of bone disease.

404. Pharmacist-initiated comprehensive dyslipidemia protocol improves the identification and treatment of lipid disorders in an outpatient kidney and pancreas post-transplant clinic. *David J. Taber, Pharm.D., BCPS*[1], Elizabeth Ashcraft, B.S.[2], G. Mark Baillie, Pharm.D., MHA[2], Bart Lawrence, Pharm.D., BCPS[3]; (1)Wingate University School of Pharmacy, Wingate, NC; (2)MUSC, Charleston, SC; (3)Pfizer Global Pharmaceuticals, 175 Beresford Creek St, Charleston, SC.

PURPOSE: The aim of this study was to determine the impact on patient outcomes with the implementation of a pharmacist initiated dyslipidemia protocol.
METHODS: This was a retrospective chart review which consisted of two groups, patients transplanted between 1/98 and 5/03 (group 1), compared with patients transplanted after the protocol implementation with at least 3 months of follow-up (group 2). The protocol was developed to provide a comprehensive set of guidelines on how to identify, diagnose, treat, and monitor dyslipidemias within the post-transplant population. Pharmacists saw patients prior to providers and used the protocol to guide and support recommendations made to the providers.
RESULTS: A total of 610 patients were included in this study, of which, 534 patients were in group 1 and 76 patients were in group 2. Patients in the two groups were well matched for both demographic features (age, race, gender, and known risk factors for dyslipidemias), as well as transplant characteristics. Group 2 had a higher percentage of patients at goal for LDL (64% vs 52%) and triglycerides (57% vs. 48%), although this did not reach statistical significance (p<0.2). However, patients in group 2 were more likely to have a follow-up FLP (91% vs. 67%; p<0.0001), and were more likely to have both their triglycerides and LDL at goal (44% vs. 28%; p<0.01).
CONCLUSIONS: The implementation of a pharmacist initiated post-transplant dyslipidemia protocol improved the identification and treatment of lipid diseases.

405. Development of a pharmacist-managed, university-based wellness center. *Christine K O'Neil, Pharm.D., BCPS, FCCP*, Hildegarde J Berdine, B.S., Pharm.D., BCPS, R. Pete Vanderveen, Ph.D., Pharm.D., BCPP, Thomas J Mattei, Pharm.D.; Mylan School of Pharmacy, Duquesne University, Pittsburgh, PA.

PURPOSE: The purpose of this project is to describe the development and implementation of a wellness clinic managed by pharmacy faculty and students within a university. The project had three goals: (1) develop pharmaceutical care & wellness programs for the university and surrounding communities (2) develop programs with intent of educating students. (3) develop and trial resources that may be used by our preceptors, specifically ambulatory preceptors in their own practice site.
METHODS: The project was conducted in three phases: (1) needs assessment of employees through health education lectures and human resources data; (2) implementation of health screenings and disease management initiatives; and (3) development of a clinical rotation and expansion of services through preceptors. The project, known as the Center for Pharmacy Care was launched in 2002. The center provides on and off campus preventive health screenings, patient education, medication and lifestyle counseling, educational seminars, tobacco cessation groups and outcome reporting for common health conditions. Preventive screenings include blood pressure, cholesterol, glucose, bone density, body composition, and facial skin analysis. The center now serves a clinical practice site, teaching site and resources for preceptors.
RESULTS: To date, the center has provided over 50 screening events, 16 health education seminars and served over 1000 individuals. Recently, the center adopted an office-style practice that allows for individual appointments and greater opportunity for continuity of care.
CONCLUSIONS: The center has evolved to be dynamic practice and service model and teaching site. Future plans include expansion of services and types of populations served.

406E. Number needed-to-treat and cost of recombinant human erythropoetin to avoid one transfusion-related adverse event in critically ill patients. *Edward T. Horn, Pharm.D.*, Kenneth M. Shermock, Pharm.D., Pamela A. Lipsett, M.D., Peter J. Pronovost, M.D., Ph.D., Todd Dorman, M.D.; The Johns Hopkins Hospital, Baltimore, M.D.

Presented at Presented at the 33rd Society of Critical Care Medicine Clinical Congress, Orlando, FL, February 20–25, 2004.

