ORIGINAL ARTICLE

Antimicrobial Stewardship at a Large Tertiary Care Academic Medical Center: Cost Analysis Before, During, and After a 7-Year Program

Harold C. Standiford, MD;[1,2] Shannon Chan, PharmD;[3] Megan Tripoli, BA;[1]
Elizabeth Weekes, PharmD;[4] Graeme N. Forrest, MBBS[5]

BACKGROUND. An antimicrobial stewardship program was fully implemented at the University of Maryland Medical Center in July 2001 (beginning of fiscal year [FY] 2002). Essential to the program was an antimicrobial monitoring team (AMT) consisting of an infectious diseases–trained clinical pharmacist and a part-time infectious diseases physician that provided real-time monitoring of antimicrobial orders and active intervention and education when necessary. The program continued for 7 years and was terminated in order to use the resources to increase infectious diseases consults throughout the medical center as an alternative mode of stewardship.

DESIGN. A descriptive cost analysis before, during, and after the program.

PATIENTS/SETTING. A large tertiary care teaching medical center.

METHODS. Monitoring the utilization (dispensing) costs of the antimicrobial agents quarterly for each FY.

RESULTS. The utilization costs decreased from $44,181 per 1,000 patient-days at baseline prior to the full implementation of the program (FY 2001) to $23,933 (a 45.8% decrease) by the end of the program (FY 2008). There was a reduction of approximately $3 million within the first 3 years, much of which was the result of a decrease in the use of antifungal agents in the cancer center. After the program was discontinued at the end of FY 2008, antimicrobial costs increased from $23,933 to $31,653 per 1,000 patient-days, a 32.3% increase within 2 years that is equivalent to a $2 million increase for the medical center, mostly in the antibacterial category.

CONCLUSIONS. The antimicrobial stewardship program, using an antimicrobial monitoring team, was extremely cost effective over this 7-year period.

Infect Control Hosp Epidemiol 2012;33(4):338-345

Antimicrobial resistance is increasing throughout the United States. Furthermore, there are fewer new antimicrobials being developed to treat these resistant organisms.[1] This has led the Infectious Diseases Society of America, the Society for Health Care Epidemiology, and the Centers for Disease Control and Prevention to recommend that hospitals develop antimicrobial stewardship programs (ASPs) to help protect our existing armamentarium as long as possible.[2] Despite this recommendation, many medical centers have not established active programs. Such programs require resources during times when competition for finances is great and return of investment is uncertain.

The University of Maryland Medical Center (UMMC) developed an ASP using an antimicrobial monitoring team (AMT) in calendar year 2001. However, after 7 years the program was discontinued in favor of using the resources to provide additional infectious diseases physicians to enhance infectious diseases consultation throughout the medical center. The rationale for this was that the infectious diseases physicians, via consultations, would provide the necessary stewardship, making the AMT superfluous. This article documents the marked cost savings that resulted after the implementation of the ASP and the AMT in 2001 and the major cost impact that resulted after the program was discontinued.

METHODS

Background

The ASP was established at UMMC in 2001, in response to the perceived need for more appropriate use and the escalating costs of antimicrobial agents. It was continued through June 2008. At the time of the implementation of the ASP,

Affiliations: 1. University of Maryland Medical Center, Baltimore, Maryland; 2. Department of Medicine, University of Maryland School of Medicine, Baltimore, Maryland; 3. Department of Pediatrics, A. I. DuPont Hospital for Children, Wilmington, Delaware; 4. Department of Pharmacy, Denver Health, Denver, Colorado; 5. Division of Infectious Diseases, Portland Veterans Affairs Medical Center, Portland, Oregon.

Received October 1, 2011; accepted December 27, 2011; electronically published March 15, 2012.

 0899-823X/2012/3304-0005$15.00. DOI: 10.1086/664909

UMMC had approximately 28,700 patient admissions per year; this has steadily increased, to 38,590 admissions in fiscal year (FY) 2010. The medical center has a very active cancer center, trauma center, and transplantation program. It has approximately 175 intensive care beds in the facility.

At the time of initiating the program, UMMC had a regulated formulary with restricted antimicrobials that required preauthorization for their use and an active pharmacy and therapeutics committee with an antimicrobial subcommittee. Despite this, annualized antimicrobial purchasing costs increased from $4.7 million in calendar year (CY) 1997 to over $8 million in CY 2000. Additionally, hospitals in Maryland were to be reimbursed for the disease entity treated (a drug-related group [DRG] system) instead of for the expenses incurred. This provided an additive monetary incentive for initiating the ASP.

