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Impact of an Antimicrobial Utilization Program on Antimicrobial Use at a Large Teaching Hospital: A Randomized Controlled Trial •

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ORIGINAL ARTICLE

Impact of an Antimicrobial Utilization Program on Antimicrobial Use at a Large Teaching Hospital: A Randomized Controlled Trial

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BACKGROUND. Multidisciplinary antimicrobial utilization teams (AUTs) have been proposed as a mechanism for improving antimicrobial use, but data on their efficacy remain limited.

OBJECTIVE. To determine the impact of an AUT on antimicrobial use at a teaching hospital.

DESIGN. Randomized controlled intervention trial.

SETTING. A 953-bed, public, university-affiliated, urban teaching hospital.

PATIENTS. Patients who were given selected antimicrobial agents (piperacillin-tazobactam, levofloxacin, or vancomycin) by internal medicine ward teams.

INTERVENTION. Twelve internal medicine teams were randomly assigned monthly: 6 teams to an intervention group (academic detailing by the AUT) and 6 teams to a control group that was given indication-based guidelines for prescription of broad-spectrum antimicrobials (standard of care), during a 10-month study period.

MEASUREMENTS. Proportion of appropriate empirical, definitive (therapeutic), and end (overall) antimicrobial usage.

RESULTS. A total of 784 new prescriptions of piperacillin-tazobactam, levofloxacin, and vancomycin were reviewed. The proportion of antimicrobial prescriptions written by the intervention teams that was considered to be appropriate was significantly higher than the proportion of antimicrobial prescriptions written by the control teams that was considered to be appropriate: 82% versus 73% for empirical (risk ratio [RR], 1.14; 95% confidence interval [CI], 1.04–1.24), 82% versus 43% for definitive (RR, 1.89; 95% CI, 1.53–2.33), and 94% versus 70% for end antimicrobial usage (RR, 1.34; 95% CI, 1.25–1.43). In multivariate analysis, teams that received feedback from the AUT alone (adjusted RR, 1.37; 95% CI, 1.27–1.48) or from both the AUT and the infectious diseases consultation service (adjusted RR, 2.28; 95% CI, 1.64–3.19) were significantly more likely to prescribe end antimicrobial usage appropriately, compared with control teams.

CONCLUSIONS. A multidisciplinary AUT that provides feedback to prescribing physicians was an effective method in improving antimicrobial use.

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The worldwide emergence of antimicrobial resistance is a major public health problem and substantially impacts patient treatment and outcomes.[1] Antimicrobial resistance continues to increase among bacteria that cause disease in both community and hospital settings.[2-5] The relationship between antimicrobial use and antimicrobial resistance is complex, but a growing body of data strongly suggests that higher levels of antimicrobial usage are associated with higher levels of antimicrobial resistance.[6-9] The persistent increase in antimicrobial resistance has created concern that we are entering a "post–antibiotic era," in which some bacterial infections will no longer be treatable.[10,11]

Antimicrobial use in hospitalized patients is common, with patients in the intensive care units receiving antibiotics on 70% of their intensive care unit–days and patients on the general inpatient wards receiving antibiotics on at least 40% of their inpatient-days.[12] Studies have documented that up to 50% of all in-hospital antimicrobial use is inappropriate.[13,14] The inappropriate use of antimicrobials represents an important patient safety issue, because inappropriate use may be associ-

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ated with adverse patient outcomes, increased cost of medical care, and increased antimicrobial resistance among nosocomial pathogens.[1]