STUDENT, RESIDENT, FELLOW RESEARCH IN PROGRESS

These papers describe original research by students, residents, and fellows in therapeutics, pharmacokinetics, pharmacodynamics, pharmacoeconomics, and pharmacoepidemiology in which the research effort is still on-going. The abstract title and authors are published in Pharmacotherapy; the full abstract will be published in the meeting program book.

407. Utilization of fenoldopam to preserve renal function in coronary artery bypass graft patients. *Matthew Dormarunno, B.S., Pharm.D.candidate*, Jim Curtis, Pharm.D.; Borgess Medical Center, Kalamazoo, MI.

408. American College of Clinical Pharmacy (ACCP) survey: assessment of student interest in clinical pharmacy. *Sindhu A Mathew, Pharm.D., candidate*, Karen Sweiss, Pharm.D., candidate, Hina Ahmed, Pharm.D. candidate, Przemyslaw Radwanski, Pharm.D. candidate, Larisa Cavallari, Pharm D; University of Illinois at Chicago, Skokie, IL.

409. A comparison of pharmacist-obtained medication history and Usual Care Model in the emergency department. *Katharine A Crites, Pharm.D.*[1],

Sara J. Smith Shull, Pharm.D., M.B.A.[1], Richard A. Walker, M.D.[2]; (1)The Nebraska Medical Center, Omaha, NE; (2)University of Nebraska Medical Center, Omaha, NE.

410. Impact of group education on metabolic syndrome. *Daniel S. Longyhore, Pharm.D.*[1], Terry L. Seaton, Pharm.D.[1], Gloria Rizkallah, Pharm.D.[1], Thomas A. Johnson Jr., M.D.[2]; (1)St. Louis College of Pharmacy, St. Louis, MO; (2)Mercy Family Medicine, St. Louis, MO.

411. *Helicobacter pylori* eradication therapy in decreasing long-term acid suppression therapy. *Chrystian R Pereira, Pharm., D.*, Alvin Goo, Pharm.D., Mark Doescher, M.D., M.S.P.H.; Harborview Medical Center, Seattle, WA.

412. Duration of venous thromboembolism prescribing on orthopedic patients. *Sanjeev Balu, B.Pharmacy, M.B.A*[1], F. Randy Vogenberg, RPh, Ph.D.[2], Leo Lichtig, Ph.D.[2], Paul J. O'Connor, RPh, M.B.A[2]; (1)Purdue University, West Lafayette, IN; (2)Aon Consulting Life Sciences Practice, Wellesley, MA.

413. A retrospective analysis of vitamin K dosing and INR decline during interuption of warfarin therapy for invasive procedures. *Christopher Martin, Pharm.D.*[1], Alicia M. Reese, Pharm.D., M.S.[1], Lisa E. Farnett, Pharm.D.[2], Henry I. Bussey, Pharm.D.[1]; (1)University of Texas College of Pharmacy/UT Health Sciences Center San Antonio, San Antonio, TX; (2)Anticoagulation Clinics of North America, San Antonio, TX.

414. Outcomes of dual-boosted protease inhibitor therapy following consultation with a national HIV/AIDS telephone consultation service. *Nancy N. Nguyen, Pharm.D.*, Betty J. Dong, Pharm.D.; University of California, San Francisco, San Francisco, CA.

415. Evaluation of gabapentin dosing and toxicity in patients with renal impairment. *Holli A. Winters, Pharm.D.*, Shiv Seth, R.Ph., Ph.D.; The Ohio State University Medical Center, Columbus, OH.

416. Assessment of an encapsulated dosage form for oral administration of 18-F-2D2-flurodeoxyglucose (FDG) and biodistribution of FDG administered by gavage in a rat model. *Tyler M. Smith-Strutz, Pharm.D.-Candidate*, Edward M. Bednarczyk, Pharm.D., Asit Paul, Ph.D., Lisa Martin, DVM; University at Buffalo, Buffalo, NY.

417. Itraconazole prophylaxis in adult acute leukemic patients. *Jeffrey J. Bruno, Pharm.D.*[1], Jennifer K. Long, Pharm.D., BCPS[1], Christopher Lowe, Pharm.D.[1], Jennifer Shamp, Pharm.D.[2], Robin K. Avery, M.D.[1]; (1)The Cleveland Clinic Foundation, Cleveland, OH; (2)The Ohio State University, Columbus, OH.

