

Outpatient Antibiotic Prescribing in Massachusetts, 2011–2015

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Background. The objectives of this study were to develop methods to measure population-based outpatient antibiotic prescribing in Massachusetts and to describe the findings as a first step toward institution of ongoing surveillance.

Methods. We analyzed outpatient prescription claims from the Massachusetts All-Payers Claims Database from 2011 to 2015. We grouped claims for antibiotics according to the World Health Organization's Anatomical Therapeutic Chemical Classification System using the National Library of Medicine's RXNorm database. We grouped prescribers into 17 specialties. Antibiotic use rates were calculated, and simple frequencies were used to describe patterns.

Results. The overall annual rate of outpatient antibiotic use for individuals aged 0–64 years was 696 prescriptions per 1000 people. During 2015, 68% of people in Massachusetts had no antibiotic prescription, and 17% had only 1 prescription. There was dramatic variability in antibiotic use rates by census tract within the state (rates of penicillin use ranged from 31 to 265 prescriptions per 1000 people, macrolides from 28 to 333, cephalosporins from 8 to 89, quinolones from 13 to 118). Antibiotic use rates were generally lower in urban census tracts. From 2011 to 2015, there was a 17% decline in antibiotic prescribing, with the greatest decline for macrolides (28%).

Conclusions. There was variability in antibiotic prescribing within Massachusetts by age, sex, and antibiotic class. Variation in antibiotic use across census tracts within the state was similar to the variation in use across US states. Continued measurement and detailed local population rates of antibiotic use in Massachusetts will provide feedback for local prescribers.

Keywords. antibiotic use; state; surveillance.

An estimated 2 million cases of antibiotic-resistant infections, resulting in 23 000 deaths, occur each year in the United States [1]. Improving antibiotic prescribing through stewardship is a core action to prevent resistance [2]. Outpatient antibiotic prescriptions, which account for >60% of all antibiotic expenditures in the United States [3], are an important target for stewardship. Antibiotic stewardship in outpatient settings is endorsed by the Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria (CARB) [4]. The Centers for Disease Control and Prevention and the Association of State and Territorial Health Officers encourage states to engage directly in antimicrobial resistance efforts [2, 5]. To do this requires an understanding of utilization patterns within the state.

The overall US rate of outpatient antibiotic prescriptions in 2015 was 838 per 1000 people, but it varied by region and

state [6]. In addition, rates may vary by other characteristics including age of the recipient [6] and prescribing provider specialty [7]. For example, number of physician offices per capita has been associated with increased antibiotic prescribing [8], and Massachusetts has the highest rate of active physicians per population at 47 per 10 000 civilian population [9]. Massachusetts is also unusual in that access to health care services is nearly universal among residents. In 2015, 4% of Massachusetts residents were uninsured, the lowest percent uninsured of any state [10]. Finally, health care services represent the state's largest industry category [11].

The objectives of this study were to develop reproducible methods to measure outpatient antibiotic prescribing and to describe population-based rates of outpatient antibiotic prescribing in Massachusetts as a first step toward institution of ongoing surveillance for provider and community feedback and evaluation of local stewardship programs.

METHODS

We developed and describe a 5-step method that uses publicly available data to identify, extract, and classify antibiotic prescription drugs for analysis. Details are provided in the Supplementary Data. Briefly, the method consists of using administrative claims from health care encounters [12],

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establishing a set of generic antibiotic drug names and their unique system identifiers, associating their National Drug Code [13] with the World Health Organization Anatomical Therapeutic Class drug taxonomy [14], standardization, de-duplication, and validation.

Study Population and Data Source

Massachusetts law mandates that all insurance providers report health care services claims for their members to the state's Center for Health Information Analysis (CHIA) [12]. In turn, CHIA prepares databases for government and external researchers to answer health services research questions. One of these databases, the Massachusetts All-Payers Claims Database (APCD) contains pharmacy claims for >94% of Massachusetts residents under 65 years of age. We excluded individuals age 65 years and older because a majority of adults over 65 use Medicare for primary health coverage and Medicare claims are not available in the APCD. Pharmacy claims contain information about the medication, the demographic characteristics of the prescription recipient, and the prescribing provider. We analyzed APCD files from 2011 to 2015.

Identifying Antibiotic Prescription Claims

A claim was defined as a unique record of a health care service as submitted to CHIA by the payer. Claims for prescription antibiotics were identified in the APCD Pharmacy File by linking National Drug Codes (NDCs) for each claim to a generic list of antibiotic formulations. Because a definitive, publicly available list of antibiotic NDCs is not available, we developed a comprehensive list using the National Library of Medicine's RXNorm database [15]. These formulations were, in turn, grouped according to the World Health Organization's Anatomical Therapeutic Chemical Classification System [14]. We selected those categorized for systemic use (J01). This group does not include antimycobacterials or combinations of antibacterials and tuberculostatics (J04) but could include inhaled and injected preparations.

We categorized prescribers into 17 specialty groups [16] using National Provider Identifier (NPI) codes, consistent with national reports [6, 7], and linked each antibiotic claim with its prescriber's specialty group. Individuals were de-duplicated using a secure, nonidentifiable member number assigned by CHIA. We considered several options for calculating rates (Supplementary Data) and opted to use all individuals with claims in the APCD as the numerator and all eligible members as the denominator. This allowed the greatest geographic granularity (census tract) for analysis, and the resulting rates followed trends consistent with the Centers for Disease Control and Prevention (CDC) outpatient pharmacy data standard [17]. However, the CDC method uses denominators from the American Community Survey (ACS), which are estimated from a sample of the population [18].

Descriptive Analysis

We measured claims for antibiotic prescriptions, excluding refills, among insurance plan members and calculated rates per 1000 people by calendar year, sex, and age group (0–2, 3–9, 10–19, 20–64 years). Population-wide antibiotic use was measured for major antibiotic classes and for the most frequently prescribed individual antibiotics. To describe the distribution by specialty, we measured antibiotic prescription fills per prescriber within prescriber specialty group. To describe intensity of use at the individual level, we measured the frequency with which an individual member received multiple antibiotics within the same year (0, 1, 2, 3–5, or ≥ 6). Finally, to describe in-state geographic prescription patterns, we measured prescribing rates for the 4 most frequently prescribed classes (penicillins [J01C], macrolides [J01F], cephalosporins [J01D], and quinolones [J01M]) stratified by the US census tract of residence documented in the claim. Finally, we calculated the mean and SD across census tracts to measure variability. We calculated the coefficient of variation (CV), which is the ratio of the standard deviation and mean rate ($CV = SD/mean$) [19].

RESULTS

Our study population had 17.1 million antibiotic claims prescribed for an average of 4.9 million members over the 2011–2015 study period. The overall annual rate of outpatient antibiotic claims for individuals aged 0–64 years was 696 per 1000 people (Table 1). The rate of prescriptions was highest among infants and lowest among children and adolescents aged 10–19 years. The rate of prescriptions was higher among females than males.

The 2 antibiotic classes most frequently prescribed were penicillins and macrolides. Quinolones, cephalosporins, tetracyclines, and sulfonamides/folic acid inhibitors were also commonly prescribed, but at rates far below penicillins and macrolides. The most commonly prescribed individual antibiotic agents were amoxicillin (including amoxicillin with clavulanate) and azithromycin (Table 1). Other agents, in descending order, were ciprofloxacin, cephalexin, sulfamethoxazole, and clindamycin.

Provider Characteristics

The 3 medical specialties contributing the largest proportions of antibiotic prescriptions were internists, pediatricians, and nurse practitioners (Table 2). Fifteen percent of prescriptions could not be assigned to a specialty due to missing or invalid NPI codes.

Geographic Distribution

The geographic distribution of the rate of prescriptions per 1000 people varied substantially across the 1463 Massachusetts census tracts (Figure 1). The highest rate was for penicillins (mean annual prescriptions per 1000 people across census

Table 1. Antibiotic Prescriptions by Recipient Age, Sex, and Antibiotic Class and Agent, Massachusetts, 2011–2015

Characteristic	Prescriptions, No. in Thousands (%)	Annual Rate of Prescriptions per 1000 People
Overall		
Overall	17 112 (100)	695.9
Age		
Infants (0–2 y)	1230 (7.2)	1018.5
Younger children (3–9 y)	2012 (11.8)	813.5
Older children & adolescents (10–19 y)	2325 (13.6)	630.4
Adults (20–64 y)	11 545 (67.5)	667.3
Sex		
Female	10 418 (60.9)	827.8
Male	6693 (39.1)	557.6
Antibiotic class		
Penicillins (J01C)	5300 (31.0)	215.6
Macrolides (J01F)	4355 (25.5)	177.1
Quinolones (J01M)	1749 (10.2)	71.1
Cephalosporins (J01D)	1589 (9.3)	64.6
All other antibiotics	1551 (9.1)	63.1
Tetracyclines (J01A)	1196 (7.0)	48.6
Sulfonamides and trimethoprim (J01E)	960 (5.6)	39.0
Nitrofurantoin (J01XE)	412 (2.4)	16.8
Antibiotic agent (top 6)		
Amoxicillin (J01CA04)	4632 (45.2)	188.4
Azithromycin (J01FA10)	2607 (25.4)	106.0
Ciprofloxacin (J01MA02)	911 (8.9)	46.1
Cefalexin (J01DB01)	1079 (10.5)	43.9
Sulfamethoxazole (J01EC01)	419 (4.1)	42.5
Clindamycin (J01FF01)	607 (5.9)	41.2

tracts \pm SD, 181.6 \pm 36.1), followed by macrolides (mean \pm SD, 150.5 \pm 29.1), quinolones (mean \pm SD, 61.1 \pm 12.0), and cephalosporins (mean \pm SD, 54.5 \pm 13.8). The coefficient of

variation across census tracts was 20% for all 4 drug classes. In general, urban areas had lower antibiotic use across the 4 major antibiotic drug classes. Western Massachusetts had lower rates of prescription, except for an area around and north of the city of Pittsfield. Another area of consistently lower rates was the Southeast area of the state. The area southeast of Boston had higher rates of penicillin and quinolone prescriptions but lower rates of cephalosporin prescriptions.

Table 2. Antibiotic Prescribing by Provider Type, 2011–2015

Characteristic	Prescriptions, No. in Thousands (%)
Overall	17 112 (100)
Internal medicine	2677 (15.7)
Unknown specialty	2571 (15.0)
Pediatrics	2340 (13.7)
Nurse practitioner	2256 (13.2)
Family practice	1342 (7.8)
Infants (0–2 y)	40 (3.0)
Younger children (3–9 y)	77 (5.8)
Older children & adolescents (10–19 y)	118 (8.8)
Adults (20–64 y)	1107 (82.5)
Dentistry	1339 (7.8)
Physician Assistant	1102 (6.4)
Other	1079 (6.3)
Emergency medicine	743 (4.3)
Dermatology	517 (3.0)
Obstetrics and gynecology	398 (2.3)
Surgery	225 (1.3)
Otolaryngology	210 (1.2)
Pediatric subspecialty	162 (1.0)
Urology	148 (0.9)

Intensity of Use

The percentage of individuals in Massachusetts with no antibiotic prescribed during the period 2011–2015 was highest among infants aged 0–2 years (45%) and lowest among children aged 3–9 years (36%), with little variation by age group (Figure 2). During 2015, the frequency of receiving no antibiotic was 68%, of receiving 1 antibiotic was 17%, of receiving 2 antibiotics was 8%, of receiving 3–5 antibiotics was 6%, and of receiving \geq 6 antibiotics was 1%.

Trends in Use

The rate of overall antibiotic prescriptions fell by 16.7%, from 759 to 632 prescriptions per 1000 people from 2011 to 2015 (Figure 3). Specifically, declines were observed in prescribing of macrolides (28.2%), sulfonamides (22.1%), quinolones (15.9%), penicillins (15.6%), cephalosporins (15.4%), and tetracyclines

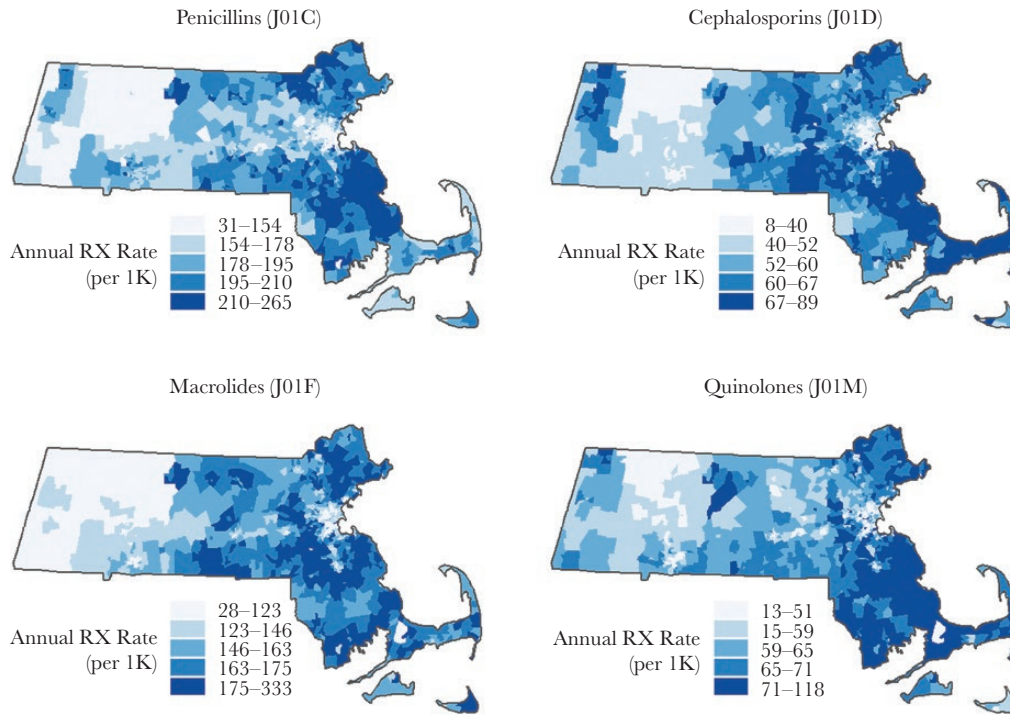


Figure 1. A–D, Antibiotic prescriptions per 1000 people, Massachusetts, 2011–2015.

(1.0%). However, there was an increase in prescribing of antibiotics in the “other antimicrobials” (J01X) category, from 17.6 to 19.8 per 1000 people.

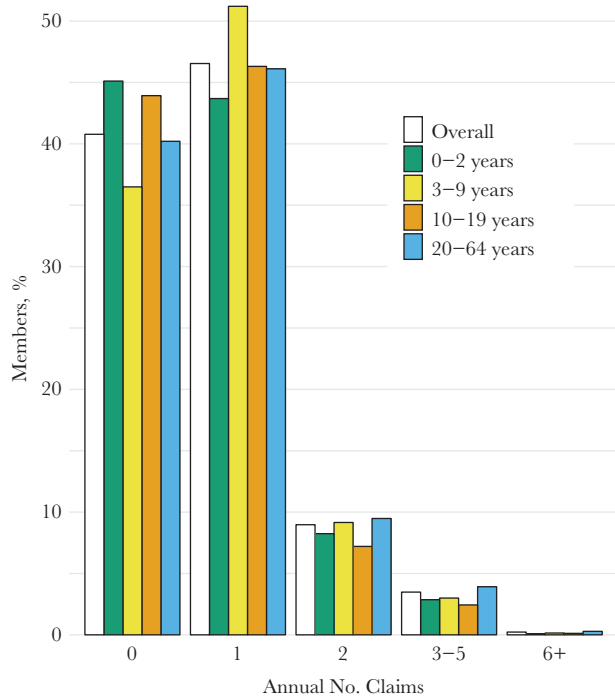


Figure 2. Antibiotic prescribing intensity by age group, Massachusetts, 2011–2015. Bars show the proportion of members of each age group who had a certain number of antibiotic prescriptions in a year.

DISCUSSION

State public health authorities are in a unique position to implement essential core functions of antibiotic stewardship by conducting population-based tracking and reporting of antibiotic use, in addition to tracking infections caused by resistant organisms. In this study, we applied existing tools to the Massachusetts APCD database to measure outpatient antibiotic prescriptions. We share these methods to support other states in calculating population-based rates by age group, sex, antibiotic class, and antibiotic agent. We found wide geographic variability in antibiotic use rates across census tracts. In fact, the variability in antibiotic prescriptions within Massachusetts was greater than that reported across states within the United States by Hicks et al. (18%) [7] and Zhang et al. (14%) [19]. These detailed characteristics of populations and providers with higher rates of prescribing can be used to focus education and monitoring. Combining these data with clinical indications for antibiotic prescriptions, particularly in areas with higher prescribing rates, will aid in shaping stewardship interventions.

Our finding that rates of antibiotic prescribing were lower in Massachusetts than other states is consistent with national data sources, albeit using different estimation methods and using public, rather than proprietary, databases [6, 7, 20, 21]. Although our population excluded individuals over 65 years old, who are known to have high rates of antibiotic use [22], even our measured age-specific rates were lower than the national rates. In particular, antibiotic use among infants in our data (1018 annual prescriptions per 1000 infants) was lower than the US rate

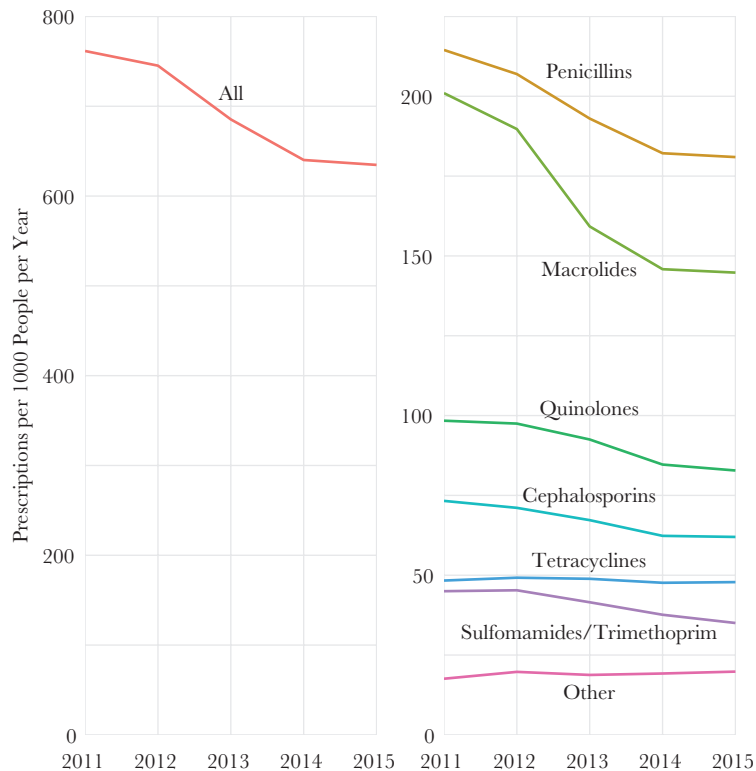


Figure 3. Trends in antibiotic prescribing by class, Massachusetts, 2011–2015.

(1287 per 1000 infants) [5]. This comparison and the observed consistency by class provide reassurance that our database is robust and our methods valid for surveillance purposes.

The method we developed resulted in a set of linked tables for antibiotic identification and classification that is comprehensive, indexed, and reproducible for routine matching against any NDC code set for analysis. Merging antibiotic classifications allows for quick aggregation, filtering, and selection of established standard antibiotic groups. Our process identified 37 386 unique NDC codes in the RXNorm database across all sources, a 6-fold increase over prior efforts relying on single-source NDC code lists for antibiotics (HEDIS AAB 6127) [23]. Subsequent selection of all matching NDC codes from a pharmacy claims file yielded 31% more claims records for analysis than past analysis selections using prior NDC code sets.

We describe a rate of decline in outpatient antibiotic prescribing of 16.7% from 2011 to 2015. Lee et al. described a decline of 25% among children and adolescents in the United States from 2003 to 2010 [24], and Mundkur et al. described a decline of 12% among adults aged 18–64 years from 2006 to 2015 [25]. Blue Cross Blue Shield, the payer for about one-third of Massachusetts residents, reported an overall decline of 11% in antibiotic prescriptions in their Massachusetts insured population [21]. Differences in the rate of decline might be due to differences in populations, distribution of prescribers, or methods. Further understanding of these differences and

an evaluation of antibiotics in the “other antimicrobials” category—the one category in which there was an increase—will help inform stewardship efforts.

Several factors may explain the lower-than-national rates and observed declines. Massachusetts providers may be early adopters of best practices, or practice and provider characteristics may lead to improved practices [26], or interventions directed toward public information are having a greater effect [27] on a more educated population [28]. Massachusetts has very high vaccination coverage [29], