

# Assessment of patient outcomes after the implementation of a pharmacist-coordinated Lipid Shared Medical Appointment (Lipid SMA) within the primary care clinic at a Veterans Affairs Hospital

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**Background:** Cardiovascular disease (CVD) remains the number one cause of death in the U.S.; CVD total mentioned deaths accounted for about 56% of all deaths in the U.S. in 2005.<sup>1</sup> Among lipids, elevated low-density lipoprotein (LDL) cholesterol has been clearly demonstrated to be independently associated with increased CHD risk.<sup>2-3</sup> The latest guideline from the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) continues to identify LDL-C as the primary target for cholesterol-lowering therapy.<sup>3</sup> In the fall of 2007, the Louis Stokes Cleveland VA Medical Center (LSCVAMC), Wade Park Division, implemented a Lipid Shared Medical Appointment (Lipid SMA) clinic. The Lipid SMA targets patients with elevated LDL-C which has not responded to usual care provided by their primary care provider.

**Objective:** To assess if there is a significant difference in the proportion of patients who achieve their LDL-C goal in the pharmacist-coordinated Lipid SMA compared to Usual Care provided by other health care practitioners in the same setting.

**Methodology:** Retrospective chart review of patients 18-89 years of age with LDL-C goal <100 mg/dL determined according to NCEP ATP III guideline who received lipid management in the pharmacist-coordinated Lipid SMA or by a primary care provider other than a clinical pharmacist between January 1, 2008 and April 1, 2009. The primary outcome was the proportion of patients who attained LDL-C goal in the Lipid SMA group compared with the Usual Care group. The study required a minimum of 73 subjects in each group to have the power to detect a 20% difference in the primary outcome. Set at a target of 80 patients in each group, charts were randomly reviewed and 78 patients were deemed appropriate for the Lipid SMA group and 80 patients for the Usual Care group according to defined inclusion and exclusion criteria. All comparisons of categorical data was performed using chi-square or Fishers's exact test when appropriate. For comparison of all continuous variables, the student's t-test was used. The study was IRB approved.

**Results:** Mean  $\pm$  SD LDL-C levels at baseline were  $133.5 \pm 28.7$  and  $126.1 \pm 24.8$  mg/dL ( $p = \text{NS}$ ) for the Lipid SMA and Usual Care groups, respectively. On the most current follow-up lipid panel, patients in the Lipid SMA and Usual Care groups had a LDL-C of  $90.8 \pm 26.1$  and  $108.6 \pm 29.8$  mg/dL respectively ( $p < 0.001$ ). In addition, 63 (81%) patients achieved LDL-C goal versus 35 (44%) in the Usual Care group ( $p < 0.001$ ). For patients achieving LDL-C goal in the Lipid SMA and Usual Care groups, mean LDL-C levels were reduced by 50 mg/dL (35%) and 38 mg/dL (29%) respectively ( $p = \text{NS}$ ). Mean time to reach LDL-C goal in weeks was  $14.7 \pm 10.2$  for the Lipid SMA versus  $29.5 \pm 14.4$  for Usual Care ( $p < 0.001$ ).

**Conclusions:** Dyslipidemia management in the pharmacist-coordinated Lipid SMA resulted in significantly more patients achieving their LDL-C goal compared to Usual Care. Patients in the Lipid SMA achieved their LDL-C goal in a significantly shorter time compared to Usual Care. Favorable outcomes obtained by the Lipid SMA are likely due to aggressive treatment and follow-up, focus on a specific disease state, and incorporation of diet/lifestyle modification education by a registered dietician. Furthermore, this study provides evidence to support the multidisciplinary team approach in the SMA model as an effective method to optimize management of patients with dyslipidemia.

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## Implementation of an Antimicrobial Stewardship Program

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**Background:** Inappropriate antimicrobial use is prevalent, leading to unnecessary costs, resistance development and patient exposure to medication. Studies also correlated an increase in resistance with the increase in antibiotic usage. Two factors shown to improve outcomes, and decrease resistance, secondary infections, and healthcare costs are appropriate antimicrobial use and infection control measures. Antimicrobial stewardship guidelines established by the Infectious Diseases Society of America (IDSA) and the Society for Healthcare Epidemiology of America (SHEA) aim to improve appropriate use by facilitating selection, dosing, route and duration of therapy in order to improve clinical outcomes and decrease unwanted effects of antimicrobial use.

**Objective:** To measure the effectiveness of the quality improvement initiative regarding antimicrobial appropriateness by comparing data before and after implementing an antimicrobial stewardship program.

**Methods:** Patients at Mercy St. Charles Hospital receiving cefepime, daptomycin, imipenem/cilastatin, or piperacillin/tazobactam admitted between October 1 and December 31, 2008 were included in the retrospective review before program implementation and those admitted between October 1 and December 31, 2009 were included in the prospective review during program implementation. The first two months of the program was implemented solely by the pharmacy resident and the third month was implemented by the rotating staff pharmacists. The program consists of daily patient monitoring with recommendations made to physicians regarding intravenous (IV) to oral (PO) changes, dose adjustments, and de-escalation or cessation of therapy as appropriate. The results are then reviewed and compared for appropriateness based on: appropriate empiric therapy, appropriate dose, antibiotics discontinued after three days of a negative work-up, antibiotics de-escalated within 24 hours of culture results and antibiotics converted from IV to PO when applicable. Costs of target antimicrobials, total antimicrobials and excess costs will also be examined.

**Results:** There were 169 patients in the retrospective review, 166 patients in the prospective review, and 110 patients in the first 2 months of the prospective review. Empiric therapy was appropriate in 83% of patients before, 91% of patients after and 93% of patients the first 2 months after program implementation. Dosing appropriateness was 80% before and after at but increased to 84% with the resident only. De-escalation within 24 hours was 72% appropriate before, 78% after and 89% during the resident review. Discontinuation within 3 days was 54% appropriate before, 73% after and 100% the first 2 months after program implementation. IV to PO was similarly appropriate before and after and increased by 5% during the resident review. Average total antimicrobial cost/patient was \$204.86 before, \$200.13 after and \$226.02 with the resident only. Average target antimicrobial cost/patient was \$161.84 before, \$171.39 after and \$195.70 during resident review. Total target antimicrobial cost was \$27,351.47 before, \$28,405.68 after and \$21,526.63 with resident monitoring.

**Conclusions:** Overall, there was high baseline appropriateness for empiric therapy, dosing, and IV to PO. Improvement was seen in de-escalation and discontinuation of therapy post program implementation. Greater improvement during the first two months suggests a designated pharmacist may have more consistent results. Total costs did not decrease but may be attributed to low cost of target antibiotics.

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# Characterization and Outcomes of Treatment with Transarterial Chemoembolization (TACE) for Hepatocellular Carcinoma (HCC) in Adults

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Background: Hepatocellular carcinoma (HCC) is a serious disease with an increasing incidence worldwide.<sup>1</sup> Approximately 75% of patients with HCC are not eligible for curative therapies such as resection or liver transplantation.<sup>2</sup> An option available to those who are not eligible for curative therapies is transarterial chemoembolization (TACE), which has been shown to have survival benefits over conservative treatment.<sup>3</sup> However, TACE treatment is not standardized and institutions have various protocols for administering TACE, use differing chemotherapeutic agents, and timing of re-treatment is not formalized.

Objective: To characterize both the patients as well as their outcomes to treatment with TACE for HCC at MetroHealth Medical Center (MHMC) and compare these outcomes with those reported in the literature.

Methodology: A retrospective chart review was conducted on patients who received at least one TACE treatment from 2000-2009 at MHMC. All adult patients (18-90+) identified through pharmacy records were included. Data was collected from MHMC's electronic medical record system, EPIC. Extensive demographic information and laboratory data was collected. All HCC treatments and treatment related details were collected. Tumor stage by AJCC criteria, performance status and patient outcomes were also assessed. Study data was analyzed through the use of descriptive statistics. Outcomes were compared to those reported in the literature.

Results and conclusions: Between May 2004 and October 2009, 15 patients were identified and 25 TACE treatments were performed. A majority of the patients were African-American men with a history of alcohol abuse, cirrhosis and Hepatitis C. Most patients were AJCC stage III, Child-Pugh score A with a good performance status. Within the study period, 27% (4/15) of patients died with 3 deaths due to progression of HCC and 1 due to multi-organ failure. Multiple TACE treatments were performed in 47% of patients but there was no association between AJCC stage and the number of treatments performed. Cisplatin was used in 96% (24/25) of TACE treatments. Overall, there was a 67% one-year post-treatment survival and a 50% 2-year post-treatment survival rate. Patients receiving a single TACE treatment had 1 and 2-year post-treatment survival rates of 50% while patients receiving  $\geq 2$  TACE treatments had 1 and 2 year post-treatment survival rates of 100% and 67%, respectively. Lo, et al.<sup>4</sup> and Llovet, et al.<sup>3</sup> conducted studies in patients with similar or more favorable baseline characteristics but unlike our study, re-treated all patients at regularly scheduled intervals unless specifically contraindicated. The 1 and 2 year post-treatment survival rates for Lo, et al. and Llovet, et al. were 57% and 31%, and 82% and 63%, respectively. Taking into consideration our results as well as outcomes reported in the literature, no recommendation can be currently made regarding a change in the TACE procedure at MHMC but some thought should be given to re-treating patients at regularly scheduled intervals as this may have some survival benefit.

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## Dexmedetomidine for procedural sedation during dressing changes for burn patients

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### **Background:**

Burn victims must undergo painful dressing changes and wound debridement frequently. These dressing changes can be traumatic and, to tolerate them, patients may require procedural sedation and analgesia. Traditionally, procedural sedation is done with agents such as propofol or midazolam, both of which can cause respiratory depression and neither provides any analgesia. Dexmedetomidine is a novel agent that produces sedation and some analgesia without causing respiratory depression. Because of these unique features, dexmedetomidine may be an ideal agent for use during dressing changes in patients with burns.

### **Objective:**

The primary objective was to evaluate the efficacy and safety of dexmedetomidine for use as a sedative agent for use during burn dressing changes.

