MAJOR ARTICLE

Impact of a Hospital-Based Antimicrobial Management Program on Clinical and Economic Outcomes

Robert Gross,[1,3] Amy S. Morgan,[4] Denise E. Kinky,[6] Mark Weiner,[2] Gene A. Gibson,[5] and Neil O. Fishman[1]

Divisions of [1]Infectious Diseases and [2]General Internal Medicine, Department of Medicine, and [3]Center for Clinical Epidemiology and Biostatistics, University of Pennsylvania School of Medicine, [4]Philadelphia College of Pharmacy, University of the Sciences in Philadelphia, and [5]Department of Pharmacy Services, University of Pennsylvania Health System, Philadelphia; and [6]Systems Consulting Company, Haddon Heights, New Jersey

Inappropriate use of antimicrobial agents results in unnecessary exposure to medication, persistent or progressive infection, emergence of resistance, and increased costs. We implemented a program to control use of restricted agents while improving care. This study compared 2 major mechanisms for improving use of antimicrobial agents: (1) recommendations made by the Antimicrobial Management Team (AMT), which included a clinical pharmacist backed up by a physician from the Division of Infectious Diseases (ID), and (2) recommendations made by ID fellows. Outcome measures included appropriateness of recommendations, cure rate, number of treatment failures, and cost of care, which were assessed for 180 patients. The AMT outperformed the ID fellows in all outcomes examined by the study (including appropriateness [87% vs. 47%; $P < .001$], cure rate [64% vs. 42%; $P = .007$], and treatment failures [15% vs. 28%; $P = .03$]), although the differences in economic outcomes between cases managed by the AMT and those managed by the ID fellows were not statistically significant. In an academic setting with a restricted formulary, the AMT demonstrated better antimicrobial prescribing than ID fellows.

Inappropriate use of antibiotics results in a variety of adverse outcomes. Overly narrow coverage increases the risk of therapeutic failure, whereas overly broad coverage increases the risk of superinfection [1]. Furthermore, injudicious use of antimicrobial agents likely contributes to the emergence of resistance. All of these effects result in increased costs [2].

Several strategies have been used to decrease injudicious antimicrobial use [3]. Formulary restrictions limit the availability of specific agents. Educational programs can increase clinicians' knowledge of judicious prescribing practices. Streamlining involves having an expert review patients' antimicrobial regimens and make recommendations to their providers about stopping or narrowing therapy [4, 5].

Each intervention has limited effectiveness [3]. Formulary restriction can be circumvented in most situations. Educational programs may influence only those committed to behavioral change [6]. Streamlining is typically applied after the antimicrobial therapies have been initiated, which allows some degree of inappropriate exposure [7]. In addition, compliance with streamlining is frequently voluntary, a circumstance that limits its effectiveness [5].

We developed and implemented a comprehensive antimicrobial management program in 1993 at the Hospital of the University of Pennsylvania in an effort to improve use of antimicrobial agents. The program incorporated the strengths of these strategies while addressing their limitations. Our primary goal was to improve the quality of patient care by ensuring the effectiveness of treatment regimens. Toward this end, we

Received 27 July 2000; revised 21 November 2000; electronically published 5 July 2001.

Reprints or correspondence: Dr. Robert Gross, Center for Clinical Epidemiology and Biostatistics, University of Pennsylvania School of Medicine, 804 Blockley Hall, 423 Guardian Dr., Philadelphia, PA 19104-6021 (rgross@cceb.med.upenn.edu).

Clinical Infectious Diseases 2001; 33:289–95

1058-4838/2001/3303-0003$03.00

restricted the use of broad-spectrum, inordinately expensive antimicrobial agents with unfavorable adverse-effect profiles in favor of narrower-spectrum agents that were less expensive and had better adverse-effect profiles. We also restricted agents, such as vancomycin, that have been linked to the emergence of resistant organisms. The program was also designed to improve clinicians' knowledge about and attitudes toward antimicrobial use.

The program was implemented in several steps. First, the formulary at the Hospital of the University of Pennsylvania was redesigned to include a single unrestricted antimicrobial agent in each class, with restricted antimicrobial agents to be released only after approval by the Antimicrobial Management Program. Second, in collaboration with the Infection Control Program and the Division of Infectious Diseases (ID) at the hospital, guidelines for appropriate therapy were developed, published in handbook form, and distributed to all residents and fellows, including the ID fellows [8]. Finally, the Antimicrobial Management Team (AMT) was created to approve use of restricted agents during weekdays; the team included a doctoral-level clinical pharmacist with postgraduate training in anti-infective therapy and the director of the Antimicrobial Management Program, an ID physician.

Antibiotic approval was provided by means of a dedicated beeper. The service was staffed by an AMT member between 8:00 AM and 5:00 PM on weekdays and by the first- and second-year ID fellows between 5:00 PM and 11:00 PM on weekdays and between 8:00 AM and 11:00 PM on weekends. Between 11:00 PM and 8:00 AM, restricted agents were released pending morning evaluation. The Antimicrobial Management Program personnel (AMT member or ID fellow) notified the pharmacy of approvals. If a request was denied, an alternative agent was suggested.

METHODS

Study design. We performed a quasi-experimental study to compare the effectiveness of the AMT with that of the ID fellows with respect to antimicrobial recommendations and clinical and economic outcomes. All antibiotic requests were recorded on standardized data cards by the ID approval staff (i.e., AMT and ID fellows); these cards included the staff member's name; the patient's age, sex, hospital service, and culture results; the antimicrobial agents requested by the caller; and the antimicrobial agents recommended by the staff.

Inpatient charts were reviewed for comorbidities, infection site, and drug allergies. Severity of illness at admission, as defined by the MedisGroup score [9], was used as a surrogate for severity of illness at the time of antimicrobial request. This measure was chosen because it has been shown, in a study of pneumonia-associated mortality rates, to perform better than several other measures of disease severity and because it was readily available for this study population [10].

Study setting and sample. The study was conducted at the Hospital of the University of Pennsylvania, a 772-bed tertiary-care medical center, and was begun contemporaneously with the initiation of the program. Eligibility criteria included age $\geq$18 years and a request on the patient's chart for restricted antimicrobial agents that was made during November 1993. Subjects were excluded if an ID physician had already been consulted before the call. Subjects were also excluded if they had died within 72 hours of the request or during the antimicrobial course but of causes deemed to be unrelated to infection by a reviewer (N.O.F.) blinded to the study group. If >1 call regarding use of antimicrobial agents was made for a particular patient, only the first call was included in the analysis.

During the study period, 265 eligible calls were logged. Figure 1 shows the breakdown of the inclusions and exclusions. Of the 210 calls that met inclusion criteria, 180 calls (86%) were made regarding patients for whom charts were available; these patients were included. Subjects whose charts were available were more likely to be female than male (72% vs. 48%; $P = .03$), and approval calls for these patients were more likely to have been made to ID fellows than to the AMT (73% vs. 52%; $P = .03$).

Table 1 shows the characteristics of the included subjects. The ID fellows received calls regarding patients in intensive care units (ICUs) more often than the AMT (24% vs. 12%; $P = .04$), and the AMT received calls regarding older subjects (median age, 60 vs. 50 years; $P = .07$). The distribution of other patient characteristics was similar among calls to ID fellows and calls to the AMT.

Outcome measures. Outcome measures included appropriateness of the antimicrobial agents, cure of infection with the first regimen, and failure of the first regimen. "Appropriateness" was defined by several criteria, all of which had to be satisfied. Use of the antimicrobial agent had to adhere to institution-specific guidelines [8] regarding spectrum and route of delivery for each indication. Doses had to be adjusted according to renal and hepatic function when indicated, and known allergies had to be avoided. If therapeutically equivalent regimens were available, the option with the lowest acquisition cost was considered to be appropriate.

The director of the AMT evaluated the recommendations in a blinded manner. To ensure masking, the research staff read aloud the information on the data collection cards to the director, omitting both the patient's and the ID approval staff member's names. Dose adjustment and drug allergies were also assessed from the cards.

