



Improved Resistance and Decreased Expense Resulting from an Antimicrobial Stewardship Program at a Community Teaching Hospital

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Abstract

Objective: The Inspira Health Network Antimicrobial Stewardship Program sought to optimize therapy through a multitude of interventions to improve patient care, increase bacterial susceptibility, and reduce healthcare expense.

Setting: Inspira Health Network includes a system of three inpatient community hospitals in southern New Jersey.

Methods: We report the 10 year experience of our Antimicrobial Stewardship Program (ASP) providing a timeline summarizing all formal interventions.

Results: During the 10 years of the ASP our hospital experienced significant decreases in antimicrobial expenditures expressed as gross cost, cost per patient admission and as a percentage of total pharmaceutical expenditures with an estimated savings of over \$4,000,000. Concurrently, we experienced a large decrease in resistant organisms including *Pseudomonas aeruginosa* and *Klebsiella pneumoniae*.

Conclusion: An ASP can be successfully pursued in the community hospital setting by utilizing key members of the existing professional staff without widespread, labor-intensive procedures. The positive results of our program came from the cooperation and hard work of its members, the relatively small size of the institution, the strong professional relationships between healthcare providers, and a consistent message relating the importance of stewardship initiatives across the healthcare system.

Background

Bacterial infections have caused significant morbidity and mortality throughout history. Over the decades since the introduction of antibiotics, countless lives have been saved through their use [1,2]. However, expanded antimicrobial use has led to undesired collateral damage antibiotic resistance and *Clostridium difficile* infection [2,3]. According to the CDC, *Pseudomonas*, *Acinetobacter*, *Enterobacteriaceae*, and *Clostridium difficile* are considered major public health threats [4]. This has led to a societal need for proper use of current treatments as well as the development of new agents to treat resistant bacteria. Over the past decade, a multitude of professional organizations including the Infectious Disease Society of America (IDSA), the Society for Healthcare Epidemiology of America (SHEA), and the Pediatric Infectious Disease Society (PIDS) among others, has aggressively promoted the implementation of antimicrobial stewardship programs [5].

Many published studies have demonstrated benefits in expenditures and doses administered, but there is little data demonstrating the desired improvement in bacterial sensitivity patterns [6,7]. Some studies have evaluated the impact of a specific intervention, such as the restriction of one agent, on resistance patterns of that specific or similar agents with varying success [7,8]. Cook et al. [9] described long-term antibiotic use and resistance benefits from a comprehensive program at a large tertiary care hospital utilizing full time pharmacists to perform stewardship activities. This article specifically details the resistance pattern and financial benefits resulting from the implementation of a multifaceted program at a community hospital lacking full time staff dedicated to antimicrobial stewardship.

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Table 1: Antimicrobial Expense.

Year	Antibiotic Expense (\$)	Pt Days	Antibiotic Expense/Pt Day (\$)	Admissions	Antibiotic Expense/ Admission (\$)	Total Drug Expense (\$)	Antibiotic Expense/ Total Drug Cost (%)
2002	642,631	46,912	13.7	10,289	62.46	2,536,041	25
2003	638,010	45,954	13.88	10,243	62.29	2,665,760	24
2004	715,071	56,436	12.67	12,343	57.93	3,898,575	18
2005	902,527	72,053	12.53	16,250	55.54	5,829,064	15
2006	913,211	90,301	10.11	19,238	47.47	5,671,785	16
2007	777,708	88,415	8.8	19,101	40.72	5,419,092	14
2008	775,361	85,112	9.11	18,582	41.73	5,620,776	14
2009	797,782	85,646	9.31	20,198	39.5	5,959,936	13
2010	796,555	86,725	9.18	20,508	38.84	5,628,160	14
2011	699,090	83,877	8.33	21,245	32.91	5,449,451	13
2012	573,916	85,155	6.74	21,955	26.14	5,741,822	10
2013	610,580	85,283	7.16	22,883	26.68	5,972,483	10
2014	617,994	85,239	7.25	24,180	25.56	6,253,637	10
2015	567,828	83,093	6.83	22,360	25.39	7,368,558	8

Table 2: *Klebsiella pneumoniae* Antimicrobial Susceptibilities (%) all locations, all sites of infection.