Developing the ASP and the AMT

Leadership of the initiative was established within the infection control program and by working closely with the pharmacy department. The program was developed by the medical director for infection control and the infectious diseases clinical pharmacist and vetted at a number of meetings with key hospital personnel, including the director of pharmacy, the chief of infectious diseases, the vice president of quality for the medical center, and the chief medical officer. Essential and central to the ASP was the establishment of an AMT. This team consisted of (1) an infectious diseases physician with an initial dedicated effort to the program of 25% that subsequently increased to 50% and (2) a clinical pharmacist with infectious diseases training with a dedicated effort to the program of 80%. A data analyst with a dedicated effort of 5% and direction of the program was incorporated in the infection control program and required no additional resources.

Responsibilities of the AMT

The duties of the team were to provide an active computer-assisted real-time review of antimicrobial orders for the designated restricted antimicrobials and to provide active intervention when necessary. During their review, the team attempted to (1) identify ineffective or excessive antimicrobial coverage, (2) assure that the orders adhered to policies and guidelines, (3) discontinue unnecessary double coverage, (4) determine patients whose treatment could be converted safely from parenteral to oral therapy (IV-PO), and (5) suggest infectious diseases consults for difficult and complex cases. The team prioritized for review those patients receiving restricted antimicrobial agents and those areas of the medical center not served by specialized infectious diseases physicians such as were present in the trauma center.

Preauthorization Using the "BUGS Beeper"

Prior to the stewardship program, preauthorization for the use of certain antimicrobial agents was required, and this consent was provided by the infectious diseases consult service. To improve the process, a "BUGS beeper" program was developed. In this a beeper, activated by dialing "BUGS," was carried by the on-duty infectious diseases fellows on a rotational schedule. The fellow was supervised by the infectious diseases–trained faculty member assigned to the antimicrobial team. If preauthorization was not provided, the attending physician on the requesting service could directly call the attending physician on the antimicrobial team. If the conflict was still not resolved, a dose of the antimicrobial agent would be administered and an infectious diseases consult would be obtained in order to clarify the situation. Initially, an on-duty fellow carried the beeper until 10:00 p.m., but this was soon extended to 24 hours, 7 days a week. The program was initiated in late January 2001 and became fully implemented by July 2001 (beginning of FY 2002).

Development of Guidelines and Policies

To provide consistency for the physicians ordering the antimicrobials and for the antimicrobial team monitoring their use, guidelines and policies were developed where applicable. The AMT frequently provided leadership when formulating these guidelines, but attempts were made to have those most involved with their use participate in the development. When the policies and guidelines were written, they were approved through the normal channels, including the antimicrobial subcommittee of the pharmacy and therapeutics (P&T) committee, the parent P&T committee, and the medical executive committee, when appropriate.

Financial Goals

The financial goals for the antimicrobial program, which were based on those of other programs using an active interventional model at the time, were purposefully conservative: to save 10%–20% of the costs of antibiotics, based on an antimicrobial budget of $6 million per year over a 3-year period (a savings of $600,000–$1,200,000 over the 3-year period).[3]

Data Analysis

The actual costs for the antimicrobials were determined by the pharmacy service, and they represented the purchasing cost for the drug per unit. These costs were obtained by the pharmacy administration, independent of the antimicrobial team. The data program captured the utilization of antimicrobials, which was defined as those antimicrobials ordered by the provider who was caring for the patient and dispensed by the pharmacy. Any unused medication returned to the pharmacy was subtracted from this amount. Initially, these utilization data were captured using the Mega Source program. The data in this program were transferred using Monarche into Access, so that they could be categorized and manipulated into a usable database. On October 7, 2002 (second quarter of FY 2003), PharmNet was initiated. During this changeover, there were no data collected for the first 7 days

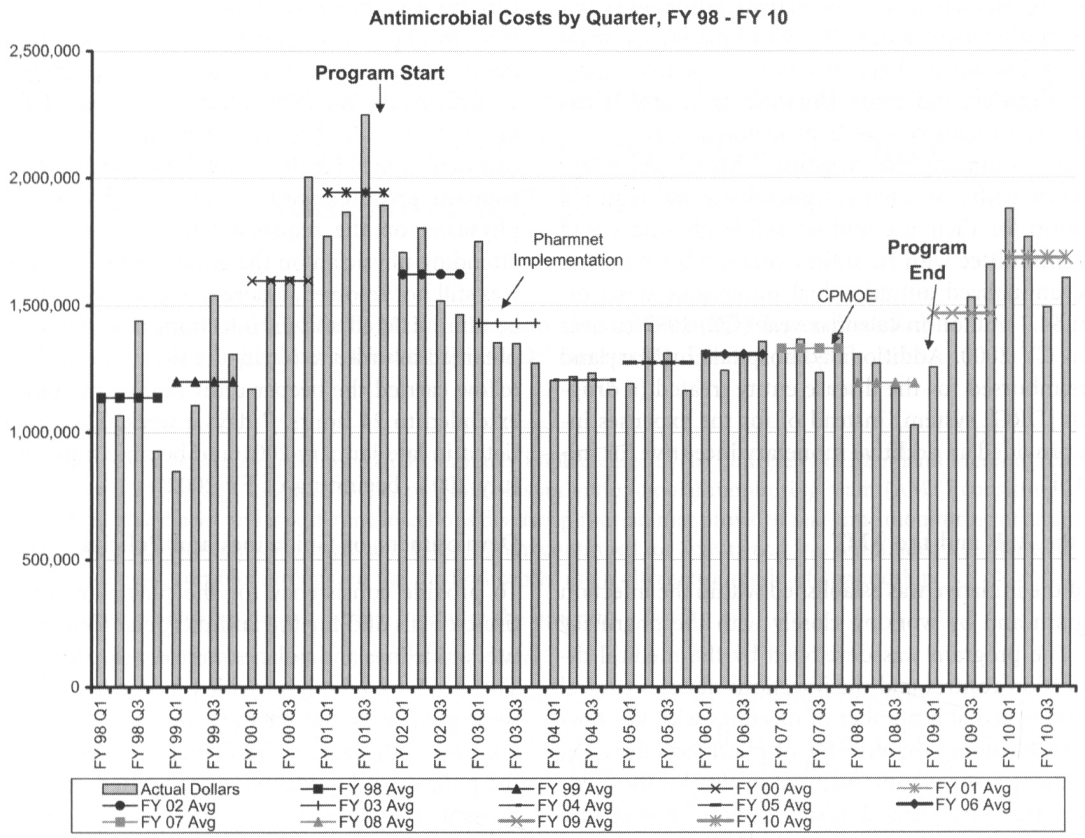

FIGURE 1. Quarterly costs of all antimicrobials, beginning with the first quarter of fiscal year 1998 (July 1997) and continuing through the 4th quarter of fiscal year (FY) 2010 (June 1, 2010). The solid horizontal lines represent the average cost for each fiscal year. The beginning and end of the antimicrobial stewardship program in the 3rd quarter of fiscal year 2001 and ending in the 4th quarter of fiscal year 2008, respectively, are indicated with arrows.

of that quarter. Instead, data for this period were estimated by extrapolating costs for the remaining portion of the quarter. Data from the PharmNet program were transferred into Access so that they could be categorized in a manner similar to the data from the Mega Source program.

Beginning in May 2004, PharmWatch (Cereplex; now owned by Premier), a decision-support program designed to assist in antimicrobial utilization, was used to evaluate for a 3-month period one-half of the patient population monitored by the antimicrobial team. Results of this evaluation have been reported previously.[4] The use of this program was subsequently expanded to include the entire hospital.

Defined Daily Doses (DDDs)

DDDs were determined according to dosages recommended by the World Health Organization (http://www.whocc.no/atc_ddd_index/). When no daily dosage was suggested by that organization, one was assigned that was thought to represent a typical daily dosage for adults with normal renal and hepatic functions. When a dosage amount was assigned, it was not changed throughout the evaluation period. The DDDs are expressed per 1,000 patient-days.

Quality Indicators

To monitor the safety of the stewardship program, we monitored selective quality indicators for the medical center including length of stay, readmissions within 30 days, and 30-day mortality. The DRG case mix index was monitored to ensure that changes in outcomes were not related to this index.

Statistical Analysis

The χ^2 test was used to compare the annual and cumulative reductions of antibiotic usage overall and then after introduction and after discontinuation of the AMT. To examine the trend in the prevalence of antimicrobial utilization over time, the results were compared using the χ^2 test for trend. For all analyses, the threshold for establishing statistical significance was set at $P < .05$. Statistical analyses were completed using the SPSS statistical package (ver 16).

https://doi.org/10.1086/664909 Published online by Cambridge University Press

RESULTS

Cost Savings after Implementation of the ASP

The utilization costs by quarter for the medical center from FY 1998 through FY 2010 are presented in Figure 1. (For example, the fiscal year for 2001 extends from July 1, 2000, through June 30, 2001.) The overall upward trend of costs that occurred from FY 1998 through the third quarter of FY 2001 (prior to the time of implementation of the ASP) is readily apparent. Similarly, the downward trend that occurred after the program was fully implemented (beginning in FY 2002) is marked, particularly in the first 3 years. Thereafter, a relatively stable period exists from FY 2004 until the first quarter of FY 2009, at which point the program was terminated. Following this termination, the costs for antimicrobials increase dramatically for the next 2 years.

The yearly costs before the stewardship program was implemented (FY 2001), for the 7 years of the program's existence (FY 2002–FY 2008), and for 2 years after it was terminated (FY 2009–FY 2010), including dollars per patient-days, are presented in Table 1. These costs are further separated into antimicrobial categories. The total expenditures for antimicrobial agents were reduced from $44,181 to $23,933 per 1,000 patient-days (45.8%; $P = .04$) over the duration of the program. In terms of costs for the hospital, a reduction of $2,949,705 occurred for the medical center within the first 3 years after implementation of the ASP.

By antimicrobial category, for FY 2001 (baseline), almost one-half ($3.7 million) of the entire budget of $7,774,588 went to pay for antifungal agents, with an additional $3.5 million (45%) paying for antibacterial agents. Together, these 2 categories were responsible for 93% of the antimicrobial costs. After the program began, the majority of the cost savings occurred in the antifungal category, which were reduced by $2,251,976 (60.7%) over the 3-year period, driven primarily by treatment guidelines for fungal infections in the medical center ($P = .003$). However, costs of antibacterial agents were also reduced by $513,044 (14.6%) over this 3-year period after the program was implemented ($P = .035$). Reductions are noted for the beta-lactam antibiotics as a group (10.2%), which include the carbapenems (primarily imipenem), the cephalosporins, and the penicillins (see Table 2). There was a slight reduction in the use of the antipseudomonal penicillins, primarily piperacillin/tazobactam, whereas use of the aminopenicillins (primarily ampicillin/sulbactam) increased. Reductions were also noted for the miscellaneous antimicrobial agents as a group, including vancomycin, quinipristin/dalfopristin, and metronidazole. The cost of the quinolones was reduced by 47% over the 3-year period. From FY 2004 to FY 2008, costs appeared to stabilize, decreasing by only $48,220 (1%); however, when patient-days are considered, this was a decrease of $3,785 per 1,000 patient-days, or 13.7%

Switch from Intravenous to Oral Delivery

An early intervention initiated by the stewardship program was the switch from intravenous to oral routes of delivery when the oral intake of other drugs was apparent and when the bioavailability of the antimicrobial agents permitted it. This was subsequently instituted as a policy. The reduction of costs resulting from this initiative was $179,285 in FY 2002 compared with baseline (FY 2001). The savings resulting from this switch were most apparent for fluconazole ($142,534) and linezolid ($19,597).

The increases in costs by antimicrobial category after the program was discontinued also is noted in Table 1, with the effects on specific antimicrobials presented in Table 2. There was an immediate increase in cost of $1 million during the first year after the program was discontinued and an additional increase of $873,184 during the second year, which represents an increase in cost of 41.2% for the 2-year period over the last year of the program (FY 2008; $P = .025$). After the discontinuation of the program, the increased costs primarily occurred in the antibacterial category, particularly the agents acting against gram-positive organisms, including vancomycin, linezolid, and daptomycin (see Table 2; $P = .002$). Also during

TABLE 1. Cost of Antimicrobials by Category, Before, During, and After the Antimicrobial Stewardship Program

	Before	During							After	
	FY 2001	FY 2002	FY 2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010
Antibacterials	3,503,878	3,017,828	3,189,081	2,990,834	3,117,084	3,283,178	3,498,911	3,183,232	4,020,487	4,751,641
Antifungals	3,710,465	2,926,270	2,011,050	1,458,489	1,605,573	1,513,837	1,343,056	1,154,256	1,268,795	1,268,498
Antimycobacterials	17,416	16,919	14,843	17,765	27,985	16,518	15,498	10,336	34,879	66,135
Antiparasitics	5,056	5,839	2,822	2,387	2,832	3,124	4,698	5,647	9,637	11,416
Antivirals	424,627	470,503	441,811	345,674	333,553	403,628	441,576	403,324	503,220	609,474
Total	7,774,588	6,490,231	5,667,893	4,824,883	5,094,800	5,227,490	5,315,848	4,776,663	5,869,764	6,742,948
Total per 1,000 patient-days	44,181	35,974	30,951	27,718	27,031	28,146	27,363	23,933	27,833	31,653
Savings (loss) from previous year		1,284,357	822,338	843,010	(269,917)	(132,690)	(88,358)	539,185	(1,093,101)	(873,184)

NOTE. Costs are in US dollars. FY, fiscal year.

https://doi.org/10.1086/664909 Published online by Cambridge University Press

TABLE 2. Utilization Costs for Selected Antibacterial and Antifungal Agents Before, During, and After the Antimicrobial Stewardship Program

