Antibiotic Self-stewardship: Trainee-Led Structured Antibiotic Time-outs to Improve Antimicrobial Use

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Background: Antibiotic use is an important quality improvement target. Nearly 50% of antibiotic use is unnecessary or inappropriate. To combat overuse, the Centers for Disease Control and Prevention (CDC) proposed “time-outs” to reevaluate antibiotics.

Objective: To optimize antibiotic use through trainee-led time-outs.

Design: Before–after study.

Setting: Internal medicine (2 units, 46 beds) at a university hospital.

Patients: Inpatients (n = 679).

Intervention: From January 2012 until June 2013, while receiving monthly education on antimicrobial stewardship, resident physicians adjusted patients’ antibiotic therapy through twice-weekly time-out audits using a structured electronic checklist.

Measurements: Antibiotic costs were standardized and compared in the year before and after the audits. Use was measured as World Health Organization defined daily doses (DDDs) per 1000 patient-days. Total antibiotic use and the use of moxifloxacin, carbapenems, antipseudomonal penicillins, and vancomycin were compared by using interrupted time series. Rates of nosocomial Clostridium difficile infection were compared by using incidence rate ratios.

Results: Total costs in the units decreased from $149 743CAD (January 2011 to January 2012) to $80 319 (January 2012 to January 2013), for a savings of $69 424 (46% reduction). Of the savings, $54 150 (78%) was related to carbapenems and $15 274 (22%) was due to other antibiotic classes. Adherence with the auditing process was 80%. In the time-series analyses, the only reliable and statistically significant change was a reduction in the rate of moxifloxacin use, by −1.9 DDDs per 1000 patient-days per month (95% CI, −3.8 to −0.02; P = 0.048). Rates of C. difficile infection decreased from 24.2 to 19.6 per 10 000 patient-days (incidence rate ratio, 0.8 [CI, 0.5 to 1.3]).

Limitation: Other temporal factors may confound the findings.

Conclusions: An antibiotic self-stewardship bundle to implement the CDC’s suggested time-outs seems to have reduced overall costs and targeted antibiotic use.

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See also:

Web-Only
Data Supplements

Antibiotic resistance is a major public health issue that substantially affects patient outcomes and costs (1). With new antimicrobials few in number and far off in development (2), we need to maximize the effectiveness of today’s therapy and preserve it for tomorrow by preventing resistance. This and the prevention of Clostridium difficile infection are 2 of the main goals of antimicrobial stewardship. There are several methods of stewardship (3); one of the most effective, prospective audit and feedback, uses consultants in infectious diseases or trained pharmacists to review use case by case (4). The expertise required limits the implementation of such programs (3, 4).

Given that the Centers for Disease Control and Prevention (CDC) suggests that nearly 50% of antimicrobial use is unnecessary or inappropriate (5), it is clear that widely available methods of stewardship need to be developed. In an online campaign called “Get Smart for Healthcare,” the CDC suggests that clinicians take an antimicrobial “time-out” to review the dose, duration, and indication when cultures and new clinical information become available (6).

While planning our local stewardship program, we recognized that our resources were limited and our needs great. Although it seemed logical that time-outs could lead to reduced antibiotic use, we believed that without education and a formal structure, they would be forgotten or underutilized. We developed an educational curriculum and electronic checklist to provide structure and subsequently implemented mandatory time-out audits on our internal medicine clinical teaching units. These time-out audits were integrated into routine clinical practice by our senior residents, who performed a process that we called “antimicrobial self-stewardship.”

METHODS
Setting
The study was conducted in two 23-bed internal medicine clinical teaching units in the Montreal General Hospital, a 417-bed tertiary care hospital. Each unit has an...
attending physician, a senior resident (second-year), 2 first-year residents, and 2 medical students. A third-year resident is shared between the teams who focuses their time on quality improvement projects, teaching, and procedural support. Attending physicians work a variable number of 2-week blocks per year. Resident physicians have three to four 1-month rotations per year.