418. Comparison of front loading dosages of darbepoetin alfa and epoetin alfa on clinical efficacy and fatigue measurements at Howard University Cancer Center. *Tiffany V. Goolsby, Pharm., D.*, Gladys Onojobi, M.D., Charles Agbemabiesse, M.D., Padma Kamieni, M.D., Deshondra Clark, Pharm.D., Fredric A. Lombardo, Pharm.D., Fitzroy Dawkins, M.D.; Howard University, Washington, DC.

419. Medication adherence and obstructive sleep apnea. *Cynthia A. Weber, Pharm.D., Candidate*[1], Rachel Gravel, Pharm.D.[1], Karen Farris, Ph.D.[1], Beth Bryles Phillips, Pharm.D.[1], Mark E. Dyken, M.D.[1], John M. Dopp, Pharm.D.[2], Bradley G. Phillips, Pharm.D.[1]; (1)University of Iowa, Iowa City, IA; (2)University of Wisconsin, Madison, WI.

420. Evaluation of 25 clinically important drug-drug interactions using a managed care database. *Meng-Ting Wang, M.S.*, Daniel C. Malone, Ph.D., Grant H. Skrepnek, Ph.D., Edward P. Armstrong, Pharm.D.; College of Pharmacy, University of Arizona, Tucson, AZ.

421. Evaluation of the in vitro metabolism of complementary and alternative medications (CAM) commonly used in oncology patients. *Marisa A. Navo, Pharm.D.*, Kellie L. Jones, Pharm.D., BCOP, John J. Kavanagh, M.D., Judith A. Smith, Pharm.D., BCOP; The University of Texas, M.D. Anderson Cancer Center, Houston, TX.

422. Hormone replacement therapy subsequent to the Women's Health Initiative. *Jennifer P. Askew, B.S., Pharm.D.*; New Hanover Regional Medical Center & Coastal AHEC, Wilmington, NC.

423. Pharmacokinetics of amoxicillin during pregnancy and postpartum. *Rachel J. Bennett, B.A.*[1], Thomas R. Easterling, M.D.[2], Danny D. Shen, Ph.D.[1], Darcy B. Carr, M.D.[2], Mary F. Hebert, Pharm.D., FCCP[1]; (1)University of Washington, Box 357630, Seattle, WA; (2)University of Washington, Box 356460, Seattle, WA.

424. A comparison of the triglyceride-lowering effects of pure docosahexaenoic acid versus combination docosahexaenoic plus eicosapentaenoic acid in patients with coronary artery disease and elevated triglycerides. *Lisa J. Schwellenbach, Pharm.D.*, Kari L. Olson, Pharm.D., Karen J. McConnell, Pharm.D., James D. Nash, Pharm.D., Ryan S. Stolcpart, Pharm.D., John A. Merenich, M.D.; Kaiser Permanente Colorado Region, Aurora, CO.

RESEARCH INSTITUTE

The following papers, based on Fellowships and Research Awards provided by the ACCP Research Institute, will be presented. Full titles and authors are listed, although a complete abstract may not be available for all papers at the time of this printing.

425. Aventis Infectious Diseases Fellowship: Designing pharmacodynamic target attainment indices for fluoroquinolones using genetically driven break points for *S. pneumoniae*. *Ayman M. Noreddin, M.Sc., Ph.D.*, Heather J. Smith, B.Sc., Daryl J. Hoban, Ph.D., George G. Zhanel, Ph.D.; College of Pharmacy, Univeristy of Minnesota, Duluth, MN.

426. Bayer Critical Care Fellowship: Longitudinal solute clearance in an in vitro continuous venovenous hemofiltration model. *Deborah A. Pasko, Pharm.D.*, Bruce A. Mueller, Pharm.D., FCCP, BCPS; University of Michigan College of Pharmacy, Ann Arbor, MI.

427. Merck Cardiovascular Fellowship: Evaluation of peak exercise tolerance, cardiac hemodynamics, and quality of life assessment from ribose versus placebo in subjects with left ventricular systolic with or without diastolic dysfunction. *Orly Carter, Pharm.D.*, Kirk Volkman, N.P., Edward Michael Gilbert, B.S., Greggory Stoddard, M.P.H., Mark A. Munger, Pharm.D., FCCP; University of Utah, Salt Lake City, UT.