	Before	During							After	
	FY 2001	FY 2002	FY 2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010
Antibacterials	3,503,878	3,017,828	3,189,081	2,990,834	3,177,084	3,283,178	3,498,911	3,183,132	4,020,487	4,751,641
Carbapenems	369,047	319,933	326,954	341,042	357,589	277,989	363,596	405,181	548,137	541,279
Imipenem	348,726	257,882	304,715	313,190	342,389	256,860	310,791	348,642	143,578	63
Doripenem	0	0	0	0	0	0	0	0	293,453	420,300
Meropenem	0	0	0	24,506	6,838	15,638	33,966	31,295	79,504	73,093
Ertapenem	0	0	0	3,347	8,362	5,491	18,839	25,245	32,203	47,823
Penicillins										
Piperacillin/ tazobactam	874,728	791,625	880,279	847,236	957,241	1,069,452	1,021,410	877,809	1,339,270	1,465,469
Ampicillin/ sulbactam	206,505	202,394	287,697	259,691	276,605	196,909	193,521	134,874	105,370	63,024
Cephalosporins										
Ceftriaxone	404,352	216,748	332,965	260,586	244,449	278,274	125,188	67,694	44,482	90,231
Cefepime	225,052	173,304	273,947	209,023	222,517	222,385	366,537	271,541	160,392	166,591
Total quinolones	336,773	299,349	203,674	179,896	168,783	177,561	141,323	92,831	47,410	47,348
Ciprofloxacin	155,902	83,542	32,560	27,026	35,442	55,203	79,106	62,319	21,342	17,147
Gatifloxacin	23,359	163,810	155,305	145,216	129,904	95,047	6	0	0	0
Moxifloxacin	0	0	14	56	545	16,183	60,836	30,251	25,852	29,484
Miscellaneous										
Vancomycin	177,830	160,211	136,395	111,177	132,576	149,188	188,117	193,424	249,130	469,830
Linezolid	164,396	136,922	220,484	287,461	258,030	332,132	427,656	343,725	499,845	643,968
Daptomycin	0	0	0	5,074	16,058	79,006	162,501	102,944	254,294	369,779
Tigecycline	0	0	0	0	0	0	0	187,305	274,554	199,766
Metronidazole	177,346	167,516	71,624	27,861	30,869	34,947	28,170	11,673	8,763	20,990
Quinupristin/ dalfopristin	102,858	49,912	12,724	4,158	12,782	7,679	0	8,607	4,321	10,307
Total antifungals	3,710,465	2,926,270	2,011,050	1,458,489	1,605,573	1,513,837	1,343,056	1,154,256	1,268,795	1,268,498
Amphotericin B	64,503	50,567	16,528	1,138	1,126	1,108	1,451	742	660	4,511
ABLC	1,591,090	1,977,355	1,139,801	440,191	464,585	276,213	241,977	157,147	151,587	152,960
LAMP	1,383,179	15,528	12,137	41,623	52,473	267,896	90,221	237,551	175,303	189,373
Fluconazole	604,611	461,486	369,196	361,525	342,970	337,820	251,431	51,127	54,829	31,959
Voriconazole	0	0	234,367	341,298	340,649	374,922	385,788	400,351	505,229	486,359
Caspofungin	23,949	137,780	124,073	222,690	359,473	184,608	172,443	23,956	28,162	26,958
Micofungin	0	0	0	0	0	26,155	160,841	253,678	289,640	284,304

NOTE. Costs are in US dollars. ABLC, amphotericin B lipid complex; FY, fiscal year; LAMP, liposomal amphotericin B.

this 2-year period, the costs of the antifungals as a class increased by approximately $100,000 (9.9%; $P = .34$).

Utilization Costs by Hospital Location

Cost savings after the program was implemented were observed in all 3 major areas of the medical center: the cancer center, the shock trauma center, and the main hospital (Table 3). However, the savings that occurred during the first 3 years of implementation were most apparent in the cancer center (~$2,000,000). Cost savings also occurred in the medical intensive care unit (MICU), the surgical ICU (SICU), and the transplantation service.

Discontinuation of the Program

After the program was discontinued, cost increases were most marked in the main portion of the medical center ($1,585,957), with very little added cost occurring in the cancer center. Costs in the shock trauma center also increased, but a new 12-bed ICU opened in this area at that time. Increases in costs after the ASP was terminated were also noted in the MICU and the SICU.

