ORIGINAL ARTICLE

Effective Antimicrobial Stewardship in a Long-Term Care Facility through an Infectious Disease Consultation Service: Keeping a LID on Antibiotic Use

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DESIGN. We introduced a long-term care facility (LTCF) infectious disease (ID) consultation service (LID service) that provides on-site consultations to residents of a Veterans Affairs (VA) LTCF. We determined the impact of the LID service on antimicrobial use and *Clostridium difficile* infections at the LTCF.

SETTING. A 160-bed VA LTCF.

METHODS. Systemic antimicrobial use and positive *C. difficile* tests at the LTCF were compared for the 36 months before and the 18 months after the initiation of the ID consultation service through segmented regression analysis of an interrupted time series.

RESULTS. Relative to that in the preintervention period, total systemic antibiotic administration decreased by 30% ($P < .001$), with significant reductions in both oral (32%; $P < .001$) and intravenous (25%; $P = .008$) agents. The greatest reductions were seen for tetracyclines (64%; $P < .001$), clindamycin (61%; $P < .001$), sulfamethoxazole/trimethoprim (38%; $P < .001$), fluoroquinolones (38%; $P < .001$), and β-lactam/β-lactamase inhibitor combinations (28%; $P < .001$). The rate of positive *C. difficile* tests at the LTCF declined in the postintervention period relative to preintervention rates ($P = .04$).

CONCLUSIONS. Implementation of an LTCF ID service led to a significant reduction in total antimicrobial use. Bringing providers with ID expertise to the LTCF represents a new and effective means to achieve antimicrobial stewardship.

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Long-term care facilities (LTCFs) hold an increasingly important role in the nation's healthcare system. Among people older than 65 years of age, 3.6% are residents of LTCFs.[1] In 2008, there were 1.7 million nursing home beds in 15,730 facilities, compared to only 0.95 million beds in 5,815 hospitals.[2] The US Census Bureau anticipates that between 2000 and 2050, the number of adults older than 65 years of age will double, increasing the need for long-term care beds.[1,3]

LTCF residents acquire an estimated 1.6–3.8 million infections each year and are especially vulnerable to healthcare-associated infections because of immune senescence, functional impairment, and the care environment.[4] With aging comes a decline in innate and adaptive immunity. Age-related primary immunosenescence is often exacerbated by secondary immune dysfunction related to poor nutrition, multiple comorbid and degenerative conditions, and medications with immunosuppressive effects.[5,6] According to the 2004 National Nursing Home Survey,[1] more than 75% of LTCF residents required assistance with at least 4 of the 5 activities of daily living: bathing, dressing, toileting, transferring, and eating. Furthermore, shared dining, recreational, therapeutic, bathing, and bathroom facilities increase the risk for pathogen transmission among LTCF residents, many of whom may be asymptomatic carriers of multidrug-resistant organisms and *Clostridium difficile*.[7,8]

Concern about increased risk of infection may account for the frequency of unnecessary antimicrobial use at LTCFs. Nationally, 25%–75% of antibiotic prescriptions for long-

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term care residents have been found to be inappropriate.[9] In our own LTCF, 42% of antibiotic courses were determined to be unnecessary, and an additional 22% of courses were too long.[10] Unnecessary antibiotic exposure increases the risk of selection for multidrug-resistant organisms, *C. difficile* infection (CDI), drug-drug interactions, and other adverse events.[9,11] We instituted an on-site LTCF infectious disease (LID) consultation service as a multifaceted intervention to improve the utilization of antimicrobials at our LTCF. We report the impact of the LID service on antimicrobial use and on rates of change in positive *C. difficile* tests at the LTCF.

METHODS

Setting and Intervention

In July 2009, we formed an infectious-disease (ID) service for the 160-bed LTCF affiliated with a large urban Veterans Affairs (VA) medical center. Three of the 4 LTCF wards provide skilled nursing, rehabilitation, restorative, respite, and continuing care. The fourth ward focuses primarily on dementia care. A nurse practitioner or physician assistant staffs each ward; 2 physicians staff 2 wards each. The LID consultation team consisted of an ID physician and a nurse practitioner who examined residents at the LTCF once each week and were available for remote consultation the remainder of the week. LTCF residents seen in consultation were identified by the LTCF staff or referred by the hospital-based ID consultation service. Urgent questions received the LID team's immediate attention, usually both by telephone and via the electronic medical record, while patients with more routine matters (eg, parenteral antimicrobials, concerns for chronic osteomyelitis) were seen during weekly rounds. Whenever possible, the LID team saw patients prior to making recommendations. Some concerns, such as adjusting vancomycin doses or tailoring antimicrobials to culture results, were addressed by telephone or through the electronic medical record before the LID team saw the patient. When antimicrobial treatment was indicated, the LID team based their recommendations on cultures when possible and favored narrow-spectrum agents.

Outcomes

The primary outcome was the use of antimicrobials at the LTCF, measured monthly in days of therapy (DOT) per 1,000 patient days of care (DOC). Secondary outcomes included comparison of antimicrobial classes and specific agents as well as positive *C. difficile* tests.

We used structured query language (SQL 2005; Microsoft) to obtain data regarding systemic antibiotic administration and positive *C. difficile* tests at the LTCF and the affiliated VA hospital. Using a database containing Bar Code Medication Administration data, we obtained systemic antibiotic doses given on the LTCF wards for the 36 months before (July 2006–June 2009) and the 18 months after (July 2009–December 2010) initiation of the LID service. Agents that were not on the formulary throughout the study period (ie, levofloxacin, fidaxomicin, doripenem, and ceftaroline) were included. Topical, ophthalmic, and otic agents were excluded, as were all antifungal and antiviral medications. A potential source of error relates to doses that were held, missing, or refused; these represented less than 5% of the total antibiotic doses given. For determination of DOT, duplicate doses of antibiotics given on the same day to the same patient were eliminated. DOT per 1,000 DOC was determined for the form of medication administered (intravenous/intramuscular or oral), the antimicrobial class, and individual agents.

Other studies have used both *International Classification of Diseases, Ninth Revision* (*ICD-9*) codes and positive toxin assays to measure rates of CDI in hospital settings.[12] Illnesses that develop after admission to our LTCF rarely receive *ICD-*

TABLE 1. Comparison of the Long-Term Care Facility (LTCF) and the Hospital before and after the Intervention

Variable, location	Preintervention[a]	Postintervention[b]	Reduction, %	*P* value
Antibiotics, mean DOT/1,000 DOC ± SD				
Total in LTCF	175.1 ± 28.0	122.3 ± 26.9	30.1	<.001
Total in hospital	631.8 ± 44.9	649.0 ± 38.4	−2.7	.15
Oral in LTCF	136.1 ± 25.6	93.1 ± 22.0	31.6	<.001
Oral in hospital	185.3 ± 18.8	182.3 ± 19.4	−4.5	.59
Intravenous in LTCF	39.0 ± 14.5	29.3 ± 10.6	25.0	.01
Intravenous in hospital	446.7 ± 39.0	466.7 ± 42.5	1.6	.10
Admissions, per month				
LTCF	58.6 ± 11.3	48.1 ± 7.7	18.0	<.001
Hospital	671.6 ± 36.1	720.4 ± 39.9	−7.3	<.001
Transfers to hospital, per month				
LTCF	19.0 ± 4.6	17.6 ± 4.5	7.6	.27
Hospital	Not applicable	Not applicable		

NOTE. DOT/1,000 DOC, days of therapy per 1,000 days of care; SD, standard deviation.

[a] July 2006–June 2009 (36 months).

[b] July 2009–December 2010 (18 months).