A hierarchical approach was used to define "cure," with the main criterion being microbiological eradication. If initial cultures were sterile or subsequent culture results were unavailable, clinical parameters were used, including decreased WBC count

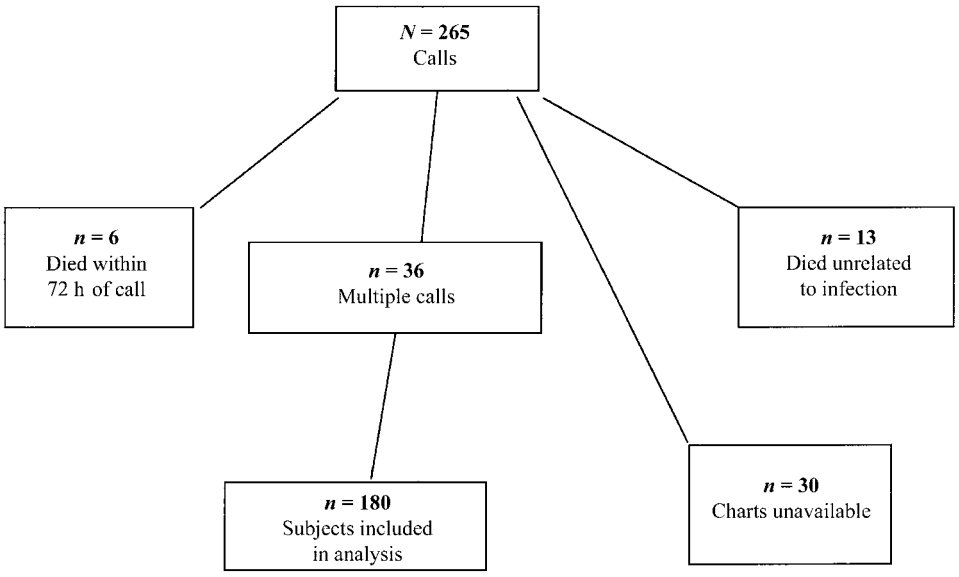

Figure 1. Breakdown of included and excluded subjects from among those for whom restricted antimicrobial agents were requested

and/or reduction of fever. Finally, if none of these were available, chart notes were used. Ten subjects in each group who received antimicrobial agents in the absence of infection (e.g., for surgical prophylaxis) could not achieve the clinical end point of "cure" and were therefore excluded from this analysis.

The definition of "failure" included a change or addition of antimicrobial agents secondary to treatment failure, to target an isolated pathogen not susceptible to the original regimen, or because the treating physicians judged clinical improvement to be insufficient. In addition, recurrence of the infection, development of superinfection, or an adverse drug effect constituted a failure. In contrast to the outcome measures of appropriateness and cure, favorable results for the outcome of failure are represented by OR < 1. All subjects were included in this analysis.

"Economic outcomes" were defined in several ways. The primary economic outcome was the cost of the hospitalization from the time of the call until discharge, which was determined using financial data from the University of Pennsylvania Health System Historical Online Warehouse, a comprehensive database of inpatient activity. We calculated total charges for each patient.

Subjects were identified retrospectively within the database by matches in name, medical record number, date of birth, and discharge date. We identified data for 163 (91%) of the 180 subjects. The accuracy of the data was confirmed by matching the length of stay with the sum of days for which there were room charges for the hospitalization. The charges were converted to costs using the ratio of costs to charges for 1993 at the Hospital of the University of Pennsylvania.

In a secondary analysis, we constructed a model of costs that were attributable directly to the infection being treated. These included the acquisition cost of the antimicrobial agent(s), room costs during treatment, microbiology laboratory costs, and ID consultation costs (if such a consultation occurred after the approval call). Costs for administration of a second course of antimicrobial agents if the initial regimen failed were also included. The cost of the personnel of the AMT was included only for calls to the AMT. The ID fellows' work was covered by training funds, supported by the hospital. An additional secondary analysis assessed the differences in drug acquisition costs alone.

We used the 1993 Hospital of the University of Pennsylvania wholesale price to calculate costs for the antimicrobial agents. Costs of administration were not included. The mean cost per culture was assessed equally for all specimens. This was determined to be $6 per culture and included wholesale costs of reagents and technician time. ID consultation costs were calculated using the Health Care Financing Administration National Physician Fee Schedule's relative value for an inpatient consultation, adjusted for the Metropolitan Philadelphia Geographic Practice Cost and converted to 1993 dollars [11]. For the base case, we included both the initial consultation and follow-up visits, at the maximum rate of $163 for the initial visit and $61 for follow-up visits. We also performed a sensitivity analysis, using the initial consultation at level 4 ($121) and follow-up at level 2 ($41).

The cost of the AMT included the salary and benefits of the pharmacist and the portion of the salary and benefits of the director of the Antimicrobial Management Program that directly supported this activity; the total was $74,810 per year for the pharmacist and $30,000 per year for the director. Costs were prorated for the month of the study and distributed evenly

Table 1. Baseline characteristics of 180 patients included in a study comparing the effects of consultation with an AMT or ID fellows on use of antimicrobial agents and treatment outcomes.

Variable	Patients whose treatment was managed by	
	AMT (n = 87)	ID fellows (n = 93)
Age, median years (range)[a]	60 (17–93)	50 (16–91)
Male sex[b]	43 (52)	47 (52)
Mean MedisGroup score [9]	1.4	1.7
Mean no. of comorbidities	1.1	0.9
Primary hospital service		
Medicine	39 (45)	45 (48)
Surgery	38 (44)	40 (43)
Other	10 (11)	8 (9)
ICU stay at time of call[b,c]	9 (12)	21 (24)
Site/source of infection		
Skin	9 (10)	10 (11)
Pulmonary	13 (15)	23 (25)
Sepsis	15 (17)	12 (13)
Gastrointestinal	15 (17)	14 (15)
Genitourinary	19 (22)	13 (14)
CNS	3 (3.5)	4 (4)
Otorhinolaryngeal	3 (3.5)	6 (6.5)
Unknown	0	1 (1)
Surgical prophylaxis	8 (9)	7 (7.5)
No infection[b]	2 (3)	3 (4)

NOTE. Data are no. (%) of patients, unless otherwise indicated. AMT, Antimicrobial Management Team; ICU, intensive care unit; ID, Division of Infectious Diseases.

[a] Borderline significant difference (P = .07).
[b] Data were not available for some patients in this category.
[c] Significant difference (P = .04).

for each call included (87 calls). One hundred dollars was added to the cost of each case managed by the AMT.

Statistical analysis. Baseline data for the groups were compared using χ^2 tests for categorical variables and the Wilcoxon rank sum test for all continuous variables. The χ^2 test was used to compare the 3 clinical outcome measures between the study groups: (1) appropriateness, (2) cure, and (3) failure. Odds ratios, 95% confidence intervals, and P values were calculated for the effect of the AMT's involvement on each outcome. Multiple logistic regression was used to control for confounding variables. Separate models were constructed for each of the 3 outcomes. The final model for each outcome included covariates that were confounding variables or were associated with the outcome with $P < .1$. Variables were removed in a stepwise manner. Since multivariate analyses yield odds ratios, not risk ratios, to make the results of the univariate and multivariate analyses comparable, we have chosen to present odds ratios. It should be noted that odds ratios regarding common events, such as those in this study, must not be misinterpreted as risk ratios.

The Wilcoxon rank sum test was used to compare costs. The bootstrap technique was used to calculate 95% confidence intervals [12]. Analyses were performed using Stata 5.0 software (Stata Corp.), and all P value calculations were 2-sided.

RESULTS

Cases managed by the AMT had better outcomes than those managed by the ID fellows, for all parameters (table 2). Separate multivariate models were constructed for the relationship between the approval group and each outcome after adjustment for potential confounding variables. Table 3 shows the variables and the associated odds ratios. After adjustment for the confounding variables, the impact of the AMT was even more strongly associated with appropriate antimicrobial use than in the univariate analysis. Other variables significantly inversely associated with appropriate recommendations included presence of malignancy or neurological disorder and non–medical service treatment.