DDDs per 1,000 Patient-Days

Since 2004, we were able to obtain DDDs per 1,000 patient-days for all of the antimicrobial agents. These are indicated in Table 4 for selected antimicrobials and for the antimicrobial categories. Overall, there was a significant decrease in DDDs from FY 2004 through FY 2008, when the program was terminated. Total antimicrobial DDDs per 1,000 patient-days decreased by 439 (29%; $P = .014$), and for antibacterial agents they decreased by 323 (27.5%; $P = .03$). DDDs per 1,000 patient-days for antifungals and antivirals were also reduced, by

https://doi.org/10.1086/664909 Published online by Cambridge University Press

TABLE 3. Comparative Costs of Antimicrobials in Specific Locations

	Before	During						After	
	FY 2001	FY 2002	FY 2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010
Cancer center	3,003,319	2,432,623	1,661,372	966,490	982,074	1,237,998	1,067,555	1,036,283	1,109,035	1,097,686
Shock trauma	798,707	641,530	600,129	690,290	656,022	669,326	701,885[a]	552,297	672,938	921,395
Main hospital	3,972,563	3,416,078	3,427,937	3,167,467	3,454,957	3,317,712	3,546,094	3,186,464	4,063,116	4,772,421
Selected units										
SICU	791,406	341,268	265,699	202,674	207,206	197,553	253,504	183,470	309,148	267,560
MICU	506,960	395,089	187,329	188,550	241,250	245,562	503,242[b]	498,723	699,179	656,267
Transplant	985,471	872,275	594,148	647,068	499,521	505,801	490,991	417,755	393,896	540,069

NOTE. Costs are in US dollars. FY, fiscal year; ICU, intensive care unit; MICU, medical ICU; SICU, surgical ICU.

[a] Increase in number of ICU beds from 24 to 36 on January 1, 2007.

[b] Increase in number of MICU beds from 16 to 29 on April 19, 2006.

24% and 57%, respectively ($P = .001$). After the program was terminated, the overall DDDs per 1,000 patient-days for all antimicrobials increased minimally during the 2-year period (5.2%; $P = .014$). However, there was an increase in the uses of cefepime (14.3%), piperacillin/tazobactam (10.5%), and antibacterials against gram-positive organisms, including linezolid (21.2%), daptomycin (113%), and vancomycin (32.3%). Echinocandin usage also increased, by 121%.

Quality Indicators

Quality indicators, including length of stay, readmissions, and mortality, are noted in Table 5. There were no significant changes in these parameters before, during, or after the program. There were no significant changes in the DRG case mix index after the program ended, indicating that changes in antimicrobial use were not caused by a change in the severity of our cases.

DISCUSSION

ASPs have been recommended to prevent antimicrobial resistance, decrease disease from *Clostridium difficile* infections, and curb adverse reactions to antimicrobials.[5-8] Nevertheless, establishing stewardship programs requires resources. This report focuses on the cost analysis of such a program and demonstrates that the establishment of an ASP incorporating an AMT can be very cost effective in a large tertiary care teaching medical center.

This program resulted in a marked decrease in costs immediately after the program was initiated and a decrease in costs of 37% within the first 3 years. In terms of dollars, this was equivalent to a $3 million decrease in yearly costs over this period of time. Most of this decrease was related to the antifungal category of antimicrobials and was centered in the cancer center and facilitated by guidelines developed addressing this area of concern. Nevertheless, there were significant cost savings with other antimicrobial categories as well. This included antibacterial agents, for which costs decreased over $500,000. The IV-to-PO-switch therapy program resulted in a decrease of $180,000 within the first year of the program. Nor was the decrease in costs entirely centered within the cancer center. The shock trauma center, which has a team of infectious diseases physicians who see the majority of the trauma patients, also experienced reduced antimicrobial costs, particularly of antibacterial agents. The main hospital also experienced reduced costs, including in the MICU, the SICU, and the transplantation service.

Although the cost of antimicrobials appeared to remain stable from 2004 to 2008, an additional reduction of 13.7% occurred when patient-days are considered, in spite of drug price inflation.[9] Also noted during this period was a decrease in DDDs per 1,000 patient-days, from 1,512 to 1,073 (29%) for all antimicrobials.

The benefit of the antimicrobial program was apparent following its introduction, but the strength of this observation is enhanced by the rapid increase in antimicrobial costs that occurred after the program was terminated. Within 2 years these costs increased by 41.2%, or almost $2 million; however, this increase was not related to an increase in the use of antifungals (which were noted to decrease on initiation of the program) but instead primarily involved antibacterial agents. Costs increased with piperacillin/tazobactam, carbapenems, and many of the agents with activity against the gram-positive bacteria, including vancomcyin, daptomycin, and linezolid. External factors may have also partially contributed to this increase in cost. The guidelines for monitoring vancomycin, which called for an increase in its dosing, were published in January 2009, 6 months after our program was discontinued.[10] Also, there was an increase in the number of clinical culture isolates of vancomycin-resistant *Enterococcus* (but not bloodstream infections) in FY 2009 and FY 2010, after the program ended, which also could have contributed to an increase in the use of daptomycin and linezolid.