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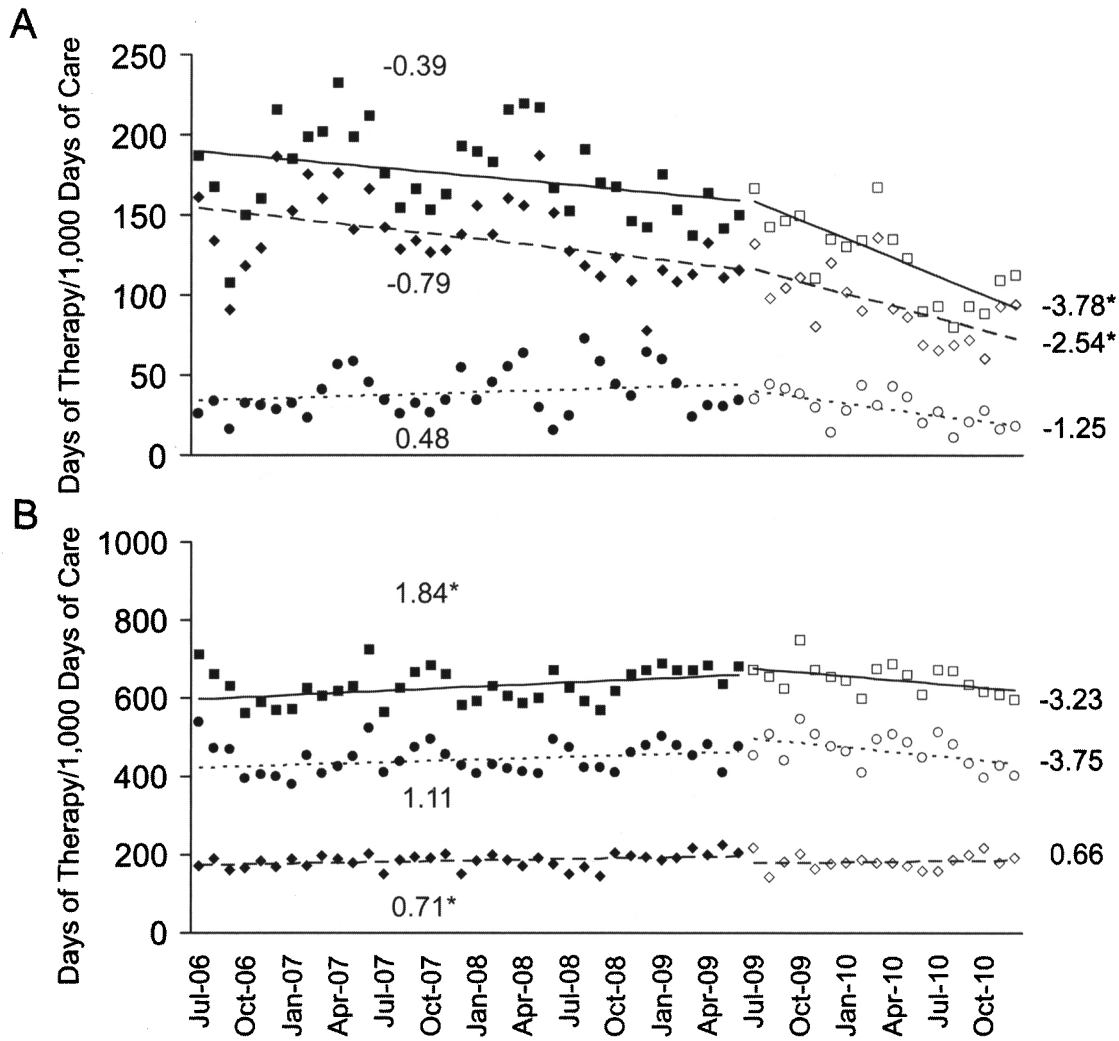

FIGURE 1. Observed rates of antibiotic use before and after initiation of the long-term care facility (LTCF) infectious diseases consultation service (LID), shown as filled and open symbols, respectively, in the LTCF (*A*) and the hospital (*B*). The corresponding lines and their slopes (indicated on the graph) represent the estimated rates of change in antimicrobial use for total antimicrobials (squares), oral agents (diamonds), and intravenous agents (circles), determined using segmented regression analysis of an interrupted time series. An asterisk indicates $P \leq .05$.

