2017

Evaluating Prescriber Adherence to Guideline-Based Treatment Pathways of a Newly Initiated Antimicrobial Stewardship Program at a Rehabilitation Hospital

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BUTLER UNIVERSITY HONORS PROGRAM

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Thesis title: Evaluating Prescriber Adherence to Guideline-Based Treatment Pathways of a Newly Initiated Antimicrobial Stewardship Program at a Rehabilitation Hospital

Intended date of commencement: 05/06/2017

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Evaluating Prescriber Adherence to Guideline-Based Treatment Pathways of a Newly Initiated Antimicrobial Stewardship Program at a Rehabilitation Hospital

A Thesis

Presented to the Department of Pharmacy

College of Pharmacy and Health Sciences

and

The Honors Program

of

Butler University

In Partial Fulfillment

of the Requirements for Graduation Honors

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April 21st, 2017

ABSTRACT

Background: Inappropriate use of antimicrobials in the healthcare setting is associated with consequences including antimicrobial resistance, *Clostridium difficile* infection (CDI), adverse drug reactions, and increased healthcare costs. To combat this, hospitals are creating antimicrobial stewardship programs (ASPs) which seek to optimize antimicrobial utilization. To date, no studies have been done to assess adherence to an ASP in a rehabilitation hospital setting. The objective of this study is to evaluate prescriber compliance to treatment pathways for common infections before and after ASP implementation.

Methods: This was a retrospective cohort study of patients admitted to the Rehabilitation Hospital of Indiana (RHI) who received an antibiotic between October 1, 2015-December 31, 2015 (pre-ASP group) and January 1, 2016-September 30, 2016 (post-ASP group) for one of the following indications: pneumonia, urinary tract infection, CDI, bone and joint infection, skin or skin structure infection, febrile neutropenia, or central/peripherally inserted central catheter line bloodstream infection. Data extracted from the hospital's electronic medical record system included patient demographic and clinical information, laboratory data, culture and susceptibility results, and antibiotic information. The primary outcome of this study was prescriber compliance to treatment pathways defined as correct drug based on the documented indication before and after the implementation of the antimicrobial stewardship program on January 1, 2016. Descriptive statistics were performed to analyze baseline characteristics and culture data, as well as antimicrobial class, indication, and overall compliance to the guideline-based treatment pathways.

Results: Data was extracted from the hospital's electronic medical record system for 381 patients (n=381) who received an antibiotic at RHI. There were 121 and 260 patients included in the pre- and post-ASP study groups, respectively. Urinary tract infections were the most common infection for which antibiotics were prescribed (n=293; 76.9%). The three most common antibiotics prescribed were ciprofloxacin (n=101; 26.5%), sulfamethoxazole/trimethoprim (n=81; 21.3%), and nitrofurantoin (n=49; 12.9%). Compliance was found to be 81% in the pre-ASP group and 78.5% in the post-ASP group (p=0.571). Overall compliance was found to be the highest (100% in both pre- and post-ASP groups) for osteomyelitis infections and CDI. Urinary tract infections had the next highest rate of compliance in both the pre- and post-ASP groups (86.5% and 81.7% respectively).

Conclusions: No difference in rates of prescriber compliance to guideline-based treatment pathways was found in the pre- and post-ASP groups. Urinary tract infections were found to be the most common indication requiring antimicrobial usage at RHI and had the third highest rate of compliance out of the infections included in this study. Our study highlights a need for further investigation regarding the impact of the ASP on appropriate antimicrobial dose, duration of therapy, administration, and de-escalation based on culture data. Additionally, our study identified a need for formal prescriber education focusing on how to utilize the treatment pathways, especially for those infections with the lowest compliance rates.