### **Methodology:**

An IRB approved, prospective evaluation of the safety and efficacy of dexmedetomidine in adult (>18 years) burn patients requiring procedural sedation for dressing changes was conducted from November 2009-April 2010. Burn unit patients were screened daily to determine eligibility for the study. Patients were excluded if they were intubated, hypotensive, or bradycardic at baseline. Dexmedetomidine was given as a 1 mcg/kg bolus over 10 minutes; followed by a continuous infusion starting at 0.5 mcg/kg/hr. The infusion could be titrated every 5 minutes by 0.2mcg/kg/hr as needed. Concomitant analgesia was administered to all patients. All medication given to the patient during the dressing change was noted. Vitals were monitored every 5 minutes for safety. Nurses and physicians subjectively evaluated their satisfaction with the quality of sedation dexmedetomidine provided for the patient.

### **Results and Conclusions:**

Over the course of the study period, 33 patients were screened for entrance into the study. Thirty-two patients were excluded for various reasons. One patient received dexmedetomidine according to the burn unit protocol for sedation during a dressing change. The dressing change was completed, the patient was adequately sedated, and his vital signs remained stable throughout the procedure. Based on this patient, dexmedetomidine may be an appropriate a good alternative for sedation during burn dressing changes. The study is currently ongoing.

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## Assessment of Nutrition Support in Acute Pancreatitis

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**Background:** Acute pancreatitis accounts for approximately 210,000 hospital admissions annually in the United States. Pancreatitis associated with organ failure and/or local complications such as necrosis, abscess or pseudocyst is considered severe and is associated with longer hospitalizations, more frequent critical care area stays and mortality rates of 10-25%. Nutrition support should be initiated when it becomes evident that the patient will not be able to consume adequate nourishment by mouth for several weeks. Practice Guidelines in Acute Pancreatitis (PGAP), endorsed by the American College of Gastroenterology, recommend the use of enteral feeding as the preferred initial nutrition support attempt because it is associated with fewer complications when compared to parenteral nutrition. For patients unable to tolerate enteral nutrition or who have a contraindication to enteral nutrition, parenteral nutrition is recommended.

**Objective:** To determine the proportion of patients who received initial nutrition support in accordance with PGAP who are placed on nutrition support at AGMC.

**Methodology:** IRB approved observational, retrospective cohort study was performed to evaluate initial nutrition support in acute pancreatitis. Patients were included if they were admitted to AGMC between January 1st 2006 and December 31st 2009,  $\geq 18$  years of age at the time of admission, had a discharge diagnosis of acute pancreatitis, and were placed on nutrition support. Patients admitted on parenteral or enteral nutrition will be excluded. Data to be collected include type of nutrition received, patient demographics, cause of pancreatitis, readmission, contraindications to enteral nutrition and the prescribing physician service. The primary outcome was the proportion of patients who received initial nutrition support in accordance with PGAP. Secondary outcomes included the assessment of the rate of subsequent hospital visits within seven days secondary to acute pancreatitis and to identify physician service initiating nutrition support.

**Results and conclusions:** This study evaluated 1452 patient charts with 166 patients meeting inclusion criteria. The majority of patients included in this study were caucasian men (73, 57%) with an average age of  $55 \pm 16$  years. Seventy-eight patients (47%) had nutrition support initiated in accordance with PGAP. A total of 116 patients did not have a documented contraindication to enteral nutrition, and of these, 76% of patients were placed in parenteral nutrition which was not in accordance with PGAP. In regards to ordering service, surgery had the highest percentage of patients (63%) whose initial nutrition support choice was in accordance with PGAP ( $p=0.010$ ). The medicine service had the lowest percentage of patients (33%) whose initial nutrition support choice was in accordance with PGAP ( $p=0.040$ ). Eighteen patients were found to have a documented subsequent hospital visit; 61% of these patients' initial choice of nutrition support was in accordance with PGAP ( $p=0.204$ ). No statistical association between PGAP compliance and ordering service, except the medicine service, or subsequent hospital visit was found in this study.

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## Evaluation of an Intensive Insulin Use Protocol in the ICU

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**Background:** The benefit of intensive insulin therapy in the intensive care unit (ICU) setting has been called into question by recently published studies, including VISEP<sup>1</sup> and NICE-SUGAR.<sup>2</sup> In contrast to previous studies demonstrating mortality benefit with intensive insulin therapy<sup>3</sup>, NICE-SUGAR found increased mortality among adults in the ICU setting with intensive glucose control.<sup>2</sup> The insulin infusion protocol used at our institution in all ICUs has recently been changed to reflect this new data, with less stringent targets (110 to 150 mg/dl) for blood glucose. In this study, we will assess efficacy of the revised insulin protocol in achieving glucose targets, quantify rates of hypoglycemia and assess healthcare provider adherence to the protocol.

**Objectives:** 1) Evaluate the efficacy and safety of the revised insulin protocol in the ICUs at our institution. 2) Assess healthcare provider adherence to the updated insulin protocol.

**Methodology:** This concurrent non-interventional chart review will include 110 consecutive patients in the medical, surgical, cardiothoracic, cardiac and neurologic ICUs receiving an insulin infusion for at least 48 hours. Inclusion criteria were patients age 18 years or older admitted to an ICU after December 1, 2009 and started on an intensive insulin protocol while in the ICU. Patients with diabetic ketoacidosis were excluded. Subjects receiving insulin infusions were identified via a report generated from the EPIC<sup>®</sup> integrated medical record. Data collected for each subject included baseline demographic information (age, gender, weight, diagnosis, history of diabetes mellitus, nutrition status and concurrent steroid use), insulin infusion rates, rate adjustments and blood glucose measurements. Outcome measures for efficacy included insulin dose, mean daily blood glucose, time to target glucose and percentage of glucose readings at target. Safety outcome measures included incidence of hypoglycemia and treatments administered for hypoglycemia. Rates of insulin protocol adherence were determined, with adherence defined as fewer than five incorrect incidents within a 48 hour time period. Data was analyzed using descriptive statistics.

**Results and Conclusions:** To date, 83 patients have been enrolled in the study. Mean blood glucose for all ICUs was 149 ± 17 mg/dl. Median time to goal blood glucose was 7 h (range 0-31h). Blood glucoses remained in the target range 47% ±16% after the goal BG was reached, with a median duration of infusion of 4.7 days (range 2-23.6 days). Hypoglycemia defined as BG<70 mg/dl occurred in 12% of subjects, with the majority (10 of 12 episodes) occurring after one or more episodes of non-adherence in the preceding 6 hours. No episodes of severe hypoglycemia (BG< 40 mg/dl) occurred in the sample. Improvements are needed with respect to protocol adherence. Most non-adherence events were related to inappropriate dose changes. The current ICU protocol in place at the Cleveland Clinic is effective in achieving the targeted BG range without episodes of severe hypoglycemia. Further education to promote adherence to the protocol is warranted.

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# Evaluation of the efficacy and safety of palifermin to reduce mucositis in allogeneic stem cell transplant patients

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**Background**<sup>1-3</sup>: Patients undergoing stem cell transplantation (SCT) for treatment of hematologic malignancies commonly experience severe oral mucositis as a result of chemotherapy and/or radiation. Palifermin, a human recombinant keratinocyte growth factor, is FDA-approved for the prevention of oral mucositis in patients undergoing SCT with myeloablative chemotherapy. Recently, the Cleveland Clinic incorporated palifermin into several allogeneic SCT regimens due to increased methotrexate (MTX) doses. Data are limited regarding the efficacy of palifermin in allogeneic SCT patients and the cost associated with palifermin is significant. In light of the recent integration of palifermin into several regimens, validation of efficacy and safety is warranted.

**Objective:** To compare the incidence of severe mucositis in allogeneic SCT patients receiving palifermin versus standard care.

**Methodology:** This was an IRB-approved retrospective, non-interventional chart review that included patients  $\geq 18$  years of age that received an allogeneic SCT with a treatment regimen containing chemotherapy and myeloablative total body irradiation and/or MTX. Patients were excluded if previously enrolled in trials utilizing keratinocyte growth factors. The primary endpoint was the incidence of World Health Organization Grades 3 or 4 mucositis. Secondary endpoints evaluated included: utilization of intravenous/transdermal narcotic analgesia and total parenteral nutrition (TPN) and the incidence of bacteremia and time to neutrophil count recovery. Adverse events related to palifermin use were evaluated. Descriptive statistics, T-tests, and Fisher's exact tests were utilized to evaluate primary and secondary objectives.

**Results and conclusions:** In the nine palifermin and 63 control patients, no difference was found for the primary outcome of the incidence of WHO Grades 3 or 4 mucositis (56 vs. 51 percent,  $P = \text{NS}$ ), respectively. For the secondary endpoints, there was no difference in the incidence of narcotic usage (89 vs. 83 percent,  $P = \text{NS}$ ) or amount of morphine equivalents utilized (median [range], 631 [38 - 1676] vs. 257 [1 - 8520] mg,  $P = \text{NS}$ ) between the palifermin and control groups, respectively. No difference was noted in the incidence and duration of TPN usage (33 vs. 32 percent,  $P = \text{NS}$ ; median [range], 6 [5 - 19] vs. 8 [4 - 19] days,  $P = \text{NS}$ ) or incidence of bacteremia (33 vs. 40 percent,  $P = \text{NS}$ ) between the palifermin and control groups, respectively. The time to neutrophil count recovery in palifermin or control patients did not differ between groups (median [range], 15 [12 - 42] and 15 [8 - 43] days,  $P = \text{NS}$ ), respectively. Significantly higher incidences of rash (78 vs. 38 percent,  $P = 0.034$ ) and mouth changes (22 vs. 0 percent,  $P = 0.014$ ) were found in the palifermin patients versus control patients, respectively. Overall, palifermin did not impact the incidence of mucositis in allogeneic SCT patients nor did it influence narcotic and TPN requirements, time to neutrophil recovery, or the incidence of bacteremia.

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## Evaluation of Osteoporosis Treatment After Hip Fracture

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Background: Patients with hip fractures are estimated to have a 10% to 20% increased risk of mortality within one year, and a 2 to 6 fold increased risk of future fractures.<sup>1-4</sup> Due to the increased risk of recurrent fractures and subsequent complications, current guidelines recommend osteoporosis treatment in those with a prior low impact hip fracture.<sup>2,5</sup> However, recent data indicate that patients with low impact hip fractures do not receive appropriate osteoporosis therapy upon hospital discharge.<sup>3,5-6</sup> The purpose of this study is to determine the prevalence of osteoporosis treatment at discharge among patients admitted to Akron General Medical Center (AGMC) for low impact hip fracture.

Objective: To determine the proportion of patients discharged with osteoporosis treatment of those admitted to Akron General Medical Center for low impact hip fracture.