9 codes, and thus these data severely underestimated the rate of CDI. Accordingly, we used the number of positive *C. difficile* tests per 1,000 DOC to measure the CDI rate. We evaluated positive *C. difficile* tests in the 21 months before (October 2007–June 2009) and the 18 months after (July 2009–December 2010) initiation of the LID service and then calculated the number of positive *C. difficile* tests per 1,000 DOC. The data pertaining to *C. difficile* test results prior to October 2007 were erratic and thus excluded.

Analysis

The mean DOTs per 1,000 DOC for total, oral, and intravenous antibiotics administered at the LTCF before and after initiation of the LID service were compared by means of a Student *t* test. We then used segmented regression analysis of an interrupted time series to control for antibiotic use and adjust for potential serial correlation of the observations.[13] The mean number of admissions and the mean number of transfers from the LTCF to the affiliated VA hospital per month were included in the model as covariates. Within this regression framework, we tested the significance of changes in the level and slope of the regression lines before and after the LID service began. We checked for autocorrelation by using the Durbin-Watson statistic (range, 1.7–2.0; values close to 2 indicate no serial correlation), followed by a generalized least squares estimation using the Prais-Winsten method.[14] Seasonal variation (by months) was tested by fitting a model for each outcome without month terms and then plotting the residuals of that model against the month. We did not identify any patterns suggestive of seasonality. For a control, we ap-

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TABLE 2. Change in the Rates of Antibiotic Use and of Positive *Clostridium difficile* Tests in the Long-Term Care Facility (LTCF) and the Hospital

	Change in intercept				Change in slope			
Form, location	Mean	LCI	UCI	*P* value	Mean	LCI	UCI	*P* value
Antibiotic use								
Total, LTCF	7.8	−26.2	41.8	.65	3.4	0.3	6.5	.03
Total, hospital	−14.9	−67.8	37.9	.57	5.1	0.4	9.7	.03
Oral, LTCF	2.5	−27.5	32.4	.87	1.8	−1.0	4.5	.21
Oral, hospital	18.7	−2.4	39.7	.08	0.0	−1.8	1.8	.96
Intravenous, LTCF	6.3	−11.6	24.1	.48	1.7	0.1	3.4	.04
Intravenous, hospital	−32.8	−80.1	14.5	.17	4.9	0.76	9.0	.02
Positive *C. difficile* test per 1,000 DOC								
LTCF	−0.20	−0.79	0.38	.48	0.1	0.00	0.1	.04
Hospital	0.79	−0.11	1.69	.09	0.0	−0.79	−0.1	.93

NOTE. DOC, days of care; LCI, lower confidence interval; UCI, upper confidence interval.

plied the same model (absent the covariate of transfers from the LTCF to the hospital) and analysis to systemic antimicrobials used at the hospital.

To compare the use of antibiotic classes and individual agents before and after initiation of the LID service for, we used a Student *t* test with a Bonferroni adjustment to account for multiple comparisons. To determine the estimated rates of change for positive *C. difficile* tests, we again used segmented regression analysis of an interrupted time series to assess the significance of changes in the level and slope of the regression lines before and after the introduction of the LID service, using the data obtained from the hospital as a control. No covariates were included this model. All statistical analyses were performed with Stata (Stata Statistical Software; rel 12).

RESULTS

LID Consultation Service

The LID service saw an average of 7 patients and fielded 5–10 phone calls each week. During the study period, the LID service saw 250 individuals, with a total of 291 consults. Nearly one-third of the consults required only 1 visit; the remaining patients required an average of 3.6 visits (range, 2–20). More than 95% of the recommendations made by the LID team were followed. The most common reason for the LTCF staff to consult the LID service was CDI, which is endemic in our region.[15] The LID service reduced the time from symptom onset to symptom recognition and diagnostic testing for CDI, promoting more rapid initiation of treatment and isolation precautions.[16] The second most common reason for consultation was conditions that were ultimately deemed noninfectious, including asymptomatic bacteriuria, colonized wounds, and heart failure exacerbations.