BACKGROUND

The inappropriate use of antimicrobials is a definite and serious problem in the healthcare setting. According to the Centers for Disease Control and Prevention (CDC), 20-50% of all antibiotics prescribed in United States (US) acute care hospitals are either unnecessary or inappropriate.[1] The most common inadvertent consequences of misusing antimicrobials include antimicrobial resistance, *Clostridium difficile* infection (CDI), adverse drug reactions, and increased health care costs.[2]

The prevalence of infections caused by multidrug-resistant organisms (MDROs) continues to increase. Currently, around two million people are infected with antibiotic-resistant organisms each year with 23,000 deaths.[3] Unlike other medications, both the use and misuse of antibiotics accelerates the spread of resistant organisms that can impact the health of patients who aren't even directly exposed to them.[1] Multi-drug resistant organism infections, including methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococcus (VRE), and extended-spectrum beta-lactamase (ESBL)-producing gram-negative rods, are associated with increased mortality, prolonged hospital stays, and higher hospitalization costs.[4] New MDROs have emerged for which there are limited to no effective treatment options such as carbapenem-resistant Enterobacteriaceae (CRE). Infections with CRE are very difficult to treat and are deadly in up to 50% of patients who become infected.[5]

To further compound the issue of resistance, today's antibiotic pipeline is nearly dry with only a "handful" of large pharmaceutical companies and smaller biotech firms engaged in antibiotic development.[6] Between 1999 and 2014, the FDA only approved two systemic antibiotics representing an 88% drop from the mid-1980s.[7] This can largely be attributed to the fact that pharmaceutical companies can make greater profits on drugs

used for chronic conditions such as HMG-CoA reductase inhibitors and antidepressants.[7] Consequently, the rate of emergence of antimicrobial resistance far exceeds new antimicrobial discovery and development.[8,9]

Clostridium difficile infection is the leading cause of healthcare-associated diarrhea in adults and its incidence has markedly increased over the past decade.[8] In 2011, CDI was estimated to cause almost half a million infections in the US and 29,000 deaths.[5] Prior antibiotic use is one of the most important risk factors for developing CDI, and antibiotic misuse or overuse strongly contributes to the infection proliferation and transmission.[8,10] Broad-spectrum antibiotics, especially cephalosporins and fluoroquinolones, as well as clindamycin are considered high-risk for CDI development.[11] Prevention of CDI is best achieved by utilizing infection control recommendations and careful antibiotic use.[5]

A third consequence of inappropriate antimicrobial utilization is the increased risk of adverse drug reactions and toxicities. Antibiotic-associated diarrhea occurs in 10-25% of patients treated with amoxicillin-clavulanate and 2-5% of patients treated with cephalosporins, fluoroquinolones, macrolides, and tetracyclines.[12] Nephrotoxicity has been reported with intravenous aminoglycosides, amphotericin, and vancomycin.[12] Up to one-quarter of women treated with a short course of oral antibiotics develop symptomatic vulvovaginal candidiasis.[12] Fluoroquinolones are associated with tendon rupture, retinal detachment, and delirium.[12] Life-threatening dermatologic complications such as Steven-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) have been implicated with sulfonamides and beta-lactams.[12] Patient groups most at risk for adverse reactions include the elderly, patients with renal dysfunction or significant cardiac disease, and

those on multiple medications.[12] Since antibiotics can cause numerous unpleasant adverse effects including life-threatening allergic reactions, it is important to decide if the efficacy outweighs the potential for toxicity.[2]

Along with increasing the risk to patient safety, the inappropriate use of antibiotics can increase otherwise avoidable healthcare costs. Unnecessary and duplicative antibiotics in 500 US hospitals over a 4-year period was associated with an estimated $12 million in excess costs and 148,589 days of redundant therapy.[13] Seventy-eight percent of hospitals had evidence of potentially unnecessary combinations of antibiotics being administered for two or more days over the time period, resulting in an estimated $163 million that could be saved when considering all US hospitals.[13]

To help combat inappropriate antibiotic use, hospitals are creating antimicrobial stewardship programs. An antimicrobial stewardship program (ASP) is an institutional antimicrobial management program, usually led by an infectious disease physician and clinical pharmacist, which seeks to optimize antimicrobial use.[14] Antimicrobial stewardship programs help prescribers apply evidence-based knowledge to treat infections and optimize doses while minimizing adverse drug reactions.[14] The primary goal of antibiotic stewardship is to optimize clinical outcomes while reducing toxicity, the selection of pathogenic organisms like *C. difficile*, and the emergence of resistance.[15] A secondary goal is to decrease health care costs without adversely impacting quality of care.[15]

The Rehabilitation Hospital of Indiana (RHI) is an acute care specialty-based rehabilitation hospital located in Indianapolis and owned by both Indiana University Health and St. Vincent Health. The hospital mainly specializes in the rehabilitation of

stroke, spinal cord injury, and traumatic brain injury patients by providing inpatient medical care as well as daily physical and occupational therapy. At the beginning of 2015, RHI formed an Antibiotic Stewardship Committee. The committee is composed of a champion physician, clinical pharmacist, infectious disease physician, program facilitator, quality director, infection control nurse, and nursing program director. Goals of the committee include the following: safe and appropriate antibiotic dosing, responsible use of broad spectrum agents, optimized duration of therapy, reduced antimicrobial expenses, and preventable antimicrobial resistance.