Methodology: This study is a descriptive, retrospective chart review of patients with low impact hip fractures admitted to AGMC between January 1, 2005 and December 31, 2008. Participants with low impact hip fracture were identified via ICD – 9 codes through electronic billing records. Patients eligible for inclusion were those 18-49 years of age on oral corticosteroid therapy or any patient greater than 49 years of age. Patients were excluded if they had a hip fracture secondary to trauma, a pathological hip fracture, or comfort care status. Data collection included demographic information, home osteoporosis medications, prior fracture, oral corticosteroid use, diagnosis of osteoporosis upon admission or at discharge, prescribed osteoporosis treatment at discharge, and osteoporosis treatment at any readmission one year following the initial fracture. The data was analyzed via descriptive statistics to determine the proportion of patients admitted with low impact hip fracture were prescribed osteoporosis medications upon discharge. Also, descriptive statistics were used to evaluate the secondary outcomes, while Chi square testing was used to determine if there were any existing trends between years evaluated.

Results and Conclusions: Of the 580 patients identified, 440 patients were included in this study. All patients were 50 years of age or older with a mean age of 80.3 years. Of those included, 74.3% were female and the rate of previous fracture was 15.2%. Upon discharge, only 95 patients (21.6%) were prescribed any osteoporosis medication and of these patients only 17 (5%) were newly started on therapy. Patients diagnosed with osteoporosis were more likely to be discharged from the hospital with osteoporosis medications compared to those that did not have a diagnosis (53.6% vs. 14%). Although the majority of patients were discharged by the Orthopedic service, the General Medicine service had a greater rate of prescribing osteoporosis medications at discharge (19.7% vs. 32.3%). The prevalence of prescribing osteoporosis medications between the years evaluated varied greatly; a significant difference between years was noted, however where the difference occurred is unknown ( $p = 0.002$ ). There were 219 patients readmitted to AGMC for any reason of the 440 included in the study. Overall, only 37% of the patients were readmitted with osteoporosis medications. Despite recently released guidelines, this study demonstrates that osteoporosis treatment is not prescribed consistently after low impact hip fracture at AGMC.

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## Evaluation of a pharmacist-managed epoetin alfa clinic in outpatients with non-dialysis dependent chronic kidney disease

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**Background:** Erythropoiesis stimulating agents (ESAs) are indicated in the treatment of anemia secondary to chronic kidney disease (CKD) to increase hemoglobin in order to positively impact a patient's quality of life.<sup>1,2</sup> Few published studies have evaluated the role of clinical pharmacists in managing epoetin alfa in outpatients with non-dialysis dependent chronic kidney disease.<sup>3,4</sup> Kaiser Permanente of the Ohio Region implemented a pharmacist-managed epoetin alfa clinic in May 2008 to improve appropriate use of epoetin alfa.

**Objective:** To assess the safe and effective use of epoetin alfa in a pharmacist-managed ESA clinic by evaluating adherence to NKF-KDOQI guidelines and the epoetin alfa package insert, and to determine those factors of the clinic that are correlated with patient satisfaction.

**Methodology:** The study included both a retrospective chart review and a patient satisfaction survey. The chart review included 162 patients on epoetin alfa for at least one year, with a diagnosis of anemia secondary to CKD, and not requiring dialysis. The collected data included: demographics (age, gender, race, history of diabetes mellitus or hypertension, and stage of CKD); frequency of hemoglobin, transferrin saturation, and ferritin testing within a 12 month period; the percentage of time these values were in therapeutic range; administration of IV iron; and the amount of epoetin alfa doses held. For the patient satisfaction surveys, 247 surveys were mailed to patients currently enrolled in the clinic. The survey evaluated knowledge about disease state and satisfaction with staff interaction. Data for the study was analyzed using descriptive statistics, z-test, and regression analysis.

**Results and conclusions:** There was a statistically significant improvement in adherence to laboratory monitoring in the pharmacist-managed group as compared to usual care. There was also a statistically significant difference in time hemoglobin and transferrin saturation spent in range, but no statistically significant difference with ferritin.

Additionally, IV iron was more likely to be administered in the pharmacist-managed group than usual care. During the first 19 months of the clinic, 1,188 doses of epoetin alfa were held group due to hemoglobin approaching or exceeding > 12 g/dL. Overall, currently enrolled patients responded that they are satisfied with the pharmacist-managed clinic.

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## Vincristine dose modification during concomitant use of fluconazole in pediatric cancer patients

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### Background: <sup>1-3</sup>

Vincristine is an antineoplastic, vinca alkaloid that is a common agent used in the treatment of pediatric acute lymphoblastic leukemia (ALL). Vincristine causes cell death by inhibiting microtubule formation in the mitotic spindle, which is also responsible for the neurologic toxicities seen in patients (due to the structural changes in the axon of nerve cells). Vincristine is hepatically metabolized and is a major substrate of the CYP3A4 enzyme system. Theazole antifungals are known inhibitors of the CYP3A4 enzyme, which could lead to increased levels of vincristine and possibly, profound toxicity for the patient. Published case reports have described neurologic toxicities associated with concomitant administration of itraconazole (for fungal prophylaxis) and vincristine in pediatric cancer patients. However, the use of fluconazole and its potential drug interaction with vincristine has not been studied or reported in the literature.

### Primary Objective:

The primary study objective is to determine the frequency of vincristine dose modifications due to increased toxicity experienced by pediatric patients who received concomitant administration of fluconazole for fungal prophylaxis compared to a historical control group.

### Methodology:

The study was a non-interventional, retrospective chart review utilizing the electronic medical record. Patients were included if they met the following criteria: diagnosis of ALL between the ages of  $1 \leq 18$ , and receiving vincristine based chemotherapy. Patients were excluded if they received a differentazole for the treatment or prophylaxis of fungal infections or if they received a potent inhibitor or inducer of CYP3A4. The following data were collected from the patient's medical record: age, gender, height, weight, disease risk stratification, chemotherapy and antifungal prophylaxis doses/frequencies/dates/dose adjustments, CYP3A4 interacting drugs, autonomic and peripheral neurotoxicities, and sodium and bilirubin levels. Study data were entered into Microsoft Access and analyzed between the treatment and historical control groups.

### Results:

A total of 36 patients were evaluated for the study. There was no increase in vincristine dose modifications secondary to neurotoxicity in patients receiving fluconazole compared to the historical control group (0% vs 4.5%;  $p = \text{NS}$ ). Patients in the control group were more likely to experience an early vincristine induced neurotoxicity compared to the patients receiving fluconazole (77% vs 36%;  $p = 0.01$ ), but there was no difference in the number of patients who experienced delayed neurotoxicity (45% vs 14%;  $p = 0.07$ ). The most commonly reported early neurotoxicities were constipation and abdominal pain while the most frequent delayed toxicity was motor/sensory neuropathy.

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# Impact of a Clinical Pharmacist on Glycemic Control in the Intensive Care Unit

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Background: Clinical pharmacists are valuable members of the multidisciplinary team in intensive care units (ICU), as evidenced by the scientific literature.<sup>1,2</sup> The impact of clinical pharmacists on glycemic control in the ICU, however, has not previously been investigated. Hyperglycemia is associated with increased morbidity and mortality, increased risk of infection, and decreased healing capacity.<sup>3-5</sup> This study will determine if addition of a clinical pharmacist to the ICU multidisciplinary team will improve glycemic control.

Objective: To determine the impact of a clinical pharmacist on glycemic control in the intensive care unit.

Methodology: The primary outcome of this retrospective chart review was the percent of patients with  $\geq 80\%$  blood glucose results  $\geq 140$  mg/dL during a 24-hour period. Patients  $\leq 18$  years old or admitted for diabetic ketoacidosis were excluded. Secondary outcomes included type of hyperglycemia treatment and rate of hypoglycemia (glucose  $\leq 60$  mg/dL). Using a power of 80% and alpha of 0.05, 136 patients per group were required. Blood glucose results for patients admitted to the ICU from January 1 – March 31, 2009, were collected to establish baseline. A clinical pharmacist participated in ICU multidisciplinary rounds Monday through Friday, September 1 – November 30, 2009. Follow-up glucose results were collected. Results were analyzed with the Chi square test.

Results and Conclusions: At baseline, 42% (57/136) of patients had at least one 24-hour period of hyperglycemia. Twenty-five patients (25/57; 44%) received only sliding scale insulin therapy as hyperglycemia treatment. Hypoglycemia occurred in 13 patients (10%). With a pharmacist, 37.5% (51/136) had at least one 24-hour period of hyperglycemia ( $p$ -value=0.46). Twelve patients (12/51; 24%) received only sliding scale insulin therapy as hyperglycemia treatment ( $p$ -value=0.026). Hypoglycemia occurred in 12 patients (9%;  $p$ -value=0.83). The overall rate of hyperglycemia was decreased with a pharmacist in the ICU, but the result was statistically insignificant. The number of patients receiving sliding scale insulin alone was significantly reduced in the pharmacist group without a concomitant increase in hypoglycemia. Evaluating the dose and titration of basal insulin in the ICU is a potential clinical pharmacist opportunity.

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# Evaluation of the Frequency, Acknowledgement and Appropriate Documentation of Critical Drug Interactions

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**Background:** Computerized physician order entry (CPOE) is an efficient system for decreasing injury from critical drug interactions (CDIs). CPOE can reduce CDIs when clinical decision support features such as drug-drug interaction (DDI) alerts are activated in the system. At the Louis Stokes Cleveland Veterans Affairs Medical Center (LSCVAMC) there are both significant and critical DDI alerts in the CPOE patient record system. Significant drug interactions do not require a provider comment, but CDIs do require both the provider and the pharmacist to place a comment that specifies the action taken. If the provider does not have a satisfactory comment, it is up to the pharmacist to contact the provider to ensure that he/she is aware of the of the interaction and has weighed the risks and benefits of ordering the interacting drug pair for the patient.

In January 2009, the pharmacy staff reviewed CDIs and determined twenty-five CDIs to educate pharmacy staff on and added recommendations in the CPOE system for the provider. The goal of this additional safety check was to have the provider realize the interaction and adjust the drug choice prior to the order being reviewed by the pharmacist. A note template was added to the computerized chart (May 2009) to allow pharmacists the ability to better communicate with provider when entering CDIs.

**Objective:** To determine the frequency, acknowledgement, and appropriate documentation of specific critical drug interactions in both the inpatient and outpatient settings at LSCVAMC.