In 1999, Carling et al evaluated the cost of parenteral antimicrobials in 14 acute care hospitals and found that those 5 facilities that included a system for active prospective intervention that involved a clinical pharmacist and a staff-level infectious diseases–trained physician cost (per 1,000 patient-days) 3%–30% below the mean for all of the hospitals ana-

TABLE 4. Defined Daily Doses per 1,000 Patient-Days of Selected Antimicrobials

	During program					After program	
	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010
Total antibacterials	1,174	1,023	1,023	990	851	868	867
Quinolones	123	103	100	96	88	81	78
Moxifloxacin	1	1	6.9	41	36	32	32
Gatifloxacin	99	81	59	0	0	0	0
Ciprofloxacin	17	19	28	54	52	49	46
Cephalosporins	201	177	181	190	163	152	159
Cefepime	57	54	57	70	56	59	64
Penicillins							
Piperacillin/tazobactam	98	92	100	91	76	95	84
Carbapenems	25	24	19	26	28	30	30
Doripenem	0	0	0	0	0	14	21
Imipenem	23	23	17	20	22	8.3	0
Meropenem	2.5	0.7	1.6	3.1	2.8	5.4	3.9
Ertapenem	0.5	1.3	0.8	2.7	3.3	2.9	5.1
Miscellaneous							
Linezolid	16.0	12.5	16.5	20.2	15.6	19.6	18.9
Daptomycin	1.0	2.2	7.4	10.9	6.8	10.2	14.5
Vancomycin	85.1	92.6	107	106	99	98	131
Colistin	0.3	0	0	0.1	0.1	3.2	7.7
Tigecycline	0	0	0	0	8.7	13.2	9.2
Antifungals	150	129	129	123	120	139	142
Fluconazole	78	63	66	61	69	71	66
Voriconazole	28	22	27	24	25	31	29
Caspofungin	4.6	9.1	5.7	7.2	0.4	0.4	0.4
Micafungin	0	0	2.2	9.2	14	23	31
Total antivirals	142	99	125	116	63	79	81
Total antimicrobials	1,512	1,303	1,321	1,272	1,073	1,125	1,129

NOTE. FY, fiscal year.

lyzed, and all 5 had costs that were below the those of the 9 hospitals that used only passive measures.[3] Passive measures included measures such as automatic stop orders, antimicrobial order forms, limited formularies, measures to control contact between pharmaceutical representatives and prescribers, educational intervention (eg, institutional guidelines for antibiotic use), and restricted antibiotic susceptibility reporting by the microbiology laboratory. It was partially on the basis of this report that we established an active program with an AMT for active prospective antimicrobial monitoring and intervention.

Prior to initiating the program with the team, there was restriction of antimicrobials and a preauthorization process was in place. Although this process was made simpler using a "BUGS" beeper to call for preauthorization, the basic process that was in use prior to the initiation of the program remained in effect. The addition of the AMT, through real-time monitoring, assured that this preauthorization process was followed and that the information given at the time of the request was accurate. Furthermore, after the program was terminated, use of the "BUGS" beeper for authorization continued but the antimicrobial team was no longer present to assure that the information given to request the antimicrobials was accurate and that the release of the antimicrobials adhered to the policies of the medical center and were appropriate in the treatment situation. Thus, the major implementation in the program was the addition of the AMT.

Another component of the ASP, which enhanced the effectiveness of the AMT, was the use of a computer decision support system.[4] Indeed, this was developed to do what the AMT was already doing, but to make the team more efficient in their duties. This computer program organized and alerted the AMT when restricted drugs were ordered and indicated where the patient resided, other medications the patient was receiving, and microbiologic laboratory results. In addition to notifications of patients receiving "restricted" antimicrobials, some other alerts included notification if a patient was receiving double antimicrobial coverage or no antimicrobial coverage for an identified pathogen and identification of potential candidates for the switch from IV to oral therapy and patients who had received 5 days of antimicrobial therapy without the isolation of potential pathogens. In a carefully controlled blinded study, it was projected that this system saved the UMMC over $600,000, compared with the use of the antimicrobial team without the decision-support system if it were used in the major portion of the medical facility

TABLE 5. Hospital Quality Statistics Before, During, and After the Stewardship Program