During the latter part of 2015, antimicrobial treatment pathways were developed for the following most common infections encountered at RHI: pneumonia, bone and joint infections, urinary tract infections (UTI), febrile neutropenia, CDI, skin and skin structure infections, and catheter-related bloodstream infections. The RHI guideline-based treatment pathways were created using the most up-to-date Infectious Diseases Society of America (IDSA) guidelines as of 2015 and only included antimicrobials on the RHI formulary. The RHI guidelines indicate appropriate empiric therapy, directed therapy, alternative agents, and those antibiotics that have prescribing restrictions (Appendix A). During the implementation phase, antimicrobial order forms were created to change the prescribing process. Although there are currently no electronic hard stops when prescribers order restricted antibiotics, the clinical pharmacist must contact the provider and confirm proper indication for the agent before verifying and processing the order. There are some antibiotics requiring an internal medicine or infectious disease consult before they can be ordered (Appendix B). If the prescribing physicians follow the treatment pathway flowsheets before prescribing an antibiotic, there ideally would be

little to no clinical pharmacist intervention necessary at the time of ordering. The objective of the proposed study is to evaluate prescriber compliance to the outlined treatment pathways based on the appropriateness of the antimicrobial regimen prescribed for the indication.

THESIS STATEMENT

Following introduction of an ASP in a rehabilitation hospital, it is predicted that a higher percentage of prescribers are adhering to guideline-based treatment pathways when prescribing antimicrobial agents in comparison with the period prior to ASP implementation.

STUDY OBJECTIVE

The objective of the proposed study is to evaluate prescriber compliance to the outlined treatment pathways based on the appropriateness of the antimicrobial regimen prescribed for the indication.

NEED FOR STUDY

Effective January 1, 2017, the Centers for Medicare & Medicaid Services (CMS) issued a new requirement stating that hospitals must have an ASP to participate in Medicare and Medicaid reimbursement.[16] Additionally, the National Action Plan for Combating Antibiotic-Resistant Bacteria, issued by the White House in March 2015, calls for the establishment of ASPs in all acute care hospitals by 2020.[11] Antimicrobial stewardship programs can be implemented in a variety of ways in any hospital.[3] There are no studies that exist which evaluate the effectiveness of ASPs in a specialty rehabilitation hospital setting. In the time since the antimicrobial stewardship program was initiated at RHI on

January 1, 2016, there has not been any significant research conducted to examine the extent of the program's success. Due to its recent implementation, it is not yet practical to look at the effects of the program on reducing resistance or healthcare costs. It is first necessary to examine whether prescribing physicians are complying with the guideline-based treatment pathways outlined in the program before further metrics can be conducted.

METHODS

This was a retrospective cohort study conducted at RHI and IRB-approved by Butler University. Eligible patients were identified using a pharmacy computer system-generated report of patients with antibiotic orders for selected indications during the specified time frame. Patients were included if they were greater than 18 years of age and received an antibiotic at RHI between October 1, 2015 and September 30, 2016 for one of the following indications: pneumonia, UTI, CDI, bone and joint infection, skin or skin structure infection, febrile neutropenia, or central/peripherally inserted central catheter line bloodstream infection. Patients were excluded if they received an antibiotic for less than 24 hours. The pre-ASP group included patients receiving an antibiotic between October 1, 2015 and December 31, 2015 (Quarter 4 2015). The post-ASP group was comprised of patients receiving an antibiotic between January 1, 2016 and September 30, 2016 (Quarters 1-3 2016). Data was extracted from the hospital's electronic medical record system, and included patient demographics (age, gender, actual body weight, antibiotic allergies), laboratory data (white blood cell count, serum creatinine), temperature, antibiotic indication, culture and susceptibility results (culture location, isolate, susceptibility to antibiotic), and antibiotic information (drug, class, dose,

route, frequency, doses administered, total days of therapy). It was also documented whether prescribers followed the guideline-based pathways when prescribing an antibiotic for individual patients (correct drug based on the documented indication) and if the antibiotic was de-escalated appropriately (guideline-based, narrowest spectrum) when culture and susceptibility results were available. The primary outcome of the study was the percentage of prescribers who adhered to the guideline-based pathways.

Statistical Analysis:

Continuous data was described using mean and standard deviation (SD) for variables considered to be normally distributed and median and interquartile range (IQR) for variables considered to be non-normally distributed. Baseline demographics and clinical characteristics were compared between pre- and post-implementation period groups using independent samples t-tests, chi-squared analyses, and Mann-Whitney tests for non-parametric data. Chi-square analysis was used to compare the primary outcome and the appropriateness of antibiotic therapy in pre- and post-implementation periods. P-values of less than 0.05 were considered statistically significant. Statistical analyses were conducted using Statistical Package for Social Sciences version 23.0 (SPSS, Inc., Chicago).

RESULTS

A total of 381 patients were identified who met inclusion criteria with 121 and 260 included in the pre- and post-ASP study groups, respectively. Females comprised 64 patients of the pre-ASP group (52.9%) and 138 patients of the post-ASP group (53.1%). The mean age of patients in the pre-ASP group was 60 years of age and 58 years of age in the post-ASP group. The majority of patients in the cohort had no documented

antibiotic allergies (n=288; 75.6%). Out of the 277 patients that had cultures obtained, 217 were positive (78.3%). Cultures were obtained for 108 patients (89.3%) in the pre-ASP group with the majority (n=92; 85%) being urine cultures. Ninety-two (85%) of all cultures obtained in the pre-ASP group were positive. In the post-ASP group, cultures were obtained for 169 patients (65%) with the majority also being urine cultures (n=155; 92%). Positive cultures were documented in 125 patients (79%) of the post-ASP group. Appendix D lists the isolates found in each group. The most prevalent isolates for both groups were *Escherichia coli* (23% of pre; 30% of post) and *Klebsiella pneumoniae* (16% of pre; 14% of post).

Urinary tract infections were the most common infection for which antibiotics were prescribed (n=293; 76.9%). Appendix E shows the prescribing rates for other included infections. The three most common antibiotics prescribed were ciprofloxacin (n=101; 26.5%), sulfamethoxazole/trimethoprim (n=81; 21.3%), and nitrofurantoin (n=49; 12.9%). First generation cephalosporins (n=31; 8.1%) and third generation cephalosporins (n=22; 5.8%) also had higher prescribing rates. A complete table of frequencies of antibiotic classes prescribed is shown in Appendix F.

Compliance to the guideline-based treatment pathways was found to be 81% in the pre-ASP group and 78.5% in the post-ASP group (p=0.571). Appendix G shows compliance per quarter. Overall compliance was found to be the highest (100% in both pre- and post-ASP groups) for osteomyelitis infections and CDI. Urinary tract infections had the next highest rate of compliance in both the pre- and post-ASP groups (86.5% and 81.7% respectively). Rates of compliance for pneumonia were 71.4% in the pre-ASP group and 72.7% in the post-ASP group. Cellulitis infections had the lowest rates of

compliance with only 27.3% in the pre-ASP group and 52% in the post-ASP group. Compliance rates based on indication per quarter are displayed in Appendix H.

The three most common classes of antibiotics prescribed were fluoroquinolones, sulfonamides, and urinary agents (nitrofurantoin and fosfomycin). In the pre-ASP group, prescribers utilized fluoroquinolones appropriately 95% of the time and 97.4% in the post-ASP group. Sulfonamides had a compliance rate of 88.5% in the pre-ASP group and 85.5% in the post-ASP group. Urinary agents had a higher rate of compliance with 95% in the pre-ASP group and 100% in the post-ASP group. Appendix I displays compliance rates based on antibiotic class in both pre- and post-ASP groups.

DISCUSSION

In this cohort, we found no statistically significant difference in rates of prescriber compliance to guideline-based treatment pathways both before and after implementation of an antimicrobial stewardship program at RHI. The 2016 Infectious Diseases Society of America/Society for Healthcare Epidemiology of America (IDSA/SHEA) guidelines "Implementing an Antibiotic Stewardship Program" recommend that ASPs develop facility-specific clinical practice guidelines and algorithms to standardize prescribing practices based on local epidemiology for common infectious diseases.[11] Several studies have shown that the implementation of facility-specific guidelines has led to statistically significant increases in the likelihood of adequate initial therapy, use of narrower-spectrum regimens, earlier switch from IV to oral therapy, and shorter duration of treatment without adversely affecting clinical outcomes.[11] In this cohort, there was no difference in prescriber compliance to guideline-based treatment pathways both before and after implementation of an antimicrobial stewardship program at a rehabilitation

hospital. While our study did not find a significant increase in appropriate antibiotic prescribing after facility-specific guideline-based treatment pathway implementation, it is reassuring that prescriber compliance remained consistent in all quarters except the first quarter following implementation.

We hypothesized that a higher percentage of antimicrobial orders would be compliant with the guideline-based treatment pathways after implementation of an ASP in comparison with the period prior to ASP implementation. There are several potential reasons as to why a significant increase in appropriate antibiotic prescribing was not found. Although the official start of the ASP was documented as January 1, 2016, the program was not implemented all at once. Accounting for the gradual implementation period where all the details were still being worked out may explain why compliance rates for Quarter 1 of 2016 were much lower than Quarters 2 and 3 of the post-implementation group.

One of the largest factors contributing to the insignificant difference in rates of compliance to treatment guidelines may be a lack of formal prescriber education and/or lack of prescriber "buy-in" to the ASP and treatment pathways. The ASP was presented to the Rehab Physicians Committee and the scope, objectives, measuring of utilization, guidelines were discussed and approved. Since the program was approved and supported by leadership present in the committee, all physicians are expected to comply with the program. However, there were never any formal educational sessions held with physicians and medical residents at RHI to introduce them to the program, educate them on how to utilize the treatment pathways, or explain the process for ordering restricted antimicrobials. Because of this lack of formally delivered information, physicians may

not understand the benefit and importance of the ASP and may be hesitant to change their prescribing habits. Education is an essential element of an ASP to influence prescribing behavior and increase the acceptance of stewardship strategies.[15] Regularly scheduled education sessions would likely aid prescribers in understanding how to utilize the outlined treatment pathways, the benefits of the ASP, and which areas to focus on for improvement in compliance (i.e. specific infection, antibiotic class, etc.).

The IDSA/SHEA guidelines for developing an institutional program to enhance antimicrobial stewardship outline core strategies which should be incorporated into all stewardship programs. The core strategies include two methods to impact antimicrobial use in hospitals: preauthorization and prospective audit and feedback.[14] ASPs should decide whether to include one strategy or a combination of both based on availability of facility-specific resources.[11] Preauthorization, or formulary restriction, is a strategy in which the ASP creates a formulary and decides which antimicrobials will require authorization before they can be prescribed.[11] Although RHI has developed a list of restricted antimicrobial agents (Appendix A) and antimicrobials which require an internal medicine or infectious disease consult (Appendix B), there is currently no formal system in place to stop prescribers from ordering an antimicrobial on one of those lists. It is the sole responsibility of the clinical pharmacist to recognize the antimicrobial as restricted and initiate contact with the prescriber to verify proper indication. According to the updated 2016 IDSA/SHEA guidelines, outcome studies from preauthorization have shown decreased antibiotic use and resistance, particularly among gram-negative pathogens, while not displaying any adverse effects for patients.[11] In one study, the initiation of preauthorization in a county teaching hospital was associated with a 32%

decrease in total parenteral antibiotic expenditures and increased susceptibility of gram-negative isolates.[11] If RHI could incorporate a hard or soft stop into their electronic antibiotic order set when prescribers attempt to order a restricted antimicrobial, it would likely minimize the incidence that these agents are used inappropriately, and may increase compliance to the treatment pathways.