428. Merck Infectious Diseases Fellowship: Evaluation of the in vitro activities of arbekacin, daptomycin, linezolid, quinupristin-dalfopristin, and tigecycline alone and in combination against two clinical strains of vancomycin-resistant *Staphylococcus aureus* (VRSA) in an in vitro pharmacodynamic infection model. *Vanthida Huang, Pharm.D.*, Michael J. Rybak, Pharm.D.; Anti-Infective Research Laboratory, Eugene Applebaum College of Pharmacy & Health Sciences, Wayne State University, Detroit, MI.

429. Ortho Biotech Pharmacogenomics Fellowship: Discordance of slow acetylator phenotype and genotype for *N*-acetyltransferase (NAT-2) in a Hmong population. Robert J. Straka, Pharm.D., FCCP, *R. Todd Burkhardt, Pharm.D.*, Nicholas P. Lang, M.D., Kelly Z. Hadsall, Pharm.D., Ter Vang, Pharm.D., Michael Y. Tsai, Ph.D.; University of Minnesota, Minneapolis, MN.

430. Ortho-McNeil Infectious Diseases Fellowship: Detection of gliotoxin, a mycotoxin produced by *Aspergillus fumigatus*, in experimental and human Asperigillosis. *Nathan P. Wiederhold, Pharm.D.*[1], Russell E. Lewis, Pharm., D.[2], Jingduan Chi, Ph.D.[1], Xiang Y. Han, M.D.[1], Krishna V. Komanduri, M.D.[1], Dimitrios P. Kontoyiannis, M.D., D.Sc.[1], Randall A. Prince, Pharm.D.[1]; (1)University of Texas M.D. Anderson Cancer Center, Houston, TX; (2)University of Houston College of Pharmacy, Houston, TX.

431. Roche Laboratories Transplantation Research Fellowship: Lack of effect of oral iron administration on mycophenolate mofetil pharmacokinetics in stable renal transplant recipients. *Daniele K. Gelone, Pharm.D.*, Jeong M. Park, M.S., Pharm.D., Kathleen D. Lake, Pharm.D., FCCP, BCPS; University of Michigan, Ann Arbor, MI.

432. Roche Laboratories Transplantation Research Fellowship: A single-center pilot study to determine the pharmacokinetics of various immunosuppressants in transplant recipients who have undergone gastric bypass surgery. *Christin Rogers, Pharm.D.*[1], J. Wesley Alexander, M.D.[2], Rita R. Alloway, Pharm.D.[1], Joseph Austin, M.D.[3], Robyn Boardman, Pharm.D.[1], Michael Cardi, M.D.[1], Sharad Goel, M.D.[1], Hope Goodman, M.P.T.[1], Shaoming Huang, M.D.[1], Shahzad Safdar, M.D.[1], Jennifer Trofe, Pharm.D.[1], Sander Vinks, Pharm.D., Ph.D.[1]; (1)University of Cincinnati, Cincinnati, OH; (2)Kidney and Hypertension Center, Cincinnati, OH; (3)Children's Hospital, Cincinnati, OH.

433. ACCP Career Development Research Award: T-cell subset responses to hepatitis A vaccine. *Mary S. Hayney, Pharm.D., FCCP, BCPS*[1], Nicholas A. Wiegert, B.S.[1], Frances L. Pelsue, B.S.[2]; (1)University of Wisconsin, Madison, WI; (2)University of Minnesota, Minneapolis, MN.

434. ACCP Pharmacotherapy Investigator Development Research Award: In vitro evaluation of antiviral agents for the treatment of cervical cancer expressing human papillomavirus (HPV) genotype. *Judith A. Smith, Pharm.D., BCOP*[1], William Figg Sr., Pharm.D.[2], Melinda M. Neuhauser, Pharm.D.[3], Diane C. Bodurka, M.D.[3], Charles F. Levenback, M.D.[3]; (1)The University of Texas, M.D. Anderson Cancer Center, Houston, TX; (2)National Cancer Intitute/National Institutes of Health, Bethesda, M.D.; (3)National Institute of Health, Bethesda, M.D.

435. Amgen Biotechnology Investigator Development Research Award: Development of a controlled-release injectable gel system for epoetin alfa. *Joanna Q. Hudson, Pharm.D.*, Yichun Sun, Ph.D., S. Casey Laizure, Pharm.D., BCPS, Atul Shukla, Ph.D., Shipeng Yu, B.S.; University of Tennessee, Memphis, TN.