Antimicrobial Use at the LTCF

After initiation of the LID consultation service, total antimicrobial use decreased by 30.1% ($P < .001$), with a greater reduction in oral agents (31.6%; $P < .001$) than in intravenous agents (25.0%; $P = .008$; Table 1). Antimicrobial use at the affiliated VA hospital did not change over the same period. We also analyzed the change in antibiotic use over time, using segmented linear regression of an interrupted time series (Figure 1). In the preintervention period, the rate of total antibiotic use at the LTCF did not change significantly ($P = .55$), while it increased at the hospital ($P = .03$). The slight decline observed in rate of oral antibiotic use at the LTCF in the preintervention period ($P = .18$) amplified significantly in the postintervention period ($P = .04$). In contrast, the rate of oral antibiotic use at the hospital increased significantly in the preintervention period ($P = .03$) and did not change in postintervention period ($P = .44$). Rates of intravenous antibiotic use at the LTCF and the hospital did not change between the pre- and postintervention periods ($P > .05$ for all intravenous antibiotic rates). Comparison of the change in intercepts in the time series analysis revealed no immediate effect of the LID service on antimicrobial use (Table 2).

Figure 2 compares antibiotic use (in DOT per 1,000 DOC) before and after the start of the LID consultation service for several antimicrobial classes and some individual agents. Fluoroquinolone use decreased by 38% ($P < .0001$). Ciprofloxacin accounted for the majority of this change (41% decrease; $P < .0001$). Sulfamethoxazole/trimethoprim use decreased by 38% ($P < .0001$), while nitrofurantoin use remained unchanged. Frequently employed as a first-line agent for CDI, metronidazole administration decreased by 22% ($P = .005$). In contrast, oral vancomycin, for which the only indication is CDI, increased by 89% ($P = .005$). The LID consultation service also led to statistically significant reductions in tetracyclines (64%; $P = .0001$) and clindamycin (61%; $P = .0015$), both of which are used infrequently.

The LID consultation service also influenced administration of β-lactams. Use of β-lactam/β-lactamase inhibitor combinations decreased significantly (28%; $P = .0005$). The greatest reduction was in piperacillin/tazobactam use (48%; $P = .005$), followed by amoxicillin/clavulanate (28%; $P =$

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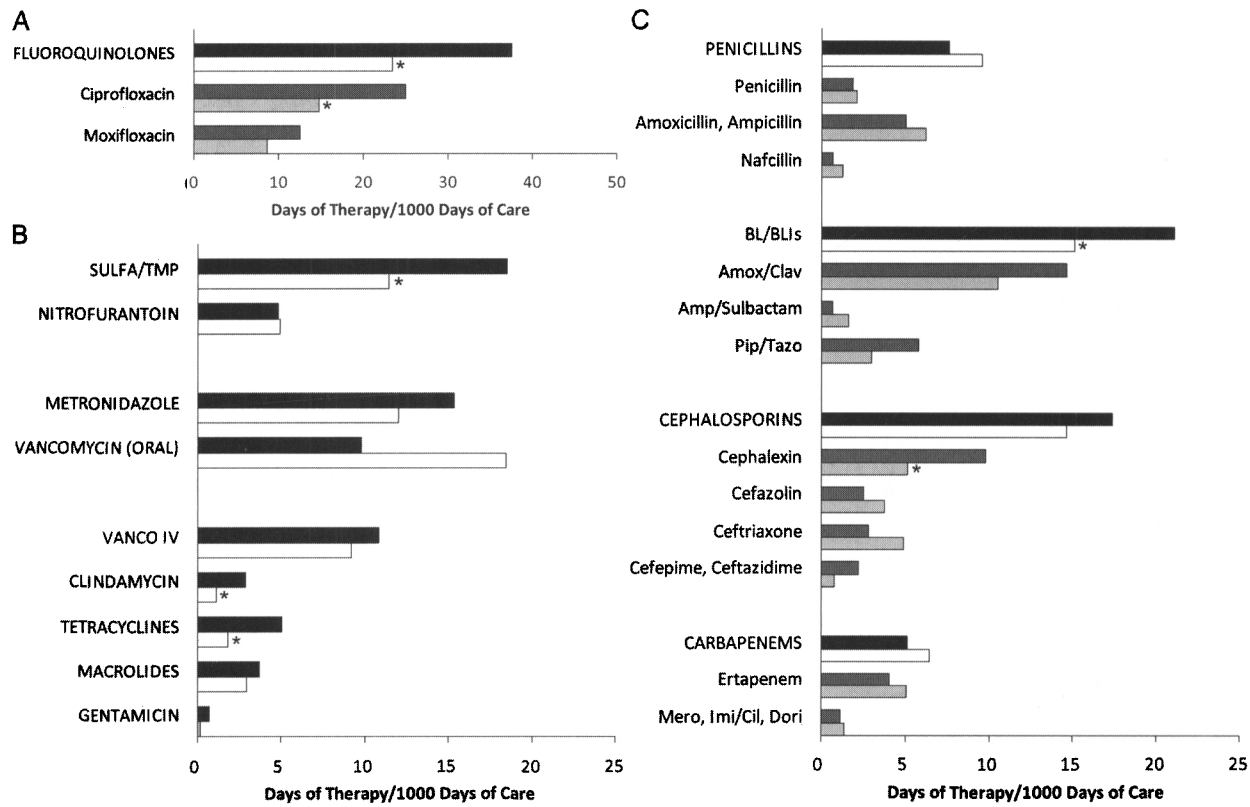

FIGURE 2. Comparison of mean use of fluoroquinolones (*A*), other non-β-lactams (*B*), and β-lactam antimicrobials (*C*). Bars depict the mean days of therapy per 1,000 days of care for drug classes before and after initiation of the long-term care facility infectious diseases consultation service for drug classes (black and white bars, respectively) and for individual antibiotics (dark and light gray bars, respectively). Asterisk indicates that the result is significant at $P \leq .0017$ with Bonferroni correction. Amox/Clav, amoxicillin/clavulanate; Amp/Sulbactam, ampicillin/sulbactam; BL/BLIs, β-lactams/β-lactamase inhibitors; Mero, Imi/Cil, Dori, meropenem, imipenem/cilistatin, doripenem; Pip/Tazo, piperacillin/tazobactam; Sulfa/TMP, sulfamethoxazole/trimethoprim; Vanco IV, intravenous vancomycin.

0.003), although these changes were not statistically significant. Total cephalosporin use declined by 16% ($P = .01$), with a significant decrease only for cephalexin (48%; $P < .0001$). In contrast, cefazolin administration increased by 51% ($P = 0.30$). Among extended-spectrum β-lactams, administration of the antipseudomonal agents cefepime and ceftazidime decreased by 65%, while ceftriaxone use increased by 75%. Interestingly, the use of carbapenems increased by 37% ($P = .50$) after initiation of the ID consultation service. None of the changes among these broad-spectrum antibiotics reached statistical significance.

Positive *C. difficile* Tests at the LTCF

At the LTCF, the rate of positive *C. difficile* tests in the preintervention period showed a trend toward increasing ($P = .09$), whereas in the postintervention period the trend was reversed ($P = .21$; Figure 3). The difference between the slopes in the pre- and postintervention periods is significant ($P = .04$; Table 2). While the rate of positive *C. difficile* tests did not change significantly over time for the 2 individual time periods, the difference in the rates between the 2 time periods was significant, indicating an improvement in the postintervention period. In contrast, the rate of positive *C. difficile* tests at the hospital presented a nearly identical increase in the pre- and postintervention periods ($P = .02$ and .05, respectively), without a significant difference in the slopes between the 2 periods ($P = .93$).

DISCUSSION

Most LTCF antibiotic stewardship strategies have focused on education, using booklets, teaching sessions, formulary guidelines, physician feedback, and diagnosis and treatment algorithms.[17-19] In our facility, Zabarsky et al[20] used an educational intervention directed at LTCF nurses and successfully decreased inappropriate submission of urine cultures, antibiotic prescriptions for asymptomatic bacteriuria, and total days of antibiotic therapy. Building on these efforts, we developed an alternative approach to achieve antibiotic stewardship, specifically, a program through which we brought subspecialty expertise to the LTCF. This intervention reduced total antibiotic use and the rate of change for positive *C.*

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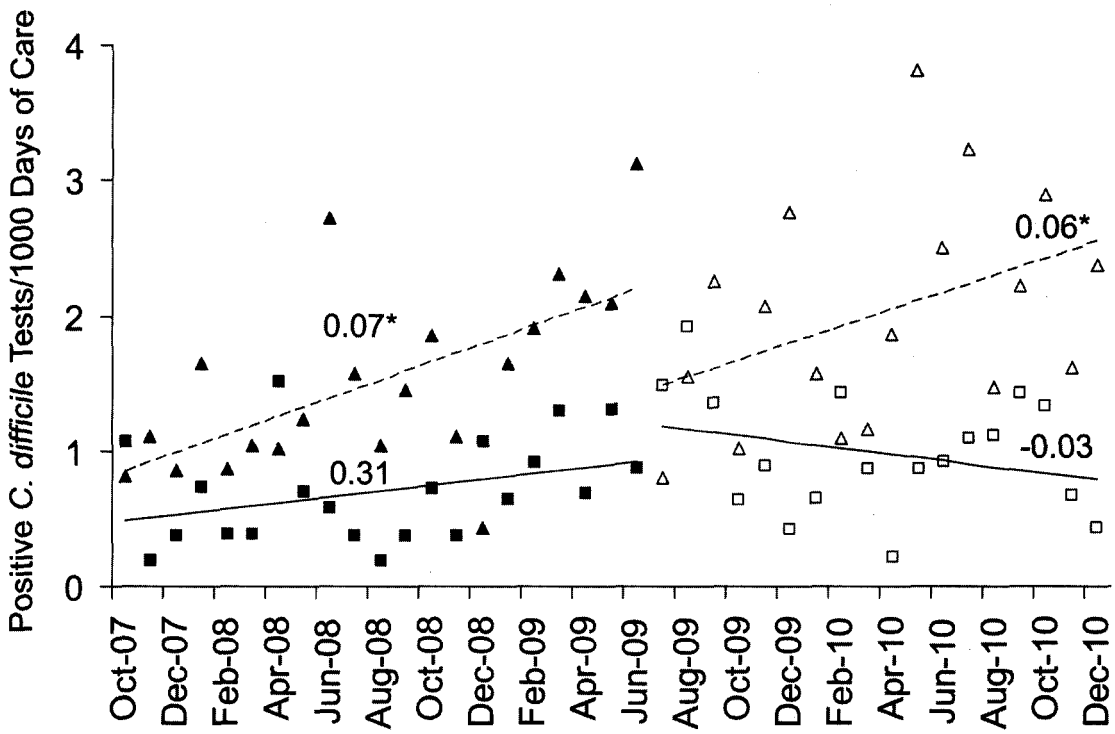

FIGURE 3. Observed rates of positive *Clostridium difficile* tests at the long-term care facility (LTCF; squares) and the hospital (triangles) before (filled symbols) and after (open symbols) initiation of the LTCF infectious diseases consultation service (LID). The corresponding lines and their slopes (noted on graph) represent the estimated rates of change for positive *C. difficile* tests at the LTCF (solid lines) and the hospital (dashed lines), determined using segmented regression analysis of an interrupted time series. An asterisk indicates $P \leq .05$.

difficile tests at the LTCF. Although total antimicrobial use at the LTCF showed a slight decline in the preintervention period, it declined significantly after initiation of the LID service.