Various approaches, including physician education, hospital formulary restriction of antimicrobials, required approval of selected antimicrobials, antimicrobial prescribing guidelines, computer-assisted antimicrobial prescribing, and antimicrobial order forms, have been undertaken in an attempt to reduce inappropriate antimicrobial use. However, it remains unclear which approaches are effective and whether these measures are sustainable.[15-22] Multidisciplinary antimicrobial utilization teams (AUTs) that include clinicians (eg, infectious diseases [ID] physicians) as well as pharmacy and microbiology personnel are thought to be an important mechanism for improving antimicrobial use, but data remain limited with regard to the impact of such an approach on the reduction of inappropriate antimicrobial usage and antimicrobial resistance.[17,23-26] There have been few randomized trials that evaluate methods to improve antimicrobial usage.[19,20,22] To better define the role of a multidisciplinary AUT in the improvement of antimicrobial use, we conducted a randomized controlled trial to determine the efficacy of a multidisciplinary AUT, compared with the efficacy of indication-based antimicrobial prescribing guidelines (standard of care at our institution), in optimizing antimicrobial use at a large university-affiliated public hospital.

METHODS

Study Design and Setting

We conducted a randomized controlled trial to compare the efficacy of a multidisciplinary AUT with that of indication-based antimicrobial prescribing guidelines in optimizing use of 3 antimicrobial agents by the internal medicine services at Grady Memorial Hospital (Atlanta, Georgia). The study was approved by the Emory University Institutional Review Board and the Grady Research Oversight Committee. Grady Memorial Hospital is a 953-bed, urban, public teaching hospital affiliated with Emory University School of Medicine. Twelve internal medicine teams that are staffed by physicians from Emory University and that treat inpatients at Grady Memorial Hospital and function independently of one another were included. Each of the 12 internal medicine teams consisted of a faculty attending physician, a senior resident (postgraduate year 3), 2 junior residents (postgraduate year 1), and 1 or 2 medical students. Physicians may rotate on the internal medicine service more than once during the year and may be assigned to a different team on different months. The internal medicine teams care for patients on the general medical wards and step-down units but not on the medical intensive care unit.

The teams were randomly assigned to 1 of 2 antimicrobial utilization strategies during the 10-month period October 2002–July 2003: (1) interaction with a multidisciplinary AUT (intervention group) or (2) indication-based antimicrobial prescribing guidelines that represented the standard of care (control group). Each month, 6 internal medicine teams were randomly assigned to the intervention arm and 6 teams were randomly assigned to the control group by means of a random number list. The AUT consisted of an ID physician (faculty member M.D.K.) and an ID clinical pharmacist (PharmD) who worked closely with microbiology personnel for acquisition of clinical microbiology results. The AUT provided structured feedback to prescribing physicians on the appropriateness of antimicrobial use. Structured verbal feedback consisted of either a short phone conversation or a face-to-face meeting on the indication for which the antimicrobial was being prescribed and a recommendation for a more optimal antimicrobial choice (as defined by hospital criteria for appropriate antimicrobial use [Appendix]).

All medical teams, regardless of randomization allocation, received at the start of each month pocket-sized cards that contained the Grady Memorial Hospital guidelines for use of antimicrobial agents, including guidelines for the use of the targeted study drugs: piperacillin-tazobactam, vancomycin, and levofloxacin. The AUT received a daily list from the pharmacy of all new orders for piperacillin-tazobactam, vancomycin, and levofloxacin. The medical records (including charts, pharmacy records, and laboratory results) of patients who were examined by the 12 teams and who received one of these antimicrobials were reviewed by an AUT clinical pharmacist (J.B.W., H.L.G., or M.P.) and/or the ID fellow (B.C.C.). Each medical record was reviewed individually by one of the reviewers. Only one reviewer was needed to review charts each day. Data were collected using standardized report forms. A daily audit of microbiologic data, including results of cultures of blood, sputum, and urine samples and drug susceptibility profiles of causative organisms, was conducted for patients who were receiving piperacillin-tazobactam, vancomycin, and levofloxacin. These antimicrobials were chosen on the basis of previous data that showed particularly high use of these drugs at our institution when benchmarked against use at other institutions.

Each antimicrobial prescription was reviewed to determine whether the criteria for appropriate antimicrobial use were met. The criteria used to define "appropriate" antimicrobial use are outlined in the Appendix. For patients receiving more than one of these antimicrobial agents, an independent assessment of use was made for each drug. The assessment of appropriateness of use was made by the director of the AUT (M.D.K.) on the basis of a verbal report from the reviewer and data from the standardized report form. The AUT director was blinded to team allocation (intervention or control) to prevent bias when determining whether criteria for optimal use were met.

If the antimicrobial use did not meet the criteria for "appropriate" use, the AUT director made recommendations for alternative antimicrobial therapy; if the prescription was writ-

ten by a physician on one of the teams randomly assigned to the intervention, then the recommendations were communicated to the prescribing physician by one of the PharmDs or the ID fellow. Recommendations were not communicated to the control group unless failure to do so could seriously jeopardize the patient (eg, use of an antibiotic without in vitro activity against the isolated pathogen, which occurred in less than 1% of the control group prescriptions). In complicated cases, the AUT recommended that the intervention group seek advice from the ID consult service. Intervention and control teams were not informed that the study was taking place.

Definitions

Initial antimicrobial use (within 72 hours of starting therapy) was defined as any antimicrobial treatment initiated for empirical coverage while microbiologic results were pending or for definitive therapy in which a pathogen was already known. Empirical antimicrobial use was defined as antimicrobial use that occurred within 72 hours of initiation of therapy while microbiologic culture results were pending or antimicrobial use in situations after 72 hours of initiation when microbiologic cultures did not yield a pathogen.

Definitive (therapeutic) antimicrobial use was defined as any antimicrobial use at a time when microbiologic culture results and susceptibility data were available. This could have occurred at initiation of therapy or after empirical antimicrobial use was initiated once microbiologic culture results were available.

End antimicrobial use was defined as the final choice of antimicrobial regimen selected for the indication being treated. This category includes definitive antimicrobial use in which a pathogen was isolated or empirical antimicrobial use in which no pathogen was ever isolated or for which microbiologic cultures were never obtained.

Study Outcomes

The primary outcomes included (1) the proportion of prescriptions for empirical therapy that was appropriate, (2) the proportion of prescriptions for definitive therapy that was appropriate, and (3) the proportion of end antimicrobial usage that was appropriate. Secondary end points included (1) the volume of inappropriate antimicrobial use in defined daily doses (DDDs),[27] (2) the duration of inappropriate antimicrobial use in days, (3) the hospital length of stay, and (4) the clinical outcome of in-hospital mortality. The primary and secondary outcomes were focused on antimicrobial usage measures with comparisons between the control and intervention groups.

Statistical Analysis

Sample size calculations. Assuming a baseline proportion of inappropriate use for target antimicrobials of 35% (with inappropriate use data based on preliminary usage data from Grady Memorial Hospital), review of at least 330 antimicrobial prescriptions in each arm would allow for detection of a 10% reduction in inappropriate antimicrobial use at $\alpha = .05$ and $\beta = 0.80$.

Data analysis. Data analyses were performed using SAS software, version 9.1 (SAS Institute). Baseline data for the intervention and control groups were assessed at the randomization unit level (internal medicine team), with aggregation of the data according to randomization units. The unit of analysis was on the level of prescriptions written for each of the targeted drugs. Risk ratios (RRs), 95% confidence intervals (CIs), and *P* values for the intervention effect on categorical outcomes were estimated with univariate log-binomial regression models. Continuous variables were compared using a 2-sample *t* test or Wilcoxon rank-sum test. Variables associated with appropriate end antimicrobial usage were initially assessed by univariate analysis. Multivariate analysis was performed using a multiple log-binomial regression model to control for confounding and effect modification; we took into account the hierarchy principle. Two-way interactions between the intervention status variable and probable effect modifiers were examined (significant interaction was found between intervention status and ID consultations). Confounding assessment following by precision considerations was performed. Backward selection model building was used

TABLE 1. Baseline Characteristics of Patients Who Had Antimicrobials Prescribed by Physicians on Internal Medicine Teams in the Intervention or Control Groups