Interventions

The study investigators included consultants in infectious diseases, critical care medicine, and general internal medicine with expertise in the management of hospitalized patients. Through consensus, we developed a 30-minute teaching session (Data Supplements 1 and 2, available at www.annals.org) that addressed the importance of antibiotic stewardship, our guidelines for the most common infectious diseases encountered, and how to perform self-stewardship. These sessions were given monthly to all rotating housestaff.

Our stewardship team (Drs. Lee and Frenette) developed an online checklist (Data Supplement 3, available at www.annals.org) that formalized each time-out audit into a step-by-step process meant to approximate how an infectious diseases specialist might approach prospective audit and feedback. We specifically targeted 4 key antimicrobials: 1) carbapenems, which were the most expensive class with the broadest spectrum of activity; 2) moxifloxacin, which was chosen to reduce *C. difficile* infection and to reduce gram-negative exposure to the quinolones; 3) piperacillin–tazobactam, which is the most widely used broad-spectrum antibiotic at our institution; and 4) vancomycin, because it is potentially overused in patients without risk factors for infection with β-lactam–resistant gram-positive organisms and is associated with nephrotoxicity.

To limit workload, we chose to implement audits twice weekly. On each audit day, the senior resident would apply the checklist to all patients receiving antibiotics. Each unit audited required 30 minutes to complete. Residents were reminded to perform the audits by the unit pharmacists, but performance was not directly observed. At the end of each month, antibiotic use was reviewed using the qualitative data from the audits and the results were fed back.

Measurements

Information on antibiotic use from 1 April 2010 to mid-January 2012 (control period) and from mid-January 2012 until the beginning of June 2013 (intervention period) was obtained from the pharmacy as World Health Organization defined daily doses (DDDs) (7). The DDDs were available by fiscal period (13 periods per year, beginning in April) and were standardized per 1000 patient-days. Cost was standardized to the June 2013 price per DDD in Canadian dollars. Because an automatic substitution from ticarcillin–clavulanate to piperacillin–tazobactam occurred in mid-2011, the lower price was used for both. Only antibacterial agents were included.

Rates of nosocomial *C. difficile* infection were calculated as the number of polymerase chain reaction–positive cases per 10 000 patient-days. In keeping with Quebec reporting standards, a nosocomial case was identified when symptoms occurred more than 3 days after admission or symptoms caused readmission in a patient who had been hospitalized on our unit within the previous 2 months and who was not a resident in a long-term care facility.

Primary outcomes were the cost and quantity of antibiotics used both overall and with a focus on our targeted drugs, and rates of *C. difficile* infection per 10 000 patient-days. Secondary outcomes were length of stay, number of monthly intensive care unit (ICU) transfers, and mortality per 10 000 patient-days.

McGill University Health Center ethics approval was obtained.

Statistical Analysis

We conducted segmented regression analysis of an interrupted time series, as described by Wagner and colleagues (8). Models were created for total antibiotic use and for each of the 4 targeted drugs or classes. Each interrupted time series can be specified as $E(Y) = \text{constant} + \beta_0*t + \beta_1*X_1 + \beta_2*t*X_1$, where $Y$ is the dependent variable (antibiotic use), $t$ indicates the order of the observations (fiscal period), and $X_1$ is a dummy variable indicating whether the observation was taken before or after the intervention. In this method, we use the preintervention period as the control for the postintervention period. If $\beta_1$ differs statistically from zero, this implies that there was a change in the absolute level of use of the drug after intervention. If $\beta_2$ differs statistically from zero, this implies that there was a change in the trend of use (slope of the line) after intervention.

The time-series analyses were done using the tsset and regress commands. Autocorrelation in the residuals was evaluated by using the Durbin–Watson method (estat dwatson command).

Rates of *C. difficile* infection and mortality before and after intervention were compared by using the $Z$ test for incidence rate ratios. Before-and-after comparisons in the average length of stay and the median monthly number of ICU transfers were compared by using the 2-tailed $t$ test and Wilcoxon rank-sum test, respectively.

All comparisons were performed by using Stata, version 11 (StataCorp).

Role of the Funding Source

This project was completed without any funding. Faculty members donated their time. Resident physicians were paid their usual salary because the time-out audits were considered clinical work. The monthly faculty time required was 1 hour, and the monthly resident time totaled 8 hours (108 hours per year).
**Table 1. Antibiotic Changes Made During the First and Subsequent Audits**

<table>
<thead>
<tr>
<th>Audit Time Frame</th>
<th>Total Audits, n</th>
<th>Audits With Change, n (%)</th>
<th>Type of Change Made, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>First</td>
<td>1062</td>
<td>154 (14.5)</td>
<td>85 (55)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>69 (45)</td>
</tr>
<tr>
<td>Second</td>
<td>271</td>
<td>24 (8.9)</td>
<td>15 (63)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>9 (38)</td>
</tr>
<tr>
<td>Subsequent</td>
<td>180</td>
<td>11 (6.1)</td>
<td>7 (64)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>4 (36)</td>
</tr>
<tr>
<td>Total</td>
<td>1513</td>
<td>189 (12.5)</td>
<td>107 (57)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>82 (43)</td>
</tr>
</tbody>
</table>

* Denominator is the total number of audits.
† Denominator is the number of audits in which a change was made.

**RESULTS**

During the intervention period (mid-January 2012 to the start of June 2013), 23 staff physicians attended a median of 6 weeks each. There were 15 senior residents who worked a median of 12 weeks each. There were a total of 1548 admissions, with 1513 time-out audits performed on 1062 unique infections involving 679 unique patients. Auditing was performed on 80% of assigned days.

Pneumonia was the most common infection (25%), followed by urinary tract infection (12%), *C. difficile* (9%), and cellulitis (7%). The top 5 classes of antibiotics used at the time of initial time-out audit were antipseudomonal penicillins (23%), fluoroquinolones (16%), glycopeptides (13%), narrow-spectrum β-lactams (12%), and third-generation cephalosporins (7%).

The initial time-out led to a change in antibiotic therapy in 15% (154) of infections audited. Among these changes, 55% involved dose or duration only and the other 45% involved a change in therapy. Changes were less frequent in subsequent audits (9%). These data are presented in Table 1. Changes were more common in patients receiving piperacillin–tazobactam (20%), a fluoroquinolone (20%), or vancomycin (14%) than in those receiving a carbapenem (6%) (Table 2). Changes or cessations that occurred before or between the time-outs were not captured.

The total annual standardized cost of antibiotics for the units decreased from $149 743 (January 2011 to December 2011) to $80 319 (January 2012 to December 2012), for a year-on-year savings of $69 424 (46% reduction). Of the savings, $54 150 (78%) was related to carbapenem use and $15 274 (22%) was due to other classes. On the basis of 108 physician-hours per year, this would represent a return of $140 to $640 per hour, excluding and including carbapenems, respectively.

In the time-series analysis, the total monthly use of antibiotics was unchanged (*P* = 0.91 for level; *P* = 0.10 for trend) and averaged 720 DDDs per 1000 patient-days per period throughout the study (Figure 1). Figure 2 shows the monthly use per fiscal period in DDDs per 1000 patient-days for moxifloxacin, carbapenems, vancomycin, and antipseudomonal penicillins. The only reliable, statistically significant change was a reduction in the trend of moxifloxacin use by −1.9 DDDs per 1000 patient-days per month (95% CI, −3.8 to −0.02; *P* = 0.048). There was a statistically significant decrease in the level of carbapenem use after intervention by 35.4 DDDs per 1000 patient-days (CI, 3.5 to 67.1; *P* = 0.030), with no change in the trend (*P* = 0.98). However, the change may have started before the intervention. There were no significant differences for piperacillin–tazobactam (*P* = 0.096 for level; *P* = 0.112) or vancomycin (*P* = 0.59 for level; *P* = 0.85 for trend). As moxifloxacin use decreased, there appeared to be a corresponding but non–statistically significant increase in combined macrolide and tetracycline use (Figure 3).