	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	Net Gain (%)	P value
# of Isolates	600	389	391	465	393	384	398	299	343	323		
Gentamicin	60	74	72	77	84	91	89	92	95	96	36	<0.001
Aztreonam	-	-	-	63	73	81	80	84	90	89	26	<0.001
Ceftriaxone	51	64	66	63	74	81	89	88	90	89	38	<0.001
Ciprofloxacin	47	53	57	61	70	78	80	83	89	88	41	<0.001
Imipenem-cilastatin/Meropenem	89	94	91	82	86	90	87	91	95	95	6	0.002
Piperacillin-Tazobactam	54	68	67	74	81	""	""	81	89	89	35	<0.001
Ampicillin-Sulbactam	42	48	51	58	68	73	72	77	79	78	36	<0.001
Trimethoprim-Sulfamethoxazole	56	60	67	64	75	79	80	82	88	85	29	<0.001

*Aztreonam not tested until 2009

""Error in lab testing materials for Piperacillin/tazobactam in 2011-2012

The majority of ASP reports are published from large academic centers many of which employ full-time faculty as their practicing physicians, have full-time dedicated antimicrobial pharmacists, and salaried house-staff including trainees in Infectious Diseases. The nature of the work force and the culture of such institutions differ greatly from that of the community hospital staffed by private practice physicians without trainees in the clinical work force.

Inspira Health Network is a comprehensive healthcare system located in southern New Jersey which includes three inpatient hospitals totaling >600 patient beds. Inspira was formed in 2012 following the merger between South Jersey Healthcare and Underwood Memorial Hospital and has approximately 34,000 admissions, 150,000 inpatient days, and 168,000 emergency department visits annually. The majority of hospital care is provided by non-employed physicians. Osteopathic training programs in Internal Medicine and Family Medicine began in Vineland in 2011.

Methods

In an effort to stem the tide of increasing bacterial resistance and antibiotic expense, Infectious disease physicians partnered with the Department of Pharmacy Services and Infection Control practitioners to create an antibiotic stewardship program in 2006 centered at the network's largest campus. A four-step strategy was

developed to improve antibiotic use. Phase one utilized our facility antibiogram to identify "high risk antimicrobials." Agents were removed from formulary if they were considered "lost", as defined by a $\geq 20\%$ resistance rate for specific bacteria on the hospital's annual antibiogram. Antibiotics approaching this point were restricted to infectious disease physicians in an effort to preserve their utility. Phase two of the stewardship initiative targeted the appropriate selection of antibiotic agents through disease specific protocols and pharmacist recommendations for patient specific de-escalation of therapy based on culture results. The third phase was the development and implementation of an automatic IV-to-PO conversion policy and appropriate antibiotic renal dosing review daily by clinical and staff pharmacists. Phase four was to reduce use of agents leading to collateral damage by targeting the use of carbapenems, extended spectrum beta-lactams, and 3rd generation cephalosporins. In addition to this stewardship implementation strategy, regular education of physicians, nurses, and pharmacists have been instrumental in optimizing antibiotic use in our facility. A constant effort is made to compare the latest research in Antibiotic Stewardship to current practices and thereby continually improve antimicrobial use. All interventions were achieved without adding any full time staff, but by refocusing current pharmacists and physicians towards stewardship initiatives as part of normal daily activities.

Timeline

2003-2005 - Surgical Care Improvement Program (SCIP) began in 2003 to restrict post-op antibiotics to 24 hrs unless indication for extended duration provided by prescriber. Publish annual antibiograms to guide empiric antibiotic selection and trend resistance patterns. Track antibiotic expense monthly to determine trends and possible cost saving initiatives. 2006-2010 - Daily review of renal function for patients receiving all nephrotoxic or renally adjusted antibiotics - contacted prescriber for adjustments when indicated based on renal dosing recommendations found in medication package inserts. Implemented pharmacy driven automatic IV-to-PO conversion of antibiotics.

Daily review of inpatient positive cultures for appropriateness of therapy by staff pharmacist. Pharmacists responsible for ordered aminoglycoside levels. 2011 - Staff pharmacist trained in Antimicrobial Stewardship through the Society of Infectious Disease Pharmacists (SIDP) to further advance program. Implemented extended infusion of piperacillin/tazobactam to optimize pharmacokinetic properties of time/MIC and reduce cost. Education of nursing regarding correct medication allergy collection. Ciprofloxacin added to formulary in addition to levofloxacin - emphasized use based on site of infection. Computerized Physician Order Entry (CPOE) introduced with diagnosis specific treatment recommendations. 2012 - Replaced ceftazidime on formulary with cefepime based on hospital antibiogram. Implemented extended infusion of imipenem/cilastatin and cefepime to optimize Pharmacokinetic properties of time/MIC. 2013 - Adopted nucleic acid testing method for accurate identification of *Clostridium difficile*. Active promotion of using alternative agents instead of tigecycline following review of published studies and hospital antibiogram [10,11]. Infectious Disease physicians providing routine education for residents.

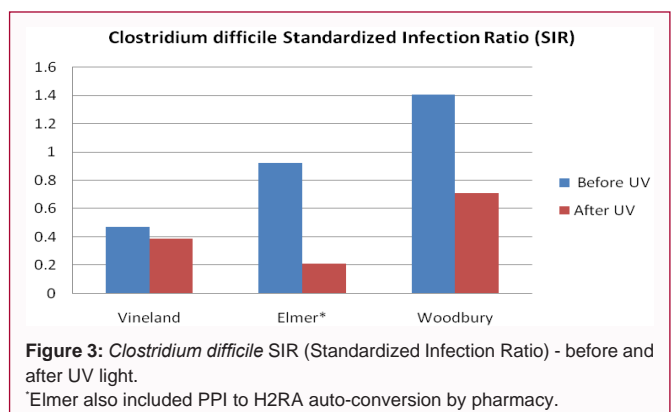
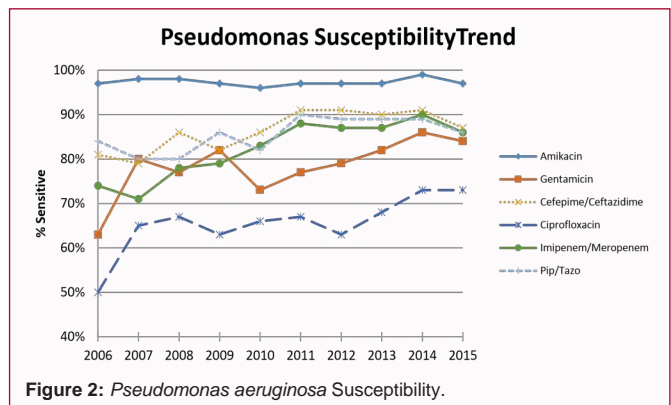
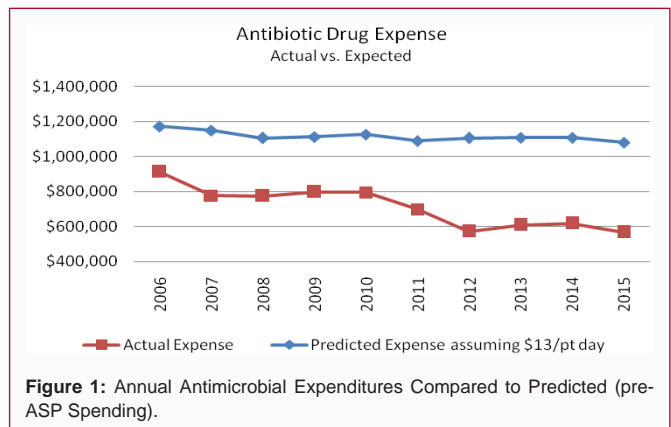
2014 - Pilot program at Elmer location to automatically convert PPIs to H2RAs in an effort to reduce *Clostridium difficile* infections. Targeted *Clostridium difficile* infection reduction through utilizing UV light to aid in disinfecting patient rooms and Operating Rooms in July. Began annual pharmacist educational sessions in appropriate antibiotic usage. Developed antibiograms for various sites of infection to develop specific empiric recommendations and guidelines. Implemented cefazolin IV push to increase enhance communication between nursing and patients.