Characteristic	Intervention group ($n = 390$ prescriptions)	Control group ($n = 394$ prescriptions)	*P*
Sex[a]			
Male	175 (45)	205 (52)	.04
Female	212 (55)	186 (47)	
Age, mean (range), years	54 (3–97)	54 (2–99)	.59
Race			
Black	305 (78)	331 (84)	.04[b]
White	35 (9)	21 (5)	
Hispanic	10 (3)	6 (2)	
Other	5 (1)	2 (1)	
Unknown	33 (9)	30 (8)	
Most common diagnoses			
Pneumonia	63 (16)	67 (17)	.75
Bloodstream infection	37 (9)	20 (5)	.02
Complicated UTI	60 (15)	50 (13)	.28
Uncomplicated UTI	20 (5)	12 (3)	.14
Asymptomatic bacteriuria	10 (3)	24 (6)	.02

NOTE. Data are no. (%) of prescriptions, unless indicated otherwise. UTI, urinary tract infection.

[a] Data on sex were available for 387 patients in the intervention group and 392 patients in the control group.

[b] Black versus all other races combined.

TABLE 2. Appropriateness of Antibiotic Use in Randomized Controlled Trial of Impact of Antimicrobial Utilization Teams

Variable	Proportion (%) of prescriptions		Risk ratio (95% CI)	*P*
	Intervention group	Control group		
Antibiotic use deemed appropriate				
Initial (<72 hours)	305/390 (78)	229/394 (58)	1.35 (1.22–1.49)	<.001
Empirical	242/294 (82)	211/291 (73)	1.14 (1.04–1.24)	.005
Definitive	92/112 (82)	60/138 (43)	1.89 (1.53–2.33)	<.001
Appropriate cultures obtained	188/270 (70)	193/286 (67)	1.03 (0.92–1.15)	.59
Changed to recommended antibiotics[a]	168/186 (90)	85/199 (43)	2.11 (1.79–2.50)	<.001
Appropriate end antimicrobial usage	367/390 (94)	277/394 (70)	1.34 (1.25–1.43)	<.001

NOTE. CI, confidence interval.

[a] In the control group, a blinded assessment of the appropriateness of the antimicrobial therapy was still made by the medical director of the antimicrobial utilization program. However, any recommendations for optimization of therapy were only recorded and never conveyed to the control group physicians.

to arrive at the final model. A *P* value of .05 or less was considered to be statistically significant.

RESULTS

A total of 784 new prescriptions were reviewed by the AUT during the 10-month study period; this included 440 (56%) for levofloxacin, 162 (21%) for piperacillin-tazobactam, and 182 (23%) for vancomycin. Demographic and clinical characteristics of the patients prescribed these antimicrobial agents are listed in Table 1. Initial antimicrobial use (within the first 72 hours of patient receipt) as well as empirical and definitive antimicrobial use were all significantly more likely to be appropriate among patients cared for by intervention teams, compared with those cared for by control teams (Table 2). Overall, 367 (94%) of 390 prescriptions that represented end antimicrobial usage among the intervention group were appropriate, compared with 277 (70%) of 394 prescriptions that represented end antimicrobial usage among the control group (RR, 1.34; 95% CI, 1.25–1.43). Among inappropriate end antimicrobial usage, 107 (42%) of 253 prescriptions were related to use of an antimicrobial agent when none was indicated or necessary and 144 (57%) of 253 prescriptions were related to use of an antimicrobial agent considered to be inappropriate by the hospital's antibiotic use guidelines (Appendix).

Internal medicine teams randomly assigned to the intervention group had a significantly shorter median duration of inappropriate use (2.0 days/prescription vs 5.0 days/prescription; $P < .001$) and lower median DDDs of inappropriate antimicrobial use (2.0 vs 4.0 DDDs; $P < .001$), compared with teams randomly assigned to the control group (Table 3). There were no differences in the in-hospital mortality rates among patients cared for by the intervention teams (11 [3%] of 390 patients died) or control teams (18 [5%] of 394 patients died) ($P = .18$). Patients treated by the intervention group also had a shorter median length of stay (7 days [range, 1–50 days]), compared with patients treated by the control group (8 days [range, 2–86 days]) ($P = .03$). An ID consult was obtained by the primary internal medicine team in only 63 (8%) of 773 episodes with available information in which an antimicrobial agent was prescribed (34 [8.8%] of 386 episodes for intervention teams vs 29 [7.5%] of 387 episodes for control teams; $P = .50$).