Multivariate modeling identified no confounding variables in the association between consultation with the AMT and cure. Furthermore, no variables other than management by the AMT were associated with cure. Multivariate modeling also identified no confounding variables for the inverse relationship between consultation with the AMT and treatment failure (table 4). Other variables associated with failure included presence of gastrointestinal comorbidity, ICU stay at the time of the call, and sepsis.

To further assess the functioning of the 2 groups, we examined both denials of requests and acceptances of recommendations. The AMT denied requests for antimicrobial agents significantly more often (25 [29%] of 87 requests denied) than did the ID fellows (8 [9%] of 93) (OR, 4.3; 95% CI, 1.8–9.9; $P < .001$). In contrast, the number of AMT recommendations accepted by the caller was similar to the number of ID fellow

Table 2. Comparison of antimicrobial treatment managed by an AMT or by ID fellows.

Outcome	No. of patients whose treatment was managed by		Unadjusted OR (95% CI)	P
	AMT (n = 87)	ID fellows (n = 93)		
Appropriate	76	44	7.7 (3.7–16.2)	<.001
Cure[a]	49	35	2.4 (1.3–4.5)	.007
Failure	13	26	0.5 (0.2–0.9)	.03

NOTE. AMT, Antimicrobial Management Team; ID, Division of Infectious Diseases.

[a] Ten subjects in each group for whom antimicrobial agents were requested for prophylaxis or in whom no evidence of infection was seen when the request was reviewed were excluded.

Table 3. Multivariate model of appropriate use of antimicrobial agents in a study of 180 patients at the Hospital of the University of Pennsylvania, November 1993.

Variable	OR (95% CI)	*P*
AMT vs. ID fellows	11.0 (4.6–25)	<.001
Surgical vs. medical service	0.41 (0.2–0.9)	.02
Other vs. medical service	0.25 (0.1–0.9)	.03
Oncological comorbidity	0.39 (0.16–0.94)	.04
Neurological comorbidity	0.21 (0.07–0.69)	.01

NOTE. AMT, Antimicrobial Management Team; ID, Division of Infectious Diseases.

recommendations accepted by the caller (AMT recommendations accepted, 73 [84%] of 87; ID fellow recommendations accepted, 76 [82%] of 93; $P = .7$)]. We also assessed whether the recommendations offered when requests were denied were appropriate. Although the AMT denied requests significantly more often than did the ID fellows, the antibiotic regimens recommended by the AMT always adhered to the guidelines (25 [100%] of 25), whereas those of the ID fellows sometimes did not (6 [75%] of 8) ($P = .05$).

We compared the reasons for which antimicrobial choices made by the AMT and by the ID fellows were deemed inappropriate. The antimicrobial agent was considered to be inappropriate if (1) the cost of the chosen agents was higher than that of an equivalent regimen; (2) the spectrum of the recommended regimen was broader than indicated by the patient's condition; (3) the spectrum of the recommended regimen was narrower than indicated; (4) the spectrum of the regimen was globally inappropriate (rather than simply too broad or too narrow); (5) the route of administration of the recommended regimen was inappropriate; (6) the dose of the chosen agents was inappropriate (table 5). Several types of inappropriate recommendations were more common to the ID fellows than to the AMT, including cost of agents, too broad a spectrum, and a globally inappropriate spectrum.

The economic analyses demonstrated lower costs for the AMT group than for the ID fellows group both in total hospital costs and in costs attributable to infection (table 6). However, these differences did not achieve traditional statistical significance in either case. The sensitivity analysis in which the cost of an ID consultation was decreased resulted in no important change from the base-case model (data not shown).

DISCUSSION

These data demonstrate, in the first comparative study of antimicrobial management strategies, that in a hospital with a restricted formulary an AMT made more appropriate recommendations and yielded better outcomes than did ID fellows. The success of this program was probably attributable to several factors. First, the director was a respected clinician who had extensive experience in the use of antimicrobial agents and provided strong and frequent support for the pharmacist. Second, this service was the primary responsibility of the pharmacist, whose job evaluation depended on the quality of her recommendations. In contrast, the ID fellows considered the service to be burdensome, distracting them from their primary activity and having little educational value or impact on fellowship evaluation. Furthermore, the fellows may have accommodated requests in order to make their daily interactions with the requesting physicians more collegial.