436. AstraZeneca Cardiovascular Investigator Development Research Award: Optimal renin angiotensin system inhibition and CAD markers.

James P Tsikouris, Pharm.D., Craig D. Cox, Pharm.D., Jan S. Simoni, Ph.D., Miranda C. Peek, B.S., Gary E. Meyerrose, M.D.; Texas Tech University Health Sciences Center, Lubbock, TX.

437. Aventis Asthma/Allergy Investigator Development Research Award: Histamine *N*-methyltransferase (HNMT) C314T gene polymorphism is associated with atopic dermatitis (AD) in Caucasian children. *Mary Jayne Kennedy, Pharm.D.*[1], Jennifer A. Loehle, M.S.[2], Janice E. Sullivan, M.D.[2], Mark A. Doll, M.S.[2], David W. Hein, Ph.D.[2]; (1)University of Louisville, Louisville, KY; (2)Kosair Charities Pediatric Clinical Research Unit, Louisville, KY.

438. Aventis Cardiovascular Investigator Development Research Award: Characterization of an aspirin-ibuprofin interaction. James J. Nawarskas, Pharm.D., *Lenka Hrebickova, Pharm.D.*, Joe R. Anderson, Pharm.D., T. Crain Timm, M.D.; University of New Mexico College of Pharmacy, Albuquerque, NM.

PURPOSE: Previous research has suggested that ibuprofen (IBU) may interfere with the ability of aspirin (ASA) to inhibit platelet aggregation (PA). Less is known regarding whether occasional use of over-the-counter IBU would interfere with the antiplatelet effect of ASA during chronic ASA treatment. The purpose of this study was to investigate whether single doses of over-the-counter IBU would affect the ability of chronic ASA to inhibit PA.

METHODS: 12 healthy volunteers participated in this prospective, randomized, crossover study. Each subject received once-daily ASA (81 or 325 mg) for 2–4 weeks, with PA assessed at the beginning (baseline) and end of this treatment period. This was followed by an additional 2–4 weeks of the same dosage of ASA. After this time, 2 single 400 mg doses of IBU were administered 4 hours apart: 20 and 24 hours, respectively, after the last dose of ASA. PA was assessed following each dose of IBU and compared to the results obtained with ASA alone at the same times post-dose. Following a 2-week washout period, each subject received the remaining dosage of ASA and the process repeated. PA was assessed using whole-blood aggregometry with collagen and arachidonic acid as pro-aggregants.

RESULTS: PA was significantly inhibited in all subjects following administration of both dosages of chronic ASA and remained inhibited to a similar extent after administration of both doses of IBU.

CONCLUSIONS: Occasional over-the-counter doses of IBU do not interfere with the ability of ASA to inhibit PA in individuals taking chronic daily ASA.

439. Aventis Infectious Diseases Investigator Development Research Award: Novel mechanisms of axole antifungal resistance. *P. David Rogers, Pharm.D., Ph.D.*, Katherine S. Barker, Ph.D., Massoumeh Z. Hooshdaran, Ph.D., George M. Hilliard, Ph.D.; University of Tennessee, Memphis, TN.

440. Ortho Biotech Pharmacogenomics Investigator Development Research Award: Influence of MDR1 genotypes on saquinavir pharmacokinetics in health human subjects. *Scott R. Penzak, Pharm.D.*, Elizabeth Formentini, R.N.C., M.S.N., Raul M. Alfaro, M.S., Judith Falloon, M.D.; National Institute of Health, Bethesda, M.D.

441. Pharmacia Health Outcomes Investigator Development Research Award: Evaluation of two Hoehl and Yahr scales modified for patient or caregiver assessment. *Gary L. Cochran, Pharm.D.*, Ekaterini M. Markopoulou, M.D., Ph.D., Susan E. Puumala, M.S., Anthony Ranno, Pharm.D.; University of Nebraska Medical Center, Omaha, NE.

442. Roche Transplantation Investigator Development Research Award: Immunosuppressant effects on P-glycoprotein function in human kidney (HK-2) cells. *Thomas C. Dowling, Pharm.D., Ph.D.*, Minori Kinjo, M.S., Tahira Iqbal, Ph.D.; University of Maryland, Baltimore, M.D.

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