Rates of nosocomial *C. difficile* infection in the full calendar year before and after intervention were 24.2 versus 19.6 per 10 000 patient-days, respectively (incidence rate ratio, 0.8 [CI, 0.5 to 1.3]). There were no differences in average length of stay (11.0 vs. 10.2 days; *P* = 0.150), median number of ICU transfers (7 vs. 5; *P* = 0.20) or...
DISCUSSION

Antibiotic self-stewardship seemed to be associated with a sizable cost reduction for our 46-bed unit. We saved almost $70 000 from the annual unit budget, using 1 hour of faculty time and 8 hours of resident physician time per month. Excluding any savings related to carbapenems, we still saved approximately $15 000 for 46 beds. If our method is generalizable to the other units of our hospital or similar units in other hospitals, the overall savings could be substantial.

Adherence with auditing was good (80%), and in general, resident physicians believed that the process improved their comfort with antibiotics and provided clinical value. Changes were common, with 1 in 7 patients having their antibiotics changed at the first audit. Subsequent audits for the same infection yielded further changes, suggesting that the residents were reevaluating at each encounter.

It is also likely that other changes occurred between audits, on the basis of clinical and microbiologic factors. Some of these changes may have happened in anticipation of the audits, owing to the Hawthorne effect. We feel that the power to cause changes in prescribing “in anticipation” should be seen as a potential strength of the intervention.

Despite a cost-savings, we were unable to demonstrate a reduction in overall antibiotic use. The metric that we used, DDDs per 1000 patient-days, may not be ideal compared with days on therapy, length of therapy, or the ratio of the two (9). Consider our most common infection, community-acquired pneumonia, for which we favored a β-lactam–macrolide (or doxycycline) combination instead a fluoroquinolone: A 7-day treatment course with 2 drugs versus a 5-day treatment course of moxifloxacin caused an increase of 9 DDDs per case of pneumonia treated.

Another reason that we did not see an improvement in total use may be our automatic hard stop on antibiotics at 7 days without reorder; this policy prevents many instances of inadvertent extended therapy. However, hard stops can also cause unintended cessations of therapy, and our time-out process should have prevented those by ensuring that the correct duration was specified in advance of discontinuation.

On visual inspection of the data, moxifloxacin use decreased and was statistically significant in the time-series of the audits, owing to the Hawthorne effect. We feel that the power to cause changes in prescribing “in anticipation” should be seen as a potential strength of the intervention.

The fiscal period started in April 2010. There are 13 fiscal periods in the financial year. The vertical line represents the first fiscal period of the intervention. The dashed and dotted lines represent the time-series model–predicted lines of best fit before and after the intervention. DDD = defined daily dose; P = period.

mortality rate per 10 000 patient-days (8.3 vs. 7.6; incidence rate ratio, 1.1 [CI, 0.9 to 1.5]).
behavior is unlikely to change without local antibiograms.

Piperacillin–tazobactam while awaiting cultures; this case well enough to narrow coverage. In addition, patients who develop nosocomial infections most often receive empiric, and no nosocomial outbreaks to explain the influx. This is particularly true when transfers happen to the former, to the best of our recollection there was no patient-days, we cannot differentiate between a few patients receiving large quantities of antibiotic or a large number of patients receiving small quantities. With respect to the latter, there was no corresponding drop in antipseudomonal agent use that would imply a shift from these agents to carbenems, and no nosocomial outbreaks to explain the period of highest use. We suggest that the carbapenem data be viewed, with due skepticism, as potentially supporting the intervention, given that use has remained well below preintervention highs.

Piperacillin–tazobactam is one of the most-used antibiotics across all services at our institution. It is significantly overused in our emergency department, where patients will receive this drug for community-acquired infections without indication for Pseudomonas coverage. Many patients are admitted while receiving this drug, and it is possible that our twice-weekly audits could not offset that influx. This is particularly true when transfers happen at night and the covering resident may not understand the case well enough to narrow coverage. In addition, patients who develop nosocomial infections most often receive empirical piperacillin–tazobactam while awaiting cultures; this behavior is unlikely to change without local antibiograms.