2015 - Began daily review of target antibiotics for appropriateness (aztreonam, cefepime, carbapenems, piperacillin/tazobactam, tigecycline, linezolid). Formed network wide Antimicrobial Use Committee to unite campus policies and procedures.

Results

Antimicrobial expenditures

Although not the primary focus, a consistently achievable goal for stewardship programs is to control expenditures for antibiotic purchasing and administration while maintaining equivalent or improved patient outcomes. While a recent report presented to the American Hospital Association showed a 38.7% increase in medication expense per admission, Inspira actually observed a decrease in antibiotic expense since 2006 [12]. Through several interventions including antibiotic restriction, IV-to-PO conversion, and culture review with de-escalation of therapy, antibiotic expense has steadily declined while seeing an increase in patient days, admissions, and overall pharmacy expense resulting from the merger of three smaller



community hospitals into a Regional Medical Center (RMC) in 2004 (Table 1). Before the antimicrobial stewardship program was started in 2006, average antibiotic expense was approximately \$13/patient day. Assuming this remained constant, savings at the Vineland campus (RMC) alone totals greater than \$4 million (Figure 1). Although unable to calculate Days of Therapy (DOT) for the years prior to 2011, it has remained relatively stable since monitoring began with values ranging between 700-760 DOT/1000 patient days annually.

Gram negative bacteria resistance

From 2006-2015, both *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* demonstrated a significant improvement in susceptibilities to several key antibiotics including β -lactams, aminoglycosides, and fluoroquinolones. For example, ceftriaxone susceptibility for *Klebsiella pneumoniae* isolates improved to 89% while the national average is approximately 80% with higher resistance rates found in

Inspira's geographical region, the northeastern United States [13] (Table 2). Similarly, significant gains in *Pseudomonas aeruginosa* susceptibility to most antibiotics were also demonstrated. MDR *Pseudomonas*, which is defined as resistance to antibiotics in three classes, improved to equal the national average of 10% [13] (Figure 2).

Clostridium difficile

Through various initiatives including general antibiotic stewardship principles, UV light disinfection of rooms, and pharmacy-based conversion of proton pump inhibitors to famotidine at the Elmer location, hospital-acquired *Clostridium difficile* infection rates decreased at each Inspira Health Network hospital. The relative rate of infection, based on the CDC defined Standardized Infection Ratio (SIR) was reduced by 18% at Woodbury, 49% at Vineland, and 78% at Elmer when comparing six quarters of data before and after mid-2014 (Figure 3). Proton pump inhibitor use was reduced by 31% at the Elmer location during this time period as a result of the pharmacy automatic conversion to famotidine.

Discussion

Antimicrobial stewardship has evolved from a primarily cost-saving measure to a CMS patient-safety mandate and CDC supported initiative. The greatest factor contributing to the success of Antimicrobial Stewardship at Inspira Health Network has been the foresight and cooperation among professionals from a variety of disciplines. The collaboration of a single Infectious Disease physician group, hospital pharmacists, and Infection Preventionists facilitated the implementation of many initiatives aimed at optimizing antimicrobial therapy throughout the hospital system. The promotion of a unified message on the necessity of stewardship convinced hospital administrators to support the program both ideologically and financially prior to widespread clinical and regulatory emphasis.

The institutional focus on antimicrobial stewardship allowed for the implementation of many initiatives over several years. Continual education, policy and procedure changes, detailed monitoring and reporting, formulary management, and daily dedication to stewardship principles led to an institutional culture change committed to optimizing antimicrobial use. The combination of multiple changes allowed Inspira to realize a statistically significant improvement in bacterial resistance while substantially reducing antimicrobial expenditures. It is impossible to attribute these outcomes to a singular intervention, which reinforces the importance of a multi-faceted approach to stewardship.

Diligence and perseverance in implementing and maintaining a collaborative program can pay dividends for years. Protocol directed therapy, culture review with de-escalation, automatic IV-to-PO conversion, antibiotic restriction, and renal dosing recommendations can all contribute to improved susceptibility patterns and monetary savings. These more sensitive bacteria allow providers to utilize

older and less costly agents which further improve the monetary benefit of stewardship programs. Through the implementation of many different stewardship initiatives, it is possible to realize many beneficial outcomes for both patients and the health system.

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