	Before	During						After	
	FY 2001	FY 2002	FY 2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010
Admissions	28,667	28,959	29,702	30,507	30,079	34,752	35,888	35,982	36,447	38,590
Patient-days	175,971	180,416	183,122	184,247	185,462	184,903	192,568	191,697	201,154	205,232
LOS	6.1	6.2	6.18	6.05	6.37	5.48	5.56	5.54	5.74	5.55
Unplanned readmissions	1,533	1,290	1,232	1,496	1,652	1,735	2,080	2,218	2,375	2,164
% of admissions	5.30	4.50	4.10	4.90	4.96	4.99	5.80	6.15	6.02	5.75
Mortality	867	901	908	876	898	1,019	970	983	948	981
% of admissions	3.0	3.1	3.1	2.9	2.9	2.6	2.8	2.7	2.7	2.5
DRG CMI	...	1.638	1.701	1.752	1.792	1.779	1.788	1.762	1.742	1.741

NOTE. DRG CMI, drug-related group case mix index; FY, fiscal year; LOS, length of stay.

for an entire year. When the stewardship program was terminated, the decision-support system was also not continued.

The stewardship program was discontinued because of some dissatisfaction over the preauthorization requirements as well as so that the funding for the program could be used to provide personnel for additional infectious diseases consultation throughout the medical center. The rationale for this change was that infectious diseases experts were the best trained individuals to make the necessary decisions for appropriate therapy in this difficult patient population and thereby could provide antimicrobial stewardship, therefore, rendering the AMT redundant. We cannot say for certain that this would not be an effective strategy, given more time. However, costs have continued to increase and the quality markers have remained stable, suggesting that more and more costly antimicrobials are being used, with no obvious increase in benefit.

In summary, the ASP with a preauthorization protocol using a "BUGS" beeper, an AMT to assure appropriate use, and computer decision-support assistance was an extremely cost-effective model for antimicrobial stewardship over a period of 7 years, and its discontinuation has proven to be very costly. On the basis of this information an ASP using an AMT has been restarted, but an automatic infectious diseases consult has replaced the preauthorization requirement for "restricted" antimicrobials.

ACKNOWLEDGMENTS

We would like to thank the following for their help in developing and maintaining the Antimicrobial Stewardship Program: for the development of the program: David Rorison, MD, MBA (senior vice president of medical affairs), Sherry Perkins, PhD, RN (vice president for clinical effectiveness), and Michael Donnenberg, MD (chief of the division of infectious diseases); from the antimicrobial team: Molly Kent, Pharm D; regarding policy and guidelines: Michael Kleinberg, MD (division of infectious diseases); and for data analysis: Marshall Bryant (pharmacy service).

Potential conflicts of interest. All authors report no potential conflicts of interest relevant to this article. All authors submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest, and the conflicts that the editors consider relevant to this article are disclosed here.

Address correspondence to Harold C. Standiford, MD, Medical Director for Antimicrobial Stewardship, University of Maryland Medical Center, 110 South Paca Street, 6th Floor, Baltimore, MD 21201 (hstandiford@umm.edu).

REFERENCES

1. Boucher HW, Talbot GH, Bradley JS, et al. Bad bugs, no drugs: no ESKAPE! an update from the Infectious Diseases Society of America. *Clin Infect Dis* 2009;48:1–12.
2. Dellit TH, Owens RC, McGowan JE, et al. Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. *Clin Infect Dis* 2007;44: 159–177.
3. Carling PC, Fung T, Coldiron JS. Parenteral antibiotic use in acute-care hospitals: a standardized analysis of fourteen institutions. *Clin Infect Dis* 1999;29:1189–1196.
4. McGregor JC, Weekes E, Forrest GN, et al. Impact of a computerized decision support system on reducing inappropriate antimicrobial use: a randomized controlled trial. *J Am Med Inform Assoc* 2006;13:378–384.
5. Carling P, Fung T, Killion A, et al. Favorable impact of a multidisciplinary antibiotic management program conducted during 7 years. *Infect Control Hosp Epidemiol* 2003;24:699–706.
6. Stevens V, Dumyati G, Fine S, et al. Cumulative antibiotic exposures over time and the risk of *Clostridium difficile* infection. *Clin Infect Dis* 2011;53:42–48.
7. Fishman N. Antimicrobial stewardship. *Am J Med* 2006;119: S53–S61.
8. Singh N, Rogers P, Atwood CW, et al. Short-course empiric antibiotic therapy for patients with pulmonary infiltrates in the intensive care unit. *Am J Respir Crit Care Med* 2000;162:505–511.
9. Hoffman JM, Shan ND, Vermeulen LC, Schumock GT, Grim P, Hunkler RJ, Hontz KM. Projecting future drug expenditures: 2007. *Am J Health Syst Pharm* 2007;64:298–314.
10. Rybak M, Lomaestro B, Rotschafer JC, et al. Therapeutic monitoring of vancomycin in adult patients: a consensus review of the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, and the Society of Infectious Diseases Pharmacists. *Am J Health Syst Pharm* 2009;66:82–98.