We believe that vancomycin showed no change because use probably varies more with the burden of methicillin-resistant Staphylococcus aureus than systematic overuse.

Fluoroquinolone use is a well-recognized risk factor for C. difficile acquisition in Quebec (10), yet we did not see a reduction in rates despite reducing quinolone use. First, the majority of patients who develop C. difficile infection on our unit have received at least 1 dose of antibiotics elsewhere. The number of patients who received antibiotics on our unit only was insufficient to make any unit-specific comparisons. Second, almost any antibiotic can cause C. difficile acquisition, not just the fluoroquinolones, and our overall use did not change. Finally, nosocomial C. difficile rates are influenced by the burden of disease present on the unit, and our reservoir fluctuates substantially on the basis of the number of patients admitted who are colonized.

Although we did not demonstrate a statistically significant effect, if we prevented even 1 case, it would be important to the individual and—at $11 285USD per case (11)—to the health care system as well.

An English-language PubMed search in August 2013 revealed 2 other studies in which a self-administered checklist was used for stewardship. Weiss and colleagues (12, 13) compared empirical antibiotic use in the intensive care unit between a group that used a self-directed checklist and a group that received face-to-face prompting by an external physician. The external physician was superior to the checklist, and furthermore, the checklist was not significantly better than baseline.

However, there are important differences between Weiss and colleagues’ studies and ours. First, they had to employ someone outside of the care team to do the face-to-face prompting. Although this did not burden the clinical team, it involved an external expert, which our self-stewardship platform was designed to avoid. Second, we provided a specific curriculum throughout our intervention; in contrast, the depth to which stewardship was taught in Weiss and colleagues’ studies is unclear. Finally, our checklist specifically addressed dose, route, duration, appropriateness to culture results, and clinical factors, whereas theirs was more limited. Whether our more structured approach would have led to different results in their center is unclear. Conversely, whether our approach would have been further supplemented by periodic external stewardship cues is also interesting.

Our approach may also offer benefits to medical student and resident education. Abbo and coworkers (14) studied medical students and Srinivasan and associates (15) resident physicians with respect to antibiotic stewardship. Both studies identified substantial knowledge deficits. Our approach ties specific education about antibiotic use in common infections with a structured tool to review and guide antibiotic use. This could potentially translate into better prescribing practices during our residents’ future careers.
Our study has limitations. We describe a single-center experience using a nonrandomized before-and-after methodology. As with any observational study, the absence of randomization and a control group limits the strength of any conclusions. We attempted to control for temporal trends by using an interrupted time series, but this is subject to the limitations of the method, including the assumption of linearity. It is possible that another model, such as a Box–Jenkins model, may have fit the data better; however, such models may be of less use in evaluating a change occurring at a specific time point, and they also require 50 to 100 data points, which we did not have.

Furthermore, although we believe that our program created some of the savings realized, we recognize that each year’s senior residents will have different practice patterns based on their own experiences and training. The cohort of senior residents during the intervention may have used antibiotics differently from those who came before, regardless of the intervention. Also, although the intervention was aimed at the resident physicians and their behavior, faculty influence can affect prescribing independent of the audits.

Finally, we tested a bundle of interventions that included education, use of a checklist, and end-of-month feedback, and we cannot separate the individual contributions of each of these components. Whether one would suffice on its own cannot be determined from our data.

Despite these limitations, we believe our data suggest that self-stewardship merits further study in other units and settings. We further suggest that when supported by educational sessions, a structured checklist, and regular feedback, the CDC’s antibiotic time-outs can aid in reducing both costs and optimizing antimicrobial use. In our center, we hope that this approach will permit a more widespread implementation of antibiotic stewardship and that by teaching self-stewardship, we will affect future prescribing, thereby turning today’s high rates of inappropriate antibiotic use into tomorrow’s historical footnote.

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Disclosures: None. Forms can be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M13-3016.

Reproducible Research Statement: Study protocol: Available from Dr. T.C. Lee (e-mail, todd.lee@mcgill.ca). Statistical code and data set: Not available.

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