Data regarding inappropriate recommendations are important for identifying the deficiencies of the ID approval service. For both groups, use of overly broad-spectrum and too-expensive antimicrobial agents was a problem, whereas errors involving overly narrow-spectrum drugs were relatively uncommon. As expected, practitioners tend to err on the side of treating too broadly. In addition, the ID fellows erred at times by choosing agents with inappropriate spectrums of activity, a finding that highlights the need for increased antimicrobial education for the fellows.

No statistically significant economic differences were demonstrated. However, the analyses suggested a trend toward cost-savings. The difference in cost of hospitalization was an order of magnitude greater than the difference in the cost of antimicrobial agents ($1396 vs. $43; table 6); thus, the cost difference, if present, must result from factors other than antimicrobial cost–saving, such as the improved outcomes yielded by the AMT. Despite the absence of significant cost differences between consultation with the AMT and consultation with the ID fellows, because the AMT yielded better clinical outcomes, use of this service is a dominant strategy.

There are several potential limitations to this study. First, this was not a randomized trial, so we were unable to control for unmeasured confounding variables. However, no confounding variables were found, and the baseline characteristics of the groups were similar, which is reassuring. Second, because the times of operation of the 2 groups were mutually exclusive, we were unable to control for time of day as a factor. If time of day influenced the results in a way that we were unable to

Table 4. Multivariate model of failure of treatment with antimicrobial agents in a study of 180 patients at the Hospital of the University of Pennsylvania, November 1993.

Variable	OR (95% CI)	*P*
AMT vs. ID fellows	0.5 (0.2–1.1)	.09
Gastrointestinal comorbidity	3.9 (1.1–14.0)	.04
Intensive care unit stay	4.8 (1.9–12.0)	.001
Sepsis	3.6 (1.3–9.8)	.03

NOTE. AMT, Antimicrobial Management Team; ID, Division of Infectious Diseases.

Table 5. Factors making AMT and ID fellow recommendations for antimicrobial treatment inappropriate.

Factor	No. (%) of consultations with AMT (n = 87)	No. (%) of consultations with ID fellows (n = 93)	OR (95% CI)	P
Cost	6 (7)	25 (27)	0.2 (0.1–0.5)	<.001
Spectrum too broad	4 (5)	21 (23)	0.2 (0.1–0.5)	<.001
Spectrum too narrow	1 (1)	5 (5)	0.2 (0–1.4)	.11
Spectrum inappropriate (other than too broad or narrow)	1 (1)	14 (15)	0.1 (0–0.4)	<.001
Antimicrobial agents not indicated	6 (7)	9 (10)	0.7 (0.2–2.0)	.5
Route inappropriate	0 (0)	2 (2)	—	.17
Dose inappropriate	0 (0)	2 (2)	—	.17

NOTE. Some recommendations were inappropriate for >1 reason. AMT, Antimicrobial Management Team; ID, Division of Infectious Diseases.

capture using other variables—the MedisGroup score [9], site of infection, ICU stay, and presence of comorbidities—then bias could have been introduced. However, there were no statistically significant differences in the characteristics of patients for whom consultations were requested on the weeknights and those for whom consultations were requested on the weekends, and the ID fellows performed comparably on weeknights and weekends. Furthermore, although the ID fellows received more requests concerning patients in the ICUs, this factor was not found to be a confounding variable in our multivariate analyses. Although these points make the presence of bias, which is common in observational studies, less likely, the possibility of bias that was introduced by unmeasured factors cannot be eliminated.

The limitations of the economic model include the fact that the "societal perspective" was not the focus. Moreover, we assessed only incremental costs incurred, by adding the AMT to a setting in which ID fellows already performed the studied service. Thus, the economic results may not be generalizable to settings in which no ID approval service is present. However, a strength of the study is that 2 separate economic models, one assessing global cost-savings and another assessing infection-specific cost-savings, both demonstrated results on a similar order of magnitude and with similar 95% confidence intervals. In each analysis, the economic difference was well in excess of the marginal cost of implementing the program ($100 per ID approval). Thus, we project that implementing an antimicrobial management program, even in settings that lack an ID approval service, will be cost-effective.