**Methodology:** Retrospective chart review of patients currently prescribed one of the following critically interacting drug pairs: nitroglycerin/varidenafil, dofetilide/moxifloxacin, methotrexate/ trimethoprim, dofetilide/hydrochlorothiazide, clarithromycin/simvastatin, erythromycin/simvastatin, cyclosporine/simvastatin, hydrochlorothiazide/lithium, allopurinol/mercaptapurine, allopurinol/azathioprine, and amiodarone/digoxin. The comparison will occur before the recommendations were added to the CPOE system (May 1<sup>st</sup>- October 31<sup>st</sup>, 2008) and after (May 1<sup>st</sup>-October 1<sup>st</sup>, 2009). The following data will be collected: age, gender, action taken by physician and pharmacist, and appropriateness of the action. Chart review data will be analyzed in a Microsoft Excel. This study was approved by the IRB committee.

**Results and Conclusions:** Currently completing data collection. Preliminary data has been collected and analyzed on 64/200 uniques. The unique CDI that has been reviewed is nitroglycerin/varidenafil. The majority of the interactions in both groups had non-specific override descriptions that were not actionable (reviewed, noted, ok). After the pharmacist education and addition of the template into the computer system there was an improvement in the documentation of CDIs in the patient's medical record. Final results to follow.

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# Stability of clozapine in oral suspension: a comparison of high performance liquid chromatography (HPLC) and mass spectrometry assays from day zero through day sixty

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**Background:** Clozapine related side effects may be dose-related, thus it is very important for patients to receive a consistent amount of medication from day to day. More research is needed to determine whether clozapine concentrations remain consistent in compounded suspensions.

For patients who cannot or will not take medications in tablet form, a liquid formulation of clozapine may be utilized; however, no commercial oral liquid or suspension exists. When a liquid formulation is utilized, clozapine suspension is compounded in the pharmacy. Very limited data is available investigating the stability of clozapine in suspension. No studies have been conducted to date using High Performance Liquid Chromatography system with Mass detector (LC – MS<sup>2</sup>) to investigate the stability of such a compounded suspension.

Depending on a patient's monitoring interval refills of clozapine suspension occur once a week or every two weeks. The limited amount of data describing the stability of clozapine suspensions makes it difficult to know if patients are receiving consistent amounts of clozapine throughout each refill. Furthermore, this compounded suspension may not remain in a controlled, refrigerated environment once it leaves the pharmacy. Given that side effects of clozapine may be dose-related, it is very important for patients to be receiving a consistent amount of medication from day to day. More research is needed to determine whether clozapine concentrations remain consistent in compounded suspensions.

**Objective:** This study seeks to determine the stability of clozapine suspension using a standard recipe by assessing the purity of clozapine in suspension at days 0, 3, 7, 14, 30, and 60 using a High Performance Liquid Chromatography system with Diode array detector (HPLC/DAD) and LC – MS<sup>2</sup>.

**Methodology:** The pharmacy resident will compound a 10mg/mL clozapine suspension using 100mg uncoated tablets of clozapine. This suspension will be dispensed into six separate 30mL aliquots (three to be stored at room temperature and three to be stored under refrigeration). The standard Louis Stokes Cleveland Veterans Affairs Medical Center (LSCVAMC) recipe will be used to compound the clozapine suspension.

A purity analysis will be conducted by the pharmacy resident on days 0, 3, 7, 14, 30, and 60 on all six aliquots utilizing an HPLC/DAD. This analysis will help to determine whether there are any minor or major breakdown products.

If any degradation products are found using the HPLC/DAD a secondary stability study will be conducted to validate the HPLC/DAD results utilizing an LC – MS<sup>2</sup>. The samples for the LC – MS<sup>2</sup> study will be batched from the proper interval time and stored at -80° C to be analyzed at the end of the study.

The null hypothesis is that the purity of the clozapine suspension at day sixty will be equal to the purity of the suspension at day zero.

**Results and conclusions:** The clozapine:protriptyline ratio decreased from day 0 to day 30, but this difference was not statistically significant. Additionally, no new peaks appeared on day 30's chromatograms. Therefore, clozapine appears stable in suspension for 30 days.

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# Tigecycline utilization for resistant infections in a community teaching hospital

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**Background:** Tigecycline is a glycolcycline intravenous antibiotic indicated for the treatment of complicated skin and skin structure infections caused by susceptible organisms including Methicillin-resistant *S. aureus* (MRSA) and vancomycin-sensitive *E. faecalis*. Tigecycline is also indicated for complicated intra-abdominal infections and community-acquired pneumonia. In addition, tigecycline has been shown to be effective for off-label use in the treatment of other MDR infections, including those caused by *A. baumannii*, *Klebsiella sp.*, *E. coli*, *E. faecium*, and *C. difficile*. Tigecycline is one of a limited number of drugs available on the market to treat MDR infections. Therefore, preventing microbial resistance to tigecycline by restricting its use is critical.

**Objective:** The purpose of this study is to evaluate tigecycline prescribing patterns at South Pointe Hospital, and to potentially improve tigecycline utilization.

**Methodology:** Approval from the Institutional Review Board was obtained prior to study commencement. Orders written for tigecycline over one year revealed 424 total patient records; 46 were randomly selected for retrospective chart review. Data points collected for each record included: patient allergies, dates of tigecycline treatment, dates of other antimicrobial therapies, organisms cultured during admission, sites of infection, and history of resistant infections over the previous two years. These data points were then used to characterize tigecycline prescribing patterns at South Pointe hospital.

**Results and conclusions:** Of the 46 patient records where a course of tigecycline was prescribed, 16 had received tigecycline previously, and 30 had positive cultures for at least one MDR organism. Tigecycline prescribed without the presence of current resistant infections accounted for 16 cases (35%); however 9 of these had documented MDR infection(s) within the past two years. Tigecycline prescribed without the presence of current resistant infections accounted for 16 cases. However 9 of these had documented MDR infection(s) within the past two years. History of MDR organisms existed in cultures of 33 of the 46 patient records (71%). Of note, 7 records (15%) lacked a current resistant infection, or an MDR infection in the past two years.

Of the 46 patient records evaluated, 16 (34%) did not have a current MDR infection, and almost half of these had no previous history of MDR infection. This data suggests tigecycline was used empirically, for non-resistant infections, or as a last-resort treatment when other therapies failed.

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## Evaluation of an Electronic Reminder to Adjust Insulin Regimens in NPO Diabetic Inpatients

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**Background:** Recent retrospective studies have found that hypoglycemia in hospitalized diabetic patients is a common problem and may be associated with increased length of stay and higher mortality rates.<sup>1-2</sup> Inpatient diabetics on insulin are at an increased risk of hypoglycemia when they become NPO (nothing by mouth). An electronic reminder was added to the NPO diet order set at the Louis Stokes VA Medical Center on September 11, 2009 reminding providers to reduce the basal insulin dose by 50% and discontinue active orders for prandial insulin and sulfonylureas for diabetic patients who become NPO.

**Objectives:** The primary objective of this study was to determine if implementation of an electronic reminder in the NPO diet order set improved insulin prescribing among NPO diabetic patients in a general medicine population.

**Methodology:** Retrospective chart review of 50 patients before and 50 patients after implementation of the electronic reminder (n=100). Eligible patients were diabetics 18 years of age and older who were admitted to a non-ICU ward between 4/11/09 and 2/11/10 who had an NPO diet order and concurrent basal insulin order. Patients were excluded if they were NPO less than 12 hours, if the NPO order was written less than 12 hours after admission, if they were on TPN or tube feeds while NPO or if they were previously included during the same admission. The primary outcomes were: the proportion of patients who had their basal insulin dose reduced by 25-75% when becoming NPO and the proportion of patients who had prandial insulin orders discontinued when becoming NPO. Secondary outcomes included: incidence of hypoglycemia, glycemic control and nursing practices. Chi-square and t-tests were used for categorical and continuous data, respectively.

**Results:** The sample was 96% male, average age 64 years, and had a mean length of stay of 12 days. The proportion of patients who had basal insulin dose reduced by 25-75% when becoming NPO was 22% before vs. 44% after the reminder was implemented (p=0.033). The proportion of patients who had their prandial insulin discontinued when becoming NPO was 24% in the before group vs. 9% in the after group (NS). There were twelve patients who experienced hypoglycemia in the 48 hour period before becoming NPO, but only one patient who experienced a hypoglycemic episode while NPO. Overall glycemic control did not differ between the groups before and after the reminder was implemented. Nurses held prandial insulin doses when the orders were not discontinued in the majority of patients: 53% before vs. 65% after. However, nurses also held basal insulin doses that had been appropriately reduced 15% of the time.

**Conclusions:** The electronic reminder increased the proportion of diabetic patients who had their basal insulin dose reduced when becoming NPO. It did not increase the proportion of patients who had prandial insulin orders discontinued when becoming NPO. Overall, hypoglycemia was rare. Further analysis of glycemic outcomes is currently in progress.

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## Inpatient Pharmacist Monitoring Program Optimizes Erythropoiesis-Stimulating Agent Utilization

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**Background:** FDA supports targeting lower hemoglobin (Hg) when treating anemia with erythropoietin stimulating agents (ESAs).<sup>1</sup> Several key organizations suggest targeting an upper limit Hg of 12 mg/dL in chronic kidney disease and myelodysplastic syndrome, and not initiating ESAs until Hg  $\leq$  10 mg/dL for chemotherapy induced anemia.<sup>2-4</sup> Hillcrest Hospital instituted a blood management program that allows ESA use preoperatively to increase Hg with the goal of decreasing blood transfusions postoperatively. Blood management experts recommend target Hg  $\leq$  13 mg/dL<sup>5</sup>; however, it is reasonable to consider lowering target Hg to  $\leq$  12 mg/dL in postoperative patients prescribed ESAs based on recent safety data regarding other causes of anemia.<sup>1</sup> Historical ESA data at Hillcrest suggest less than optimal use based on current safety guidelines.

**Objective:** To assess if pharmacist monitoring and intervention of ESA orders increased compliance with current safety guidelines.

**Methodology:** A prospective pilot study was conducted over three months. A pharmacist reviewed all orders prior to dispensing and data was compared to historical data of a similar time frame. A pharmacist contacted physicians to confirm necessity of ESA use in patients with Hg above defined target ranges. Orders received after 6 PM were processed the following day. All inpatient ESA orders were included while all outpatient ESA orders were excluded. Our primary outcome was rate of change in inappropriate orders. Secondary outcomes assessed change in pharmacist auto-substitution from epoetin to darbepoetin, change in dispense as written (DAW) epoetin orders, and change in overall darbepoetin use. Nominal data was analyzed with Chi-square using Sigma Stat 3.5 software. Descriptive data analysis included breakdown of orders by disease state, time of order, time spent processing order, and the number of orders evaluated per day.