In univariate analysis, factors associated with appropriate end antimicrobial usage included intervention by the AUT (RR, 1.34; 95% CI, 1.25–1.43), consultation with the ID service (RR, 1.15; 95% CI, 1.07–1.24), and an abnormal finding present on chest radiograph (RR, 1.13; 95% CI, 1.02–1.24) (Table 4). In multivariate analysis, independent predictors for appropriate end antimicrobial usage included AUT intervention and ID consultation; we found significant interaction between these 2 factors. The highest effect on appropriate end antimicrobial usage included AUT intervention combined with ID consultation (adjusted RR [aRR], 2.28; 95% CI, 1.64–3.19). AUT intervention without ID consultation

TABLE 3. Overall Volume and Duration of Inappropriate Antibiotic Use

Variable	Intervention group	Control group	*P*[a]
Duration of inappropriate use, median (range), days	2.0 (1–16)	5.0 (1–20)	<.001
Total volume of inappropriate use, DDDs	441	753	
Median volume of inappropriate use (range), DDDs	2.0 (0.5–16)	4.0 (0.3–16.5)	<.001

NOTE. DDD, daily defined dose.

[a] Wilcoxon 2-sample test.

TABLE 4. Univariate and Multivariate Analysis of Predictors for Appropriate End Antimicrobial Use for 784 Prescriptions

	Prescriptions		Univariate analysis		Multivariate analysis	
Variable	Appropriate end (n = 644)	Inappropriate end (n = 140)	RR (95% CI)	P	Adjusted RR (95% CI)	P
Patient associated						
<50 years old	307 (48)	59 (42)	1.04 (0.97–1.11)	.23	…	
Male sex	318/641 (50)	62/137 (45)	1.03 (0.97–1.10)	.35	…	
Black race	524 (81)	112 (80)	1.02 (0.93–1.11)	.71	…	
LOS <8 days	322 (50)	69 (49)	1.01 (0.94–1.07)	.88	…	
Abnormal chest radiograph finding	199/314 (63)	25/56 (45)	1.13 (1.02–1.24)	.01	…	
Prescriber associated						
AUT intervention	367 (57)	23 (16)	1.34 (1.25–1.43)	<.001		
With ID consultation	…	…	…		2.28 (1.64–3.19)	<.001
Without ID consultation	…	…	…		1.37 (1.27–1.48)	<.001
ID consultation (alone)	59/635 (9)	4/138 (3)	1.15 (1.07–1.24)	<.001	1.31 (1.14–1.51)	<.001
PGY >1 year	211/605 (35)	40/130 (31)	1.03 (0.96–1.11)	.36	…	

NOTE. Data are no. (%) or proportion (%) of prescriptions, unless otherwise indicated. Data were missing for some patients. AUT, antimicrobial utilization team; CI, confidence interval; ID, infectious diseases; LOS, length of stay; PGY, postgraduate year; RR, risk ratio.

(aRR, 1.37; 95% CI, 1.27–1.48) and ID consultation without AUT intervention (aRR, 1.31; 95% CI, 1.14–1.51) also independently predicted appropriate end antimicrobial usage in multivariate analysis (Table 4).

DISCUSSION

In this randomized controlled trial, we found that physicians on teams randomly assigned to the intervention group (who received structured feedback from the AUT) were significantly more likely to use antimicrobials appropriately than physicians on teams randomly assigned to the control group (who were given cards with guidelines for appropriate antimicrobial use but who received no feedback from the AUT). Feedback from the AUT resulted in a significantly higher proportion of initial antimicrobial therapy deemed appropriate in the intervention group, compared with the control group (78% vs 58%; RR, 1.35), as well as a higher proportion of end antimicrobial use deemed appropriate: 367 (94%) of 390 antimicrobials prescribed by the intervention group were appropriate, compared with only 277 (70%) of 394 antimicrobials prescribed by the control group (RR, 1.34). Patients treated by the intervention teams had a significantly shorter median length of stay, compared with patients treated by the control teams. In-hospital mortality rates were low in both arms and did not differ significantly between the 2 groups. We found that receiving feedback from both the AUT and the ID consult service was associated with the highest likelihood of appropriate end antimicrobial usage (aRR, 2.28, compared with the control group). The AUT intervention alone (intervention group) or an ID consult alone (control

TABLE 5. Summary of Randomized Controlled Trials on Antimicrobial Utilization Team (AUT) Interventions to Improve Antibiotic Prescribing Practices for Hospital Inpatients

Author, publication year	Sample size	Intervention	Primary outcome
Fraser et al [19], 1997	252 patients	AUT (ID fellow and a clinical pharmacist)	Per patient antibiotic charges decreased in the intervention group, compared with the control group. Clinical and microbiological response, antibiotic-associated toxic effects, in-hospital mortality, and readmission rates were similar for both groups.
Solomon et al [20], 2001	278 antimicrobial prescriptions	Academic detailing (clinician educators, ID physicians, and specially trained clinical pharmacist)	Number of days that unnecessary levofloxacin or ceftazidime was used was reduced by 37% in intervention group, compared with the control group. In the intervention group, 70% of unnecessary orders were discontinued; in the control group, 30%.
Dranitsaris et al [22], 2001	323 antimicrobial prescriptions	Educational intervention (clinical pharmacist without ID faculty support)	Appropriateness of cefotaxime use did not improve.
Camins et al, 2009 (PR)	784 antimicrobial prescriptions	AUT (ID physician faculty member, clinical pharmacist [PharmD])	Proportion of appropriate antimicrobial prescriptions increased: 78% vs 58% for empirical usage (RR, 1.35), 82% vs 43% for definitive usage (RR, 1.89), and 94% vs 70% for end antimicrobial usage (RR, 1.34).

NOTE. All 4 studies were performed in the United States. ID, infectious diseases; PR, present report; RR, risk ratio.

group) was also associated with significantly higher appropriate antimicrobial use, compared with no feedback at all. In our study, an ID consult was obtained in only 8% of all antimicrobial prescriptions (and this did not significantly differ between intervention and control teams). The vast majority of antimicrobial prescriptions are written without ID service consultation; therefore, having an AUT to provide feedback on antimicrobial use is important. Furthermore, our data indicated that there was an additive or synergistic effect when there was involvement of both the ID consult service and AUT feedback. In such cases, the likelihood that the antimicrobial prescription was appropriate increased by a factor of nearly 2.

Data on how best to improve antimicrobial use, including data from randomized controlled trials that assess the impact and efficacy of a multidisciplinary AUT in improving antimicrobial use in the hospital setting,[19,20] are limited. Much of what has been published are data from smaller studies that were performed for short periods, that used historical controls, or that were not randomized.[19-22,25-27] Table 5 summarizes previous randomized trials on the impact and efficacy of an AUT. Our randomized controlled trial, which was performed during a 10-month period, is the longest randomized study reported to date and has the largest number of prescriptions of antibiotics ($n = 784$) included in the analysis. To our knowledge, our study is only the second study in the hospital setting that randomly assigned groups of treating physicians, as opposed to antimicrobial prescriptions. The previous studies randomly assigned treatment groups by antimicrobial prescriptions or patients, so all treating physicians may have been exposed to the daily academic detailing intervention; this exposure could have increased bias through cross-contamination.[19,20,22] To further decrease bias in our study, the assessment of the appropriateness of therapy was performed in a blinded fashion (ie, the AUT director was blinded to the randomization group allocation of each prescription reviewed; feedback was provided to physicians on the intervention teams by a PharmD or ID fellow). Similar to previous studies, the appropriateness of antimicrobial use in this study was determined on the basis of hospital guidelines approved by the hospital pharmacy and therapeutics committee. These guidelines were developed after a review of national guidelines and evidence-based medical literature.

Our study has several limitations. First, we could not completely remove the potential for cross-contamination between the intervention and control groups during the trial. Physicians could spend more than one month on the internal medicine team, so some may have been on an intervention team one month and a control team another month. However, this would have biased the findings to the null hypothesis (ie, no difference between control and intervention groups). Another limitation was that this study was conducted among internal medicine ward teams and did not include teams working in intensive care units and on other medical subspecialties (such as the surgical services). Because there is only a single large medical intensive care unit team, it was not feasible to include that group. Because the target group of physicians included in this study were only those in internal medicine and because this study was carried out at a university-affiliated teaching hospital, care should be exercised in generalizing these results to other settings. In the control group, twice as many patients were given antibiotics for asymptomatic bacteriuria, compared with the intervention group ($P = .02$), which may potentially create bias away from the null in results. Finally, we were unable to measure the effect that our intervention had on the development of antimicrobial resistance in our hospital.

CONCLUSIONS

In a randomized controlled trial, structured feedback provided by a multidisciplinary AUT proved to be an effective method of improving antimicrobial use in a teaching hospital. This improvement was seen in the entire antimicrobial prescribing process, from empirical prescriptions to end antimicrobial use after microbiological results were available. In multivariate analysis, independent predictors for appropriate end antimicrobial use were the AUT intervention and consultation with an ID specialist. Future studies should also examine the sustainability of the impact of such a team on other medical subspecialties and for periods longer than 10 months as well as the impact on the rates of drug resistance, including multidrug resistance, of isolates.

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Potential conflicts of interest. B.C.C. reports that he is on the speakers' bureau for Wyeth Pharmaceuticals. All other authors report no conflicts of interest relevant to this article.

APPENDIX

CRITERIA FOR APPROPRIATENESS OF ANTIMICROBIAL USE

Recommendations were made with the goal of modifying antimicrobial therapy such that all criteria for optimal use were met. For any antimicrobial use to be deemed appropriate, it had to satisfy the following criteria: (1) the antimicrobial prescribed for the indication met hospital guidelines, (2) the antimicrobial prescribed had activity against the suspected or recovered pathogen, (3) the dose of the antimicrobial prescribed was adjusted in cases of renal or hepatic impairment, (4) the antimicrobial therapy was necessary, and (5) the patient had no known allergy to the antimicrobial prescribed. In addition, dose and duration of therapy were

reviewed; however, these 2 measures were not included as criteria for appropriate use. The hospital guidelines for each of the antimicrobials included in the study are listed in Table A1.

Types of recommendations made to the prescribing physician and internal medicine team included the following: (1) modification in antimicrobial choice to meet the hospital prescribing guidelines, (2) modification in antimicrobial choice to provide active spectrum against the suspected or isolated pathogen, (3) modification in dose to adjust for renal or hepatic insufficiency, (4) discontinuation of antimicrobial therapy for unnecessary use, and (5) modification in antimicrobial choice for patients with known allergies to prescribed antimicrobial

TABLE A1. Grady Memorial Hospital Guidelines for Appropriate Use of Levofloxacin, Piperacillin-Tazobactam, and Vancomycin During the Study Period

Piperacillin-tazobactam
- A. Severe diabetic skin and soft-tissue infections (eg, toxic-appearing patient who requires surgical debridement or polymicrobial isolate with high suspicion of infection with *Pseudomonas aeruginosa*)
- B. Empirical use for suspected nosocomial infections that include sepsis, intra-abdominal infection, and nosocomial pneumonia for 72 hours pending culture and susceptibility results
- C. Treatment of nosocomial infections due to:
  1. Organisms resistant to first- and second-generation cephalosporins or piperacillin
  2. Mixed infections involving aerobic and anaerobic organisms

Levofloxacin (intravenous and oral)
- A. Empirical therapy
  1. Pyelonephritis and/or complicated urinary tract infection
  2. Gastrointestinal infection likely due to *Salmonella, Shigella,* or *Campylobacter* spp
  3. Nosocomial gram-negative infections. Continued use beyond 72 hours with negative culture results or use when the organism isolated is susceptible to a first- and/or second-generation cephalosporin requires approval from the ID service.[a]
  4. Presumed treatment of "atypical" pneumonia (due to *Legionella* spp, *Mycoplasma pneumoniae,* or *Chlamydia pneumoniae*)
  5. Single dose for genitourinary surgical prophylaxis in high-risk patients (urine culture results positive or unavailable, preoperative catheter, and/or transrectal prostatic biopsy)
- B. Treatment of:
  1. Pyelonephritis/complicated urinary tract infection in patients with pathogens resistant to first- and second-generation cephalosporins
  2. Prostatitis for patients intolerant or refractory to trimethoprim/sulfamethoxazole
  3. Infections due to gram-negative organisms that are resistant to first- and second-generation cephalosporins
  4. Mycobacterial infections
     a. Multidrug-resistant tuberculosis
     b. Parenteral therapy for tuberculosis
     c. Other mycobacterial infections
  5. Susceptible *Pseudomonas* and *Enterobacter* spp infections
  6. Gram-negative infections in patients with a history of an allergy to β-lactam antibiotics
  7. Gastrointestinal infections
     a. Due to *Salmonella* or *Shigella* spp resistant to trimethoprim-sulfamethoxazole
     b. Due to *Salmonella* or *Shigella* in patients allergic to trimethoprim-sulfamethoxazole
     c. Due to *Campylobacter* spp
  8. Osteomyelitis

Vancomycin (intravenous)
- A. Empirical criteria (for 72 hours pending culture and susceptibility results)
  1. When there is a high suspicion of methicillin-resistant *Staphylococcus aureus* (MRSA) or coagulase-negative *Staphylococcus* infection with pending culture and susceptibility results
  2. Suspected pneumococcal meningitis
  3. Suspicion of life-threatening infection in children (eg, fulminant sepsis in sickle-cell patient)
- B. Treatment criteria
  1. For documented infections where the organism is not susceptible to alternative antibiotics (ie, for use in the treatment of methicillin-resistant staphylococcal infections [MRSA], coagulase-negative *Staphylococcus,* or ampicillin-resistant enterococcal infections)
  2. The patient has a *documented, severe allergy* to β-lactam antibiotics (eg, among patients with a methicillin-susceptible staphylococcal infection)
  3. Pneumococcal meningitis resistant to β-lactam antibiotics (eg, penicillin or third- generation cephalosporin)

NOTE. ID, infectious diseases.

[a] *P. aeruginosa* susceptibility to levofloxacin during the study was approximately 70%.

or potential cross-reactivity between prescribed antimicrobial and known allergy (eg, cephalosporin use for a patient with a serious penicillin allergy such as anaphylaxis).

For definitive (therapeutic) use (ie, microbiologically defined etiology), additional recommendations included the following: (1) modification of the antimicrobial choice to provide targeted antimicrobial therapy (streamlining) on the basis of culture and susceptibility results (eg, to an equally efficacious agent that may have a more narrow spectrum of activity and may be less expensive) and (2) modification of duration of therapy in accordance with evidence-based guidelines. The AUT director remained blinded to team allocation during the recommendation process. These recommendations were recorded on the case report form for both the control and the intervention groups. Inappropriate antimicrobial use was classified into 3 categories: (1) antimicrobial use that was unnecessary (eg, treatment of asymptomatic bacteriuria or use of an antimicrobial agent for patients who had colonization but no infection), (2) antimicrobial prescribed that was inconsistent with the hospital's indication-based guidelines (eg, prescribing piperacillin-tazobactam for treatment of community-acquired pneumonia), and/or (3) antimicrobial prescribed that had no in vitro activity against the suspected or isolated pathogen for the treatment of the infection. Consultation with the ID service was independent of the AUT and was readily available at the hospital; ID service consultation could be requested by all internal medicine teams.

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