The second approach, or prospective audit with intervention and feedback (PAF), requires ASP clinical pharmacists or infectious disease physicians to review antimicrobial appropriateness after they are prescribed and provide feedback to the prescriber.[11] Unlike preauthorization alone, this approach does impact resistance to a greater degree due to its usefulness in antimicrobial de-escalation and appropriate duration of therapy.[15] However, PAF is more time and resource-intensive, especially in the setting of a larger hospital.[14] The IDSA/SHEA guidelines report that PAF interventions have also been shown to improve antibiotic use, reduce resistance, and reduce CDI rates without negatively impacting patient outcomes.[11] RHI would eventually like to implement a 48-hour stop for antimicrobial review in which a clinician evaluates if the antimicrobial is still necessary, is de-escalated appropriately based on culture data, and has a stop date entered. This is currently being piloted at two other facilities within the hospital network and would likely decrease the incidence of inappropriate duration and utilization of empiric antimicrobial therapy.

There are limitations to this study including its retrospective design and relatively small sample size. Our study likely lacked necessary power. The inherent limitations of chart documentation and the variable availability of certain information could have affected our results. In many instances, it was difficult to find a clearly documented

indication for antimicrobial therapy. If an indication was listed, it was rare for prescribers to document the type/severity of the infection, making it challenging to assess the appropriateness of the prescriber's choice in antimicrobial agent. The retrospective nature of our study made it difficult to understand all prescriber considerations at the time of antibiotic regimen formulation. The prescriber may have known more about a specific patient than what was documented in the electronic medical record, warranting them to choose one antibiotic over another recommended in the guideline-based pathway.

At the start of the study, compliance was originally defined as both correct drug and correct duration based on indication since appropriate antibiotic duration guidelines are also included on the treatment pathways for each infection. However, throughout the data collection process, it became difficult to track days of antibiotic therapy for patients at RHI due to the nature of the institution. In the rehabilitation hospital setting, patients could be admitted on antibiotics, be admitted to an acute hospital during their course of antimicrobial therapy and then readmitted to RHI, or be discharged on antimicrobial therapy, making total days of therapy difficult to determine. It is important to consider that many factors contribute to appropriate antimicrobial usage besides appropriate drug choice, including appropriate dose, duration, de-escalation, and administration. This warrants a need for future studies to evaluate all of these components.

CONCLUSIONS

In this retrospective cohort study, no significant difference in rates of prescriber compliance to guideline-based treatment pathways was found after the implementation of an ASP. Urinary tract infections were found to be the most common indication requiring antimicrobial usage at RHI and had the third highest rate of compliance out of the

infections included in this study. Fluoroquinolones, sulfonamides, and urinary agents were the most prescribed antibiotic classes and were utilized appropriately 85-100% of the time in both the pre- and post-ASP groups.

Our study highlights a need for further investigation regarding the impact of the ASP on appropriate antimicrobial dose, duration of therapy, administration, and de-escalation based on culture data. Additionally, our study identified a need for formal prescriber education focusing on how to utilize the treatment pathways, especially for those infections with the lowest compliance rates. The rates of antimicrobial resistance, adverse events, and cost savings at RHI pre- and post-ASP implementation are areas of future study.

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Appendix A
Restricted Antimicrobials

Amphotericin B lipid complex	Serum creatinine >2 or 50% decrease in baseline renal function Amphotericin B failure ID consult
Cefepime	Penicillin-allergic patients Organisms resistant to piperacillin/tazobactam CNS infections
Linezolid	VRE and all alternatives resistant
Posaconazole	Transplant patients
Voriconazole	Transplant patients

Appendix B
Antimicrobials that require an Internal Medicine or Infectious Disease Consult

Ertapenem	Moxifloxacin	Daptomycin
Carbapenem	Tigecycline	Micafungin

Appendix C
Appropriate Antibiotics by Indication per Guideline-Based Treatment Pathways

Indication	Empiric Therapy	Directed Therapy
Pneumonia	Cefepime or Ceftazidime or Meropenem or Piperacillin/tazobactam PLUS Levofloxacin or Gentamicin PLUS Vancomycin	Piperacillin/tazobactam Piperacillin/tazobactam PLUS gentamicin Meropenem Vancomycin or linezolid
Osteomyelitis	Vancomycin Vancomycin PLUS piperacillin/tazobactam Ampicillin/sulbactam	Cefazolin Ceftriaxone Piperacillin/tazobactam Ampicillin/sulbactam

UTI	Nitrofurantoin SMX/TMP Fosfomycin Ciprofloxacin Ceftriaxone Levofloxacin Gentamicin	Ciprofloxacin Levofloxacin Amoxicillin/clavulanate Cefdinir SMX/TMP
Febrile Neutropenia	Ciprofloxacin PLUS amoxicillin/clavulanate Piperacillin/tazobactam Meropenem Ceftazidime Cefepime	Meropenem Vancomycin Daptomycin Linezolid Gentamicin Tigecycline
CDI	Metronidazole +/- Vancomycin	Metronidazole and/or Vancomycin
Cellulitis	Penicillin VK Ceftriaxone Cefazolin/cephalexin Clindamycin Vancomycin PLUS piperacillin/tazobactam	Penicillin VK Ceftriaxone Cefazolin/cephalexin Clindamycin Vancomycin PLUS piperacillin/tazobactam
Catheter-Related Bloodstream Infection	Vancomycin +/- Piperacillin/tazobactam +/- Micafungin	Nafcillin Vancomycin Ampicillin Ceftriaxone Meropenem Ampicillin/sulbactam Piperacillin/tazobactam

Appendix D
Isolates from Positive Cultures

Pre-ASP (N=91)			Post-ASP (N=125)		
Isolate	**Frequency**	**Percent**	**Isolate**	**Frequency**	**Percent**
E.coli	21	23.1%	*E.coli*	38	30.4%
Klebsiella pneumoniae	15	16.4%	*Klebsiella pneumoniae*	17	13.6%
Coag-negative *staphylococcus*	3	3.3%	Coag-negative *staphylococcus*	5	4%
E. coli ESBL	5	5.5%	*E. coli* ESBL	4	3.2%
Pseudomonas	9	9.9%	*Pseudomonas*	10	8%
Enterococcus	4	4.4%	*Enterococcus*	6	4.8%
Enterobacter aerogenes	2	2.2%	*Enterobacter aerogenes*	2	1.6%
Citrobacter	3	3.3%	*Citrobacter*	2	1.6%
Enterobacter cloacae	4	4.4%	*Enterobacter cloacae*	6	4.8%
C. difficile	3	3.3%	*C. difficile*	4	3.2%
Enterococcus faecium VRE	1	1.1%	*Enterococcus faecium* VRE	2	1.6%
Streptococcus	1	1.1%	*Streptococcus*	2	1.6%
Klebsiella oxytoca	1	1.1%	*Klebsiella oxytoca*	2	1.6%
Serratia	2	2.2%	*Proteus mirabilis*	8	6.4%
Stenotrophomonas	1	1.1%	*Lactobacillus*	1	0.8%
Multiple	16	17.6%	Multiple	15	12%
			Providencia stuartii	1	0.8%

Appendix E
Antibiotics Prescribed Based on Indication

Indication	Frequency (N=381)	Percent
UTI	293	76.9%
Cellulitis	36	9.4%
Pneumonia	29	7.6%
CDI	17	4.5%
Osteomyelitis	4	1%
Febrile Neutropenia	1	0.3%
UTI and cellulitis	1	0.3%
Catheter-related Bloodstream Infection	0	0%

Appendix F
Antibiotics Prescribed Based on Class

Antibiotic Class	Frequency (N=381)	Percent
Fluoroquinolone	118	31%
Sulfonamide	81	21.3%
Urinary	55	14.4%
1st generation cephalosporin	31	8.1%
3rd generation cephalosporin	22	5.8%
Glycopeptide	16	4.2%
Anaerobic	12	3.1%
Beta-lactamase inhibitor	12	3.1%
4th generation cephalosporin	10	2.6%
Penicillin	8	2.1%
Lincosamide	5	1.3%
Tetracycline	4	1%
2nd generation cephalosporin	3	0.8%
Macrolide	2	0.5%
Aminoglycoside	1	0.3%
Miscellaneous	1	0.3%

Appendix G
Compliance per Quarter

Group	Quarter	Frequency	Percent	Cumulative Percent
Pre-ASP (N=121)	Quarter 4 2015 (N=121)	98	81%	81%
Post-ASP (N=260)	Quarter 1 2016 (N=121)	90	74.4%	78.5%
	Quarter 2 2016 (N=83)	68	81.9%	
	Quarter 3 2016 (N=56)	46	82.1%	