**Results and conclusions:** Overall rate of inappropriate orders decreased from 5% to 1.2% (absolute reduction 3.8%, relative reduction 76%;  $p = 0.006$ ,  $\alpha = 0.05$ , power = 0.80) with pharmacist intervention. Total darbepoetin use increased from 59% to 77.6% ( $p < 0.001$ ,  $\alpha = 0.05$ , power = 0.80). Pharmacist auto-substitution increased from 41% to 63%; however this was not significant ( $p = 0.118$ ). One reason we may not have achieved significance for this objective is the significant increase in DAW orders (63% vs. 89%;  $p < 0.001$ ). Nephrology was the primary prescriber with 80% of the orders, and also wrote for all of the DAW epoetin dispensed. Approximately 5 orders were assessed per day, with 88% of the orders written before 1600. Each order required 10 minutes for initial assessment and processing, although the time requirement increased to 30 minutes if the order necessitated a phone call. This project shows the benefit of pharmacist monitoring of inpatient ESA orders to increase compliance with current safety guidelines.

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## Utilization of a reminder mailing to improve blood glucose log reporting in an outpatient diabetes clinic

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**Background:** Improving glycemic control reduces complications in diabetic patients.<sup>1</sup> Self-monitored blood glucose (SMBG) is a strategy that has been widely used to achieve glycemic control.<sup>2</sup> However, if patients are unwilling or unable to make therapy adjustments in response to SMBG readings, or if SMBG readings are unavailable to clinicians, this strategy will have a limited impact.<sup>3</sup>

**Objective:** To assess the impact of a reminder mailing on response rates to requests for SMBG logs.

**Methodology:** Adult diabetic patients were recruited from the Internal Medicine Center of Akron (IMCA) Diabetes Management Clinic at the time a request for an SMBG log was made from December 2009 through February 2010. Patients who did not have a mailing address or who were not independently managing their disease were excluded. The following data were collected: date of recruitment, patient demographics, date of first diabetes clinic visit, concomitant medical conditions, most recent hemoglobin A1c, and anti-diabetic medication list. A reminder mailing was sent one week before SMBG logs were due to be returned to the clinic. Compliance rates pre- and post-intervention were compared. The primary outcome is the proportion of all SMBG logs returned on-time. Secondary outcomes include the percentage of SMBG logs that are returned at all, the percentage fulfilled, the percentage of diabetes clinic appointments kept, predictors of patients bringing SMBG logs to follow-up appointments, and the number of interventions made to anti-diabetic therapy.

**Results and conclusions:** Twenty SMBG requests were made in the pre-intervention cohort versus 19 in the post-intervention cohort. Groups were well-matched for all baseline data. A trend towards more on-time SMBG requests was observed post- vs. pre-intervention (32% vs. 15%,  $P = 0.273$ ). Overall return rates were 40% and 36.8%, pre- and post-intervention, respectively ( $P = 0.839$ ). Fulfilled return rates were identical to on-time return rates. A non-significant increase in clinic appointments kept was observed post-intervention (63.2 vs. 45%,  $P = 0.256$ ). Receipt of a reminder mailer was not a significant predictor of patients bringing an SMBG log to their follow-up appointments (OR 0.69, 95% CI 0.14 – 3.27). A non-significant trend towards fewer interventions made was observed post- vs. pre-intervention (87.5 vs. 57.1%,  $P = 0.175$ ). In conclusion, we found that receipt of a reminder mailer did not increase overall return rates of SMBG logs, although receipt of a mailer was associated with a trend towards more on-time and fulfilled SMBG logs being returned. There was a trend towards fewer interventions made after receipt of the reminder mailer, as well as a trend towards more patients keeping their follow-up appointments when receiving a mailer. As a result of this study, it is not likely that a reminder mailer will be implemented into the standard of practice at IMCA at this time. However, it may be worth stressing the importance of SMBG log reporting to patients during their clinic visits, since the data showed no higher than a 40% overall return rate of SMBG logs regardless of whether a reminder mailer was used.

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# Evaluation of the safety of combination alteplase and intra-arterial glycoprotein IIb/IIIa inhibitor therapy for acute ischemic stroke

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Background: Stroke is the third leading cause of death and the leading cause of long term disability in the United States.<sup>1</sup> While ischemic strokes account for over 80% of all strokes, consistently safe and effective therapies for its management in a broad population have yet to be identified. The American Stroke Association guidelines for the management of ischemic stroke recommend the use of intravenous alteplase (rtPA) in appropriate candidates, with intra-arterial (IA) rtPA administration considered an option in certain patients.<sup>2</sup> Additional pharmacological therapies such as glycoprotein (GP) IIb/IIIa inhibitors for ischemic have been evaluated. Intravenous use of GP IIb/IIIa inhibitors is associated with increased bleeding risk without benefit and therefore not recommended.<sup>3</sup> However, IA administration of GP IIb/IIIa inhibitors are utilized in select patients although limited data exists regarding the safety and efficacy of this therapy in ischemic stroke.<sup>3-6</sup>

Objective: To evaluate the safety of combination alteplase and intra-arterial glycoprotein IIb/IIIa inhibitors for the treatment of ischemic stroke.

Methodology: This IRB-approved, retrospective chart review includes all adult patients treated for ischemic stroke at the Cleveland Clinic who received any combination of rtPA and IA GP IIb/IIIa inhibitor. Data collected includes patient demographics, location of the infarct, National Institute of Health Stroke Scale (at baseline, 24 hours, 48 hours, and hospital discharge), symptomatic intracranial hemorrhage (ICH) or other bleed within 48 hours of combination therapy, recanalization rates as determined by Thrombolysis in Myocardial Infarction Score, thrombolytic and antiplatelet medication, dose, and route used, anticoagulant and antiplatelet use prior to admit, and mortality at hospital discharge. Descriptive statistics were used to summarize the results of the study.

Results and conclusions: From 2008-2009, 18 patients received combination rtPA and IA GP IIb/IIIa inhibitor therapy for ischemic stroke and were included in this analysis. One symptomatic ICH and one bleeding event requiring transfusion occurred, representing bleeding rates similar to those in IV rtPA trials. Based on these findings, combination rtPA and IA GP IIb/IIIa inhibitor therapy for ischemic stroke appears to be safe. Future prospective studies are warranted prior to recommending combination therapy for ischemic stroke in defined patient populations.

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# Impact of Pharmacist-Provided Nursing Education on Medication History Accuracy

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**Background:** An accurate medication history is an integral part of patient assessment on admission to the hospital.<sup>1</sup> Errors in the medication history could potentiate errors in the medication reconciliation process. Since 2005, the accurate and complete reconciliation of medications across the continuum of care has been a National Patient Safety Goal of The Joint Commission.<sup>2</sup> Currently, the methods used by many hospitals to perform medication reconciliations have been shown to be inaccurate. Up to 45% of patients have at least one discrepancy on their medication history on admission.<sup>4</sup> Clinical skills are often necessary to obtain an accurate and complete medication history and pharmacists have demonstrated to be an ideal resource for obtaining medication histories due to their expertise and extensive training.<sup>1,3,5</sup> Despite this, many hospitals do not utilize pharmacists for this process due to financial barriers and staffing requirements. Currently at Summa Health System, nurses obtain medication histories and input the data into the electronic medical record (EMR).

**Objective:** The aim of this study is to identify the barriers of obtaining accurate medication histories and subsequently to test the efficacy of a pharmacist-driven educational program to overcome the modifiable barriers.

**Methodology:** This was a three phase, prospective observational study that included general-medical patients admitted by selected staff nurses. During the initial phase, patients were randomly selected using predefined inclusion and exclusion criteria. Once enrolled, a pharmacist-obtained a medication history from the patient and updated the EMR. This new list was compared to the list previously obtained by the selected nurse. All discrepancies were noted and all medication errors were resolved. After completing the initial phase, the types of discrepancies were tabulated. The information obtained in the initial phase was used in the interventional phase to develop a nursing education program. Once education was completed, identical methods to the initial phase were implemented during the final phase. The results from the initial phase were compared to those from the final phase to measure the effect of the education session. The primary outcome of the study was to evaluate the change in total discrepancies after nursing education was given. Secondary outcomes included evaluating the change in number of discrepancies by type of discrepancy and category of medication, noting the frequency of the types of discrepancies, and assessing whether over-the-counter (OTC) or prescription (Rx) medication discrepancies would decrease. Also correlations between number of medications and number of discrepancies and age as it relates to number of discrepancies were observed.

**Results and Conclusions:** In the initial phase, 46 patients were included with 509 medications being recorded, of which 205 discrepancies were identified between the nurse-obtained and pharmacist-obtained medication history. The most common type of discrepancy was medication omission (n=93) and the most common category of medications with discrepancies was prescription drugs (n=124). Nursing education was given including the results of the initial phase, clinical guidance on how to more accurately collect a medication history, and instruction of the use of a mnemonic to aid in patient recollection of OTC drugs. In the final phase, 44 patients were included with 505 medications being recorded, of which 150 discrepancies were identified between the nurse-obtained and pharmacist-obtained medication history. Similar to the initial phase, the most common type of discrepancy was medication omission (n=68) and the most common category of medications with discrepancies was prescription drugs (n=105). The difference in total number of errors per patient decreased by 10.6% (mean 4.46 vs. 3.41, p=0.096). Although not statistically significant, there may be some clinical significance seen in the decrease of greater than one discrepancy per patient. Depending on the type and severity, one medication error could cause harm to the patient. The type of discrepancy most often seen was medication omissions in both the initial and final phase. This confirms and is consistent with other recent studies.

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# Evaluation of Acid Suppression Medication Use at the Louis Stokes VA Medical Center

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**Background:** Acid suppression medications (ASM) are prescribed for a variety of indications, including treatment of gastrointestinal (GI) disorders and stress ulcer prophylaxis. ASM include proton pump inhibitors (PPIs) and histamine-2 receptor blockers. The inappropriate use of PPIs has been reported at rates as high as 65%.<sup>1</sup> Although generally believed to be benign, ASM increase gastric pH and are associated with side effects and drug interactions. The LSVAMC Pharmacy and Therapeutics Committee exhibited interest in a PPIs order set in the spring of 2009 following recent literature and a statement by the Food and Drug Administration (FDA) identifying awareness of a possible drug interaction between omeprazole and clopidogrel.<sup>2,3</sup> Omeprazole is the focus drug of this trial due to the heightened publicity about the drug interaction recently.