In response to the evidence of the effectiveness of this program and the errors in the ID fellows' recommendations, we reorganized the AMT to include the ID fellows. Under this new system, the ID fellows are encouraged to call the director of the AMT when faced with difficult cases, especially when the caller does not desire a formal ID consultation. In addition, the director reviews all recommendations made by the ID fellows and provides feedback to them on both a scheduled and an ad hoc basis.

In conclusion, this study demonstrates that a comprehensive AMT consisting of a pharmacist with ID specialist backup was better able to manage antimicrobial recommendations in a hospital with a restricted formulary than were ID fellows receiving limited backup. A randomized trial confirming the impact of this service is needed, as is an economic analysis of its cost-effectiveness outside of an academic setting. If these results are confirmed, this type of system should be implemented in hospitals where antibiotics are used injudiciously. Given our current understanding of the injudicious use of antibiotics, we

Table 6. Differences in economic outcomes among 180 patients whose antimicrobial treatment was managed by an AMT or by ID fellows.

Economic outcome measure	Median cost per group: AMT	Median cost per group: ID fellows	Difference (95% CI)	P
Total hospital cost after approval call	$6468	$7864	$1396 (−$3154 to $5991)	.08
Cost attributable to infection	$3510	$4205	$695 (−$1078 to $2985)	.10
Cost of antimicrobial agents	$79	$122	$43 (−$47 to $136)	.09

NOTE. AMT, Antimicrobial Management Team; ID, Division of Infectious Diseases.

believe that few hospitals would not benefit from this type of antimicrobial management system.

ACKNOWLEDGMENT

We thank J. Sanford Schwartz, MD, for his guidance in the analysis of this project, his advice regarding the preparation of the manuscript, and his ongoing assistance in related and unrelated projects.

References

1. Belongia EA, Schwartz B. Strategies for promoting judicious use of antibiotics by doctors and patients. BMJ **1998**; 317:668–71.
2. Gaynes R. The impact of antimicrobial use on the emergence of antimicrobial-resistant bacteria in hospitals. Infect Dis Clin North Am **1997**; 11:757–65.
3. John JF Jr, Fishman NO. Programmatic role of the infectious diseases physician in controlling antimicrobial costs in the hospital. Clin Infect Dis **1997**; 24:471–85.
4. Briceland LL, Nightingale CH, Quintiliani R, Cooper BW, Smith KS. Antibiotic streamlining from combination therapy to monotherapy utilizing an interdisciplinary approach. Arch Intern Med **1988**; 148: 2019–22.
5. Fraser GL, Stogsdill P, Dickens JD Jr, Wennberg DE, Smith RP Jr, Prato BS. Antibiotic optimization: an evaluation of patient safety and economic outcomes. Arch Intern Med **1997**; 157:1689–94.
6. Mazmanian PE, Daffron SR, Johnson RE, Davis DA, Kantrowitz MP. Information about barriers to planned change: a randomized controlled trial involving continuing medical education lectures and commitment to change. Acad Med **1998**; 73:882–6.
7. Quintiliani R, Cooper BW, Briceland LL, Nightingale CH. Economic impact of streamlining antibiotic administration. Am J Med **1987**; 82: 391–4.
8. Fishman NO, Morgan AS, Green S. Guidelines for antimicrobial therapy. Philadelphia: Trustees of the University of Pennsylvania, **1993**.
9. Iezzoni LI, Moskowitz MA. A clinical assessment of MedisGroups. JAMA **1988**; 260:3159–63.
10. Iezzoni LI, Shwartz M, Ash AS, Hughes JS, Daley J, Mackiernan YD. Severity measurement methods and judging hospital death rates for pneumonia. Med Care **1996**; 34:11–28.
11. National physician fee schedule. Baltimore: Health Care Financing Administration, **1999**.
12. Briggs AH, Wonderling DE, Mooney CZ. Pulling cost-effectiveness analysis up by its bootstraps: a non-parametric approach to confidence interval estimation. Health Econ **1997**; 6:327–40.