Appendix H
Compliance based on Indication per Quarter

Indication	Group	Quarter	Compliant (N (%))	Cumulative Percent
UTI (N=293)	Pre-ASP (N=96)	Quarter 4 2015 (N=96)	83 (86.5%)	86.5%
	Post-ASP (N=197)	Quarter 1 2016 (N=99)	76 (76.8%)	83.4%
		Quarter 2 2016 (N=55)	48 (87.3%)	
		Quarter 3 2016 (N=43)	37 (86%)	
Pneumonia (N=29)	Pre-ASP (N=7)	Quarter 4 2015 (N=7)	5 (71.4%)	71.4%
	Post-ASP (N=22)	Quarter 1 2016 (N=9)	5 (55.6%)	73.2%
		Quarter 2 2016 (N=9)	8 (88.9%)	
		Quarter 3 2016 (N=4)	3 (75%)	
Cellulitis (N=36)	Pre-ASP (N=11)	Quarter 4 2015 (N=11)	3 (27.3%)	27.3%
	Post-ASP (N=25)	Quarter 1 2016 (N=7)	4 (57.1%)	53.2%
		Quarter 2 2016 (N=10)	4 (40%)	
		Quarter 3 2016 (N=8)	5 (62.5%)	
CDI (N=17)	Pre-ASP (N=6)	Quarter 4 2015 (N=6)	6 (100%)	100%
	Post-ASP (N=11)	Quarter 1 2016 (N=5)	5 (100%)	100%
		Quarter 2 2016 (N=5)	5 (100%)	
		Quarter 3 2016 (N=1)	1 (100%)	
Osteomyelitis (N=4)	Pre-ASP (N=1)	Quarter 4 2015 (N=1)	1 (100%)	100%
	Post-ASP (N=3)	Quarter 2 2016 (N=3)	3 (100%)	100%
Neutropenia (N=1)	Post-ASP (N=1)	Quarter 1 2016 (N=1)	0 (0%)	0%
UTI and cellulitis (N=1)	Post-ASP (N=1)	Quarter 2 2016 (N=1)	0 (0%)	0%

Appendix I
Compliance based on Antibiotic Class per Group

Antibiotic Class	Group	Compliant (N (%))
Fluoroquinolone (N=118)	Pre-ASP (N=40)	38 (95%)
	Post-ASP (N=78)	76 (97.4%)
Sulfonamide (N=81)	Pre-ASP (N=26)	23 (88.5%)
	Post-ASP (N=55)	47 (85.5%)
Urinary (N=55)	Pre-ASP (N=20)	19 (95%)
	Post-ASP (N=35)	35 (100%)
1st generation cephalosporin (N=31)	Pre-ASP (N=4)	2 (50%)
	Post-ASP (N=27)	12 (44.4%)
3rd generation cephalosporin (N=22)	Pre-ASP (N=8)	6 (75%)
	Post-ASP (N=14)	7 (50%)
Glycopeptide (N=16)	Pre-ASP (N=3)	2 (66.7%)
	Post-ASP (N=13)	11 (84.6%)
Anaerobic (N=12)	Pre-ASP (N=5)	5 (100%)
	Post-ASP (N=7)	7 (100%)
Beta-lactamase inhibitor (N=12)	Pre-ASP (N=4)	0 (0%)
	Post-ASP (N=8)	4 (50%)
Penicillin (N=8)	Pre-ASP (N=2)	0 (0%)
	Post-ASP (N=6)	0 (0%)
Macrolide (N=2)	Pre-ASP (N=0)	n/a
	Post-ASP (N=2)	2 (100%)
Tetracycline (N=4)	Pre-ASP (N=0)	n/a

	Post-ASP (N=4)	0 (0%)
2nd generation cephalosporin (N=3)	Pre-ASP (N=2)	2 (100%)
	Post-ASP (N=1)	0 (0%)
4th generation cephalosporin (N=10)	Pre-ASP (N=5)	0 (0%)
	Post-ASP (N=5)	1 (20%)
Lincosamide (N=5)	Pre-ASP (N=2)	1 (50%)
	Post-ASP (N=3)	1 (33.3%)
Aminoglycoside (N=1)	Pre-ASP (N=0)	n/a
	Post-ASP (N=1)	1 (100%)
Miscellaneous (N=1)	Pre-ASP (N=0)	n/a
	Post-ASP (N=1)	0 (0%)