**Objective:** To compare the use of omeprazole and ASM at the LSVAMC before and after implementation of a quick order set.

**Methodology:** A retrospective chart review evaluated ASM use in all inpatients admitted to general medicine floors, the progressive care unit, and the medical and cardiac intensive care units during three phases: Phase 1 October 2008 (baseline prescribing habits), Phase 2 May 2009 (prescribing habits following FDA statement and literature release), Phase 3 February 2010 (after quick order implementation). One-hundred patients were enrolled chronologically in each phase in a percentage distribution based on past admission rates for each hospital ward. Information on patient demographics, diagnoses, ASM use, concurrent medication use, laboratory values, and comorbidities were collected using the LSVAMC electronic medical record system. The primary endpoint of the study compared the percent of inpatients on oral omeprazole between Phase 1 and Phase 3. Secondary endpoints compared the overall use of ASM, the percent of patients newly initiated on ASM during hospitalization, the indications for ASM use, the percent of patients prescribed both omeprazole and clopidogrel, and the rates of GI bleeding during hospitalization and up to 3 months post discharge between each of the three phases. A t-test evaluated continuous data and a chi-square test evaluated categorical data.

**Results and conclusions:** One-hundred patients were enrolled in each of the three phases (total 300 patients). The mean age was 63-65 years and the mean duration of hospitalization was 6 days. There were no differences in demographic characteristics of patients in the three phases. In Phase 1, 70% of patients received omeprazole compared to 48% of patients in Phase 3 ( $p=0.0016$ ). In Phase 2, 65% of patients received omeprazole compared to 48% in Phase 3 ( $p=0.015$ ). There was no statistically significant decrease in omeprazole use between Phase 1 and Phase 2. The overall use of ASM significantly decreased from Phase 1 to Phase 3 (75% vs 60%,  $p=0.024$ ) but not from Phase 2 to Phase 3 (69% vs 60%,  $p=0.18$ ). The use of ASM for prophylaxis decreased from Phase 1 to Phase 3 (53% to 38%) but the percent of patients with no indication documented increased (8% vs 30%, respectively). The percent of patients who were discharged on newly initiated omeprazole for treatment of a GI disorder increased from Phase 1 to Phase 2 and to Phase 3 (9%, 28%, 62%, respectively). The percent of patients who were discharged on newly initiated omeprazole for GI prophylaxis decreased from Phase 1 to Phase 2 and to Phase 3 (82%, 58%, 13%, respectively). The percent of patients receiving omeprazole in addition to clopidogrel decreased significantly from Phase 1 to Phase 2 (94% vs 54%,  $p=0.0001$ ). Data on GI bleeding rates between groups is pending. The overall use of omeprazole significantly decreased after implementation of a quick order set.

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## De-escalation of Antimicrobial Therapy: A Pilot Study

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**Background:** Fifty to sixty percent of all nosocomial infections in the US are caused by antibiotic-resistant bacteria.<sup>1</sup> Infections caused by antibiotic-resistant or multidrug-resistant (MDR) bacteria can lead to higher rates of mortality, longer ICU stays, longer hospital stays, and higher costs.<sup>2</sup>

De-escalation therapy is one strategy to combat resistance and consists of narrowing the antibiotic spectrum by changing from a broad spectrum agent to a narrow spectrum agent or by eliminating a drug from combination therapy as well as using the shortest adequate duration.<sup>3,4</sup> Modifications in antibacterial therapy should ideally occur as soon as possible with the availability of culture and susceptibility results.

Studies that have addressed de-escalation thus far have focused on patients with ventilator-associated pneumonia (VAP). One observational study showed that de-escalation led to improved outcomes as measured by mortality.<sup>5</sup> A prospective observational study of critically-ill, surgical and septic shock VAP patients did not find an increased rate of recurrent pneumonia in patients that received de-escalation therapy.<sup>6</sup>

**Objective:** The primary outcome was the association of de-escalation therapy on mortality at 30 days of hospital stay or discharge. Secondary outcomes were the assessment of the incidence of de-escalation, rate of appropriate initial therapy, rate of resolution of infection, days in intensive care, and the impact of an infectious disease service consult on these outcomes.

**Methodology:** This IRB approved, observational study assessed antibiotic therapy in patients with any single site infections of the blood, urinary tract, lungs, or a wound. Patients were included if they were 18-90 years old and were identified by positive microbiological results from lab reports. Patients with multiple site infections, pregnant women, or comfort care only/arrest or Hospice patients were excluded. Data collection included demographical information, history of antibiotics and location prior to admission, comorbid conditions and evaluation of clinical status, culture and susceptibility results, inpatient antibiotic therapy, and course of therapy. Statistical analysis was performed with an independent consultant with significance set at  $p < 0.05$ .

**Results and Conclusions:** The demographics of patients who did and did not receive de-escalation were not significantly different. The rates of comorbidities and sites of infection were also not significantly different between groups. The primary outcome showed that there was no significant difference ( $p = 0.77$ ) in mortality for patients that did or did not receive de-escalation therapy. For the secondary outcomes, there was an association between de-escalation and a higher rate of appropriate initial therapy ( $p = 0.0$ ) and a higher rate of resolution of infections ( $p = 0.008$ ). Patients with de-escalation also had a significantly shorter length of stay in the ICU at 7.3 days versus 12.5 days in patients who did not receive de-escalation ( $p = 0.022$ ). In a sub-analysis, there were no significant differences for patients that did or did not have an ID service consult. Several factors that were not examined, and may be pursued in further study, were the severity of infection, duration of treatment, multiple site infections, exclusion of colonization microbiological results and larger sample sizes. This study showed that it is feasible and beneficial to provide de-escalation therapy to patients in the ICU with single site infections of the blood, respiratory tract, urinary tract, and wounds.

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## Another Setting for Stewardship: High Rate of Unnecessary Antibiotic Use in a Long-Term Care Facility

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Background: Antimicrobial use is common in long-term care facilities (LTCFs). Excessive use of antimicrobials may lead to emergence of resistance and other adverse effects.

Objective: To determine the frequency of, reasons for, and adverse effects of unnecessary antimicrobial use in a Department of Veterans Affairs LTCF.

Methodology: We performed a 6-month retrospective study of randomly selected patients receiving antimicrobial therapy. Antimicrobial regimens were determined to be necessary or unnecessary based on published guidelines or standard principles of infectious diseases. If antimicrobial therapy was deemed necessary, further evaluation of all components of the regimen was conducted to assess appropriateness of duration of therapy and spectrum of antimicrobial coverage. Adverse effects were determined based on chart review.

Results and conclusions: Of 943 days of therapy prescribed in 70 regimens, 415 days (44%) were deemed unnecessary. Of the 415 unnecessary days of therapy, 207 (50%) were for antimicrobial regimens that were entirely unnecessary (N =29). Asymptomatic bacteriuria was the most common reason for wholly unnecessary regimens (N =16), resulting in 98 days of unnecessary therapy. Regimens that were partially unnecessary resulted in 208 (50%) days of unnecessary therapy, with longer than recommended treatment duration accounting for 193 (93%) unnecessary days of therapy. Within 30 days of completing the antimicrobial regimens, 3 patients (4%) developed *Clostridium difficile* infection, 4 (6%) developed colonization or infection with antimicrobial-resistant pathogens, and 10 (14%) had other adverse drug reactions. In our LTCF, nearly half of all days of antimicrobial therapy were unnecessary. Our findings suggest that antimicrobial stewardship interventions in LTCFs should focus on improving adherence to recommended treatment durations and eliminating inappropriate treatment of asymptomatic bacteriuria.

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## Efficacy and safety of continuous infusion of labetalol for lowering blood pressure in intracerebral hemorrhage

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**Background:** Intracerebral hemorrhage (ICH) is a medical emergency that involves a focal bleed resulting from a spontaneous rupture of a blood vessel. Management of ICH requires immediate and aggressive reduction in blood pressure (BP)<sup>1,2</sup>. Current American Stroke Association guidelines for BP management in ICH recommend the use of various antihypertensives including labetalol, nicardipine, and nitroprusside to achieve and maintain a goal systolic BP less than 160 mmHg. Labetalol can be administered as a continuous infusion at a rate of 2 mg/min until a maximum daily dose of 300 mg is reached. However, this maximum limit may be reached before the BP goal is achieved. Published data of prolonged continuous infusions of labetalol in hypertensive emergencies are limited in patients with ICH. Despite the lack of published data, continuous infusion labetalol is currently utilized at the Cleveland Clinic Neurology Intensive Care Unit for management of hypertension in patients with ICH. Therefore, this study aims at evaluating the efficacy and safety of continuous infusion of labetalol for the management of hypertension in patients with ICH.

**Objective:** The goal is to evaluate the clinical efficacy and safety of a continuous infusion of labetalol for hypertension management in patients with ICH. The primary objective consists of describing the time and the labetalol dose required to achieve the BP target. Secondary objectives include determining the use of additional antihypertensive medications needed to achieve BP goal as well as assessing for adverse events related to prolonged antihypertensive medication administration.

**Methodology:** This is a non-interventional retrospective chart review of patients admitted and treated in the Neurology Intensive Care Unit at the main campus of Cleveland Clinic with a diagnosis of ICH between January 2006 and December 2009. Descriptive statistics were used to report key patient characteristics and treatment outcomes.

**Results and Conclusions:** A total of 19 patients were included, 58% of them being male. Sixteen (84%) patients had a history of hypertension followed by diabetes in 6 (32%). All patients were hypertensive at the moment of initiation of the labetalol infusion (mean SBP 183± 26 mmHg, HR 82±14), 12 (63%) of them being intubated [GCS 9(5-15)]. Seventeen (90%) patients had received at least one IV antihypertensive medication (17 pts received labetalol, 5 hydralazine, and 3 metoprolol) prior to the initiation of the labetalol infusion. All patients reached the targeted SBP within a median of 0.75 (0.25-14.33) hrs and remained below that goal 88±12.8% of the time. The total dose of labetalol required to achieve the targeted SBP goal was 127 (5-2342) mg. Ten (53%) patients required additional rescue antihypertensive medications while on continuous labetalol infusion. The maximum recommended daily dose of 300 mg was exceeded in 6 (84%) patients with 8 (50%) of them experiencing adverse effects (AEs). Overall, 10 (53%) patients experienced AEs (8 patients bradycardia vs 3 patients hypotension, and 0 increased LFTs). This resulted in 4 (40%) patients having the labetalol infusion discontinued and 1 patient having it temporarily held. Continuous infusion of labetalol helped achieve the targeted SBP goal in all studied patients. However, even though the SBP of the majority of the patients was being maintained below that targeted goal, this was achieved with considerable side effects.