Fluoroquinolones account for 30%–44% of antimicrobial prescriptions in LTCFs, likely a reflection of their broad spectrum of activity, oral bioavailability, and ease of dosing.[21,22] In our LTCF, ciprofloxacin was being used, often empirically, for suspected urinary tract infections (UTIs). While the LTCF staff was familiar with using sulfamethoxazole/trimethoprim and nitrofurantoin for UTIs, they were also quick to adopt the LID recommendations for other narrow-spectrum drugs, such as amoxicillin and cephalexin. The LID service led to a reduction in the use of piperacillin/tazobactam, cefepime, and cetazidime, all of which have antipseudomonal activity. The corresponding increase in ampicillin/sulbactam, ceftriaxone, and penicillin use suggests that the LID service successfully directed deescalation of antimicrobial therapy. The overall use of carbapenems, however, showed a nonsignificant increase following implementation of the LID service. As a result of these data, we have implemented further efforts to reduce total carbapenem use at the LTCF.

The decline in the rate of change of positive *C. difficile* tests at the LTCF following implementation of the LID consultation service is multifactorial. In addition to decreasing total antimicrobial use, the LID team promoted narrow-spectrum agents whenever possible. Furthermore, the LID consultation service actively discouraged use of clindamycin and fluoroquinolones. Clindamycin has a long association with increased CDI risk;[23] fluoroquinolone exposure may select for the fluoroquinolone-resistant epidemic *C. difficile* strain.[24] Beyond supporting the measures implemented by infection control practitioners, the LID team also provided direct education and feedback to the LTCF staff and improved treatment of CDI through use of guideline-driven recommendations regarding the antimicrobial agents selected, the doses administered, and the length of treatment.[11] Finally, suggestions to avoid "test of cure" in asymptomatic patients and to forego testing among those in whom recurrent disease was clinically evident may have also contributed to a decline in positive *C. difficile* tests.

Our study has several limitations. We measured only total DOT but did not consider the average length of therapy or the number of antimicrobial courses initiated.[22,25] We did not focus on antimicrobials applied to specific syndromes, such as suspected UTIs or pneumonia, which also limits our ability to comment on the appropriateness of therapy. In addition, while the use of positive *C. difficile* tests to determine the rate of CDI has not been validated in an LTCF setting, Dubberke et al[12] report equivalent results regarding CDI incidence in

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acute care settings, using either *C. difficile* toxin assays or *ICD-9* codes. Furthermore, our intervention occurred at a single VA LTCF, in which all of the prescribers (2 physicians, 3 nurse practitioners, and 1 physician assistant) are full-time staff. This is atypical for most LTCFs. Less than 20% of nursing homes employ full-time staff physicians, and most LTCF medical directors typically provide primary care at 4 facilities, spending 8–12 h/wk in nursing homes seeing residents while also serving as the medical director for 2 facilities.[1,26] Finally, the ID specialists who initiated the LID service at the LTCF are full-time VA employees, and thus there were no concerns about reimbursement or insurance claims, limiting the applicability of the LID service to non-VA LTCFs.

The increasing prevalence of nosocomial pathogens and the lack of new antimicrobials under development have prompted many hospitals to implement stewardship programs to improve the use of antimicrobial agents, minimize selection for organisms with antimicrobial resistance, and reduce the incidence of CDI.[11,27] LTCFs have been slower to adopt stewardship measures. The reasons for this are multifactorial and include the lack of necessary personnel, funding, and electronic resources as well as a paucity of well-validated strategies specific to LTCFs.[27-30] A survey of LTCFs in Nebraska found that the greatest perceived barrier to effective antimicrobial stewardship was physician practice; specifically, a treat-first attitude, lack of response to input from other healthcare workers, nonparticipation in LTCF initiatives, and lack of knowledge regarding appropriate use of antimicrobials.[28] The scarcity of clinical ID expertise is perhaps the most significant challenge faced by LTCFs in conducting concurrent review and adjustment of antibiotic therapy.[27,29,30]

To our knowledge, this is the first description of effective antimicrobial stewardship at an LTCF achieved by bringing subspecialist expertise directly to the residents.[30] While labor-intensive, our intervention reduced not only total antimicrobial use but also the rate of change for positive *C. difficile* tests, providing a functional measure of the influence of the LID service. It is our hope that this success within the VA system may support measures to implement similar programs in other LTCFs.

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