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## Nesiritide Cohort Study in Total Artificial Heart Patients

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### Background:

Endogenous B-type natriuretic peptide (BNP) is produced by the ventricular cardiomyocytes. When the native ventricles are removed and a total artificial heart (TAH) is implanted in a patient it is hypothesized that this may impair their renal function and volume homeostasis due to lack of BNP.<sup>1</sup> Theoretically, administering nesiritide infusion could prevent abrupt withdrawal of endogenous BNP and improve patient outcomes. Support of this hypothesis is limited to one case report investigating nesiritide use in total artificial heart patients.

### Objective:

The goal of this study was to assess the use of nesiritide in patients with a CardioWest™ TAH at the Cleveland Clinic. The primary objective of the study was to assess the change in urine output in patients with a TAH who received nesiritide. The secondary objectives were to assess: 1) average daily nesiritide dose 2) average daily diuretic dose 3) change in serum creatinine (SCr) 4) incidence of hypotension.

### Methodology:

The study was a retrospective medical record review of adult patients who received a TAH at the Cleveland Clinic and received therapy with nesiritide. Patients who received CVVHD and patients who did not receive nesiritide infusion were excluded. In addition to demographic information, the following daily information from baseline up to 2 days after nesiritide therapy discontinuation was collected: TAH cardiac output, serum sodium, SCr, daily fluid intake and output, nesiritide daily dose, loop diuretic daily dose, vasopressor requirements, and incidence of hypotension. Descriptive statistics analysis was used to evaluate the data.

### Results and conclusions:

Between July 2005 - February 2010, 16 patients received a TAH at the Cleveland Clinic. Out of the 11 included patients, information was collected on 17 nesiritide episodes. The median duration of nesiritide therapy ranged from 12-17 days. Our findings suggest that urine output more closely follows loop diuretic use than nesiritide use. However, it was noted that the dose of nesiritide used was lower in TAH patients than package labeling (0.005 mcg/kg/min). It was also observed that SCr was higher at baseline and decreased throughout nesiritide therapy. Nevertheless, the majority of patients had normal SCr levels with values only as high as 1.7 g/dL. Additionally, SCr is likely multifactorial in the post-operative period due to fluid administration and hemodynamic instability. No problematic hypotension was observed.

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## An Evaluation of Patients with Type 2 Diabetes Followed by a Pharmaceutical Care Clinic

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**Background:** Almost 8% of the United States population is affected by diabetes mellitus and the incidence is on the rise. In light of this problem, many studies, both prospective and retrospective, have supported the notion of pharmacist managed diabetes care clinics. Diabetes care services have been offered at the Pharmaceutical Care Clinic (PCC) since 2002 at the Cleveland Clinic. A study conducted in 2004 to assess diabetes care at the PCC found a significant reduction in HbA1c. In the current study, the impact of pharmacist intervention on glycemic control was assessed while addressing some limitations of the previous study. This study provided insight on patient care at the PCC that will direct future care improvements at the Cleveland Clinic.

**Objectives:** The primary objective was to evaluate the change in HbA1c from baseline to end of 6-month period after a clinical pharmacist intervention. The secondary objectives were to evaluate a change in HbA1c from baseline to 3 and 12 months after pharmacist intervention and to determine percentage of patients with at least one HbA1c < 7% within 12 months following first visit at the PCC.

**Methodology:** A retrospective chart review included patients with an established diagnosis of type II diabetes managed by their primary care physician for at least 6 months prior to PCC enrollment. Baseline HbA1c greater than or equal to 7.5% was required for study inclusion. In addition, study subjects must have had at least two visits with the pharmacist within 6 months at the PCC between 1/2004 and 11/2008. Paired t-test and fisher's exact test were used for statistical analysis.

**Results and Conclusions:** The mean reduction in HbA1c from baseline to 6 months was 2.3% [95% CI 1.27 - 3.66 %], p=0.001. The change in HbA1c from baseline to 3 months was 2.3% [95% CI 1.54 – 2.80 %], p=0.001 and from baseline to 12 months was 2.5% [95% CI 1.50 – 4.53 %], p=0.001. Forty two percent of the (n=21) patients had at least one HbA1c less than 7% within 12 months. The study illustrates that clinical pharmacist intervention in diabetes care had resulted in significant HbA1c reduction in patients with poorly controlled diabetes.

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## Effect of omeprazole on clozapine pharmacokinetics in patients with chronic schizophrenia

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**Background:** Clozapine is a highly effective atypical antipsychotic used in refractory schizophrenia. It is hepatically transformed to N-desmethylclozapine (NDMC, norclozapine, primary metabolite) and clozapine-N-oxide (CNO) by the CYP450 system. Omeprazole is a commonly utilized proton pump inhibitor that is an inducer and inhibitor of the hepatic CYP450 1A2 isoform, as well as an inhibitor of CYP3A4, 2C19, 2C9 and 2D6. There are several case reports of omeprazole interacting with clozapine, however the observed change in clozapine concentration varies from report to report, both in magnitude and direction and there is much heterogeneity between baseline characteristics of the patients in the reported cases.

**Objective:** The primary objective of this study is to characterize the pharmacokinetics of clozapine alone and clozapine plus omeprazole in non-smoking patients with chronic schizophrenia. The secondary objective is to characterize the pharmacokinetics of NDMC and clozapine-N-oxide CNO when clozapine is administered alone and when clozapine is administered concurrently with omeprazole in non-smoking patients with chronic schizophrenia.

**Methodology:** This will be a prospective, paired, single group, pharmacokinetic study, targeted enrollment is 10 subjects. The inclusion criteria are: DSM-IV diagnosis of schizophrenia or schizoaffective disorder; male; greater than 18 years old and receiving the same dose of clozapine from the Cleveland VA Medical Center for at least 28 days. Exclusion criteria are: patient received fluvoxamine, oral ciprofloxacin, cimetidine or nicotine within 14 days of study initiation; patient is actively receiving atazanavir, nelfinavir, posaconazole, oral ketoconazole, itraconazole, oral tacrolimus, oral mesalamine, erlotinib, dasatanib, delavirdine, clopidogrel or cilostazol as part of their medication regimen; patient is consuming more than 400mg/day of caffeine, (approximately four 6 ounce cups of brewed coffee or ten 6 ounce cups of green/black tea); patient is currently on omeprazole; patient takes their first dose of clozapine after 12:00PM daily, if the patient has a documented heparin allergy and if the patient has a legal guardian. Upon enrollment into the study and after obtaining informed consent, baseline serum clozapine, NDMC and CNO pharmacokinetics will be obtained. Blood samples will be obtained just before, 0.5, 1, 2, 3, 4 and 6 hours after their morning dose of clozapine (day 1). At the end of day 1, each subject will receive a supply of omeprazole 20mg capsules, to be taken once daily in the morning at least 30 minutes prior to breakfast for 14 days. On day 15 blood samples will be obtained for the analysis of serum clozapine NDMC and CNO levels just before and at 0.5, 1, 2, 3, 4, 6, 8 and 12 hours after their morning dose of clozapine. This will be their last day of concurrent clozapine and omeprazole. Subjects will be evaluated for dietary habits of foods that can affect CYP450 1A2, medication compliance and safety and tolerability on days 8 and 15 of the study.

**Results and conclusions:** subjects are currently being recruited, results pending.

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# Potential Impact of Enterococcal PNA FISH on Antimicrobial Use at Cleveland Clinic

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**Background:** Enterococci are the third most common cause of bloodstream infections (BSIs). Risk factors for enterococcal BSIs are intravascular catheter devices, transplant and neutropenia. Associated mortality is estimated at 35%. *E. faecalis* and *E. faecium* are the most common species. *E. faecalis* is ampicillin and vancomycin susceptible and *E. faecium* is more likely to be vancomycin-resistant. PNA FISH allows for rapid identification of *Enterococcus* species. Rapid identification may allow for earlier directed therapy or sooner de-escalation. The results of this project will assist in evaluating its potential impact on clinical practice at our institution.

**Objectives:** Primary objective is to predict if PNA FISH results in earlier initiation of targeted therapy or decreases time to de-escalation of therapy. Secondary objective is a cost minimization analysis.

**Methodology:** Non-interventional, retrospective, IRB-approved chart review of patients with blood cultures positive for enterococci over a six month period. Patients included were 18 years of age or older with at least one blood culture positive for enterococci. Patients with death or discharge within 24 hours of positive blood cultures were excluded. The following data was collected: age, gender, primary service, length of stay, underlying medical conditions, culture results, enterococcal isolate, initial antimicrobial agent, time of initiation of therapy, start and stop dates of antimicrobials, reasons for changes in therapy and date of change. Data analysis included descriptive statistics. A cost minimization analysis will also be performed.

**Results and Conclusions:** 139 enterococcal episodes were analyzed. Initial empiric therapy was vancomycin (74%), daptomycin (14%), piperacillin/tazobactam (5%), linezolid (3%), ampicillin/ sulbactam (1%), ampicillin (1%), imipenem (1%) and no therapy (1%). *E. faecalis* was presumed in 52% of episodes and 48% were presumed *E. faecium*. 62% of patients were on appropriate therapy without a potential benefit of enterococcal PNA FISH. Earlier initiation of targeted therapy would have occurred in 29% and 9% may have been de-escalated sooner. Enterococcal PNA FISH results in potentially earlier targeted therapy by 2 days in patients with *Enterococcus* sp. BSIs. Cost minimization analysis will follow.

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## A comparison of vancomycin to metronidazole for the treatment of moderate to severe *Clostridium difficile*

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**Background:** *Clostridium difficile* is an anaerobic, spore-forming gram-positive bacillus that is frequently the cause of nosocomial-associated diarrhea. The severity of *Clostridium difficile*-associated disease (CDAD) can range from uncomplicated diarrhea to sepsis or even death.<sup>1</sup>

**Objective:** To evaluate the outcomes related to moderate to severe *Clostridium difficile* infection for patients receiving metronidazole or vancomycin.

**Methodology:** An observational retrospective chart review of all patients at least 18 years or older with a positive *C. difficile* toxin, diarrhea ( $\geq 3$  unformed stools in 24 hours), and at least one of the following: fever ( $>38.3^{\circ}\text{C}$ ), abdominal pain and/or leukocytosis. Patients with an intolerance to metronidazole or vancomycin, pregnant, colostomy; or diagnosis of ulcerative colitis, Crohn's disease, short bowel syndrome, bowel obstruction or death within twenty-four hours after positive *C. difficile* toxin were excluded. The following data was collected: age, gender, place of residence, past medical history; dose, route and frequency of treatment antibiotic; days to symptom resolution, treatment in the intensive care unit, prior antibiotics, day prior antibiotics were discontinued; antiperistaltic medications, bile acid sequestrants and probiotics received during treatment period. Severe *C. difficile* is defined as any of the following: septic shock, megacolon, perforation, colectomy or pseudomembranous colitis. Treatment success is defined as: resolution of diarrhea or negative *C. difficile* toxin by day 6, or discharged prior to day 6 with resolution of diarrhea. Chart review data was entered and analyzed in Microsoft Access. Descriptive data analysis included assessment of demographic data, initial study treatment, changes in study treatment, comorbid conditions, prior antibiotics, day prior antibiotics discontinued, days to symptom resolution and other ancillary medications used during treatment including: antiperistaltic medications, bile acid sequestrants and probiotics.

**Results and conclusions:** 39 patients were assessed and 34 of those patients had moderate disease and five had severe disease. None of the 39 patients were initially started on vancomycin; 34 patients were started on metronidazole, and 5 patients were started on metronidazole and vancomycin. 24 (61.5%) patients were considered to have treatment success and 15 patients (38.5%) failed treatment. Four of the five patients with severe disease had septic shock and one had pseudomembranous colitis. Three of the four patients with septic shock failed treatment, the one patient with pseudomembranous colitis was treated successfully. All the patients with severe disease were treated initially with metronidazole. 90% of the patients were on antibiotics prior to *C. difficile* infection and 46% of the patients continued on antibiotics after positive *C. difficile* toxin.

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# Therapeutic Troughs in Standard Versus Individualized Dosing of Vancomycin

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## Background

Historically, vancomycin dosing and monitoring methods have not been well-defined. In 1977, author Geraci recommended targeting trough concentrations of 5 – 10mg/L. The vancomycin guidelines published in 2009 recommend targeting troughs greater than 10mg/L to avoid resistance from organisms such as *S. aureus*, *E. faecalis* and *E. faecium*. For most infections the guidelines suggest targeting troughs between 10 – 20mg/L. However, for complicated infections (i.e. osteomyelitis, meningitis) the recommendation is made to target troughs between 15 – 20mg/L. These guidelines also acknowledge that there are two different dosing strategies (i.e 1g/dose and 15mg/kg/dose) used in the treatment of infections, however they do not specify if a method is more appropriate.

## Objective

The primary objective is to determine the proportion of patients in each dosing strategy who attain an appropriate initial target trough. The secondary objectives are to assess an appropriate initial target trough drawn before and after an approximated steady state (i.e. trough drawn after receiving at least 4 doses) and evaluate if a dosing adjustment was made when the initial trough was inappropriate.

## Methodology

This study was a retrospective chart review that conducted a search for patients who received vancomycin between January 1, 2008 and December 31, 2008. Patients were then divided into two groups based on the dosing strategy used: standard (1g every 12 or 24 hours) or individualized (15mg/kg every 12 or 24 hours). Patients were selected based on inclusion and exclusion criteria. If a patient was included, an assessment of the vancomycin dosing regimen, initial trough, whether vancomycin was appropriately dosed (i.e. initial trough reached target), and whether the dose was changed (if initially inappropriate) was performed.

## Results and conclusions

A total of 152 patients were included in the study (standard: n=94 and individualized: n=58). The standard group had 47.9% of patients attain an initial target trough, in comparison to the individualized group who had 50% of patients attain an initial target trough ( $p = 0.556$ ). Eighty-three percent (n=126) of the total study population had troughs drawn before the approximated steady state (i.e. trough drawn after receiving 2 or 3 doses). A comparison of these patients showed that 47.4% of the standard group and 43.8% of the individualized group attained an initial target trough ( $p=0.126$ ). The remaining 17% (n=26) of patients who had a trough drawn at or after the approximated steady state had 50% of the standard group and 80% of the individualized group attain an initial target trough ( $p=0.687$ ). Patients were reassessed for appropriate doses based on criteria developed for creatinine clearance and the interval administered. It was found that 33 patients in the standard group and 12 patients in the individualized group were inappropriately dosed based on this criteria. Inappropriately dosed patients were excluded and the primary objective was then re-evaluated. After excluding these patients, 39.3% of the standard group and 45.7% of the individualized group attained an initial target trough ( $p=0.059$ ). When a trough was initially inappropriate it was found that 42.3% of patients did not have a dosing adjustment made in response to this non-target trough. There were no statistically significant differences seen in the ability of standard and individualized doses to attain an initial target trough. However, there was a trend observed that favored the individualized dosing strategy. Approximately 50% of patients with non-target troughs had no dosing adjustments made.

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## Retrospective Cohort of Extended-Infusion Piperacillin/Tazobactam (RECEIPT): A Multicenter Study

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**Background:** As suggested by Lodise and colleagues<sup>1</sup>, extending the length of infusion of piperacillin/tazobactam maximizes the time free drug is available at concentrations in excess of the MIC ( $fT > MIC$ ) without the notable line access drawbacks of continuous infusions. Lodise and colleagues<sup>2</sup> demonstrated extended-infusion piperacillin/tazobactam improves 14 day mortality and decreases length of stay in patients with *Pseudomonas aeruginosa* infections and APACHE II scores of  $\geq 17$ . A multisite, retrospective study<sup>3</sup> compared extended-infusion piperacillin/tazobactam to intermittent infusion piperacillin/tazobactam in documented gram negative infections, but found no impact on 30 day mortality or length of stay.

**Methods:** A multicenter, retrospective chart review study was conducted in which fourteen corresponding authors conducted independent reviews of 399 adult patients treated with extended-infusion piperacillin/tazobactam or intermittent-infusions of cefepime, imipenem/cilistatin, meropenem, doripenem, or piperacillin/tazobactam for greater than 48 hours for treatment of any infection in which a gram negative organism is identified as the causative pathogen. Excluded were patients who received greater than 24 hours of effective antibiotics prior to initiation of study drug, patients whose infection were proven resistant to empiric therapy, or any patient inadequately treated for a concurrent resistant pathogen.

**Results:** Baseline characteristics were matched between groups excepting higher APACHE II scores in the intermittent-infusion group (15 vs. 12,  $P = 0.04$ ). More patients in the intermittent-infusion group were treated with a concomitant aminoglycoside (16.6% vs. 6.4%,  $P < 0.002$ ) Overall in-hospital mortality was decreased in patients receiving extended-infusions of piperacillin/ tazobactam from 17.7% to 9.9% ( $P = 0.025$ ). Antibiotic duration, length of stay, and length of ICU stay were not significantly impacted by extended-infusion. Subgroup analysis revealed ICU patients (14.9% vs. 22.5%,  $P = 0.14$ ) and patients with APACHE II scores  $\geq 17$  (15.9% vs. 23.4%,  $P = 0.57$ ) trended toward benefit from extended-infusion piperacillin/tazobactam over intermittent-infusions of other  $\beta$ -lactams.

**Conclusion:** Within this analysis, extended-infusion piperacillin/tazobactam provided an in-hospital mortality benefit over comparative  $\beta$ -lactams given as traditional infusions. Subgroup analysis demonstrated non-statistical benefit to using extended-infusion piperacillin/tazobactam. Pharmacodynamic dosing of piperacillin/tazobactam should be the preferred method of dosing in documented gram negative infections.

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## Atorvastatin 80 mg daily therapy for acute coronary syndrome: an assessment of short and long term tolerability

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Background: HMG-CoA reductase inhibitors, referred to as statins, lower serum cholesterol and reduce cardiovascular events in patients with coronary heart disease.<sup>1</sup> The Pravastatin or Atorvastatin Evaluation and Infection Therapy-Thrombolysis in Myocardial Infarction 22 (PROVE-IT-TIMI 22) demonstrated that an intensive lipid-lowering regimen with high-dose statin therapy (atorvastatin 80 mg) significantly reduces cardiovascular risk by 16 percent after acute coronary syndrome (ACS) compared to moderate lipid-lowering with standard dose therapy (pravastatin 40 mg).<sup>2</sup> These results led to the prescribing of atorvastatin 80 mg daily in ACS patients discharged from University of Toledo Medical Center (UTMC).

Objective: To assess use and tolerance of atorvastatin 80 mg daily in ACS patients. Specifically, if a dosage adjustment or therapy discontinuance has occurred during follow-up consultation and the documented reason for a therapy change.

Methodology: Retrospective chart review of adult patients admitted with a diagnosis of ACS discharged on a statin from UTMC during September 1, 2005 to August 31, 2009 and follow-up with UTMC Cardiology Clinic are included in the study. Subjects were evaluated for up to 36 months following discharge. The following data was collected: patient demographics, type of ACS (NSTEMI, STEMI, or unstable angina), past medical history, home and discharge medications, laboratory values (liver function tests, creatine phosphokinase, serum creatinine, and cholesterol). Data collected from follow-up visits include statin type and dose, current medications, and statin-related adverse events or intolerances. Data was collected on data collection forms using Microsoft Access and analyzed using Microsoft Excel. This study has been reviewed and approved by the UTMC IRB.

Results and conclusions: 90 patients have been included for data analysis. 58.9% of patients continued atorvastatin 80 mg and 41.1% of patients discontinued atorvastatin 80 mg through follow-up. 45.9% of patients who discontinued atorvastatin 80 mg switched to an alternative statin, 32.4% decreased the dose of atorvastatin and 21.6% were taken off of statin therapy. A total of 8.9% of patients discontinued atorvastatin 80 mg due to intolerance/adverse effects, including 1.1% with an increase in liver function tests, 2.2% with elevation in creatine kinase levels, and 2.2% who experienced myalgias. No significant complications including rhabdomyolysis or acute renal necrosis were reported. 5.6% of patients discontinued atorvastatin 80 mg due to economic issues and 22.2% had no documented reason. Based on these results, we concluded that the majority of patients continued atorvastatin 80 mg up to four years of follow-up. Limitations to the study include subjective reporting due to physician documentation, reasons for change/discontinuation of therapy were not consistently documented, compliance was not assessed, and length of follow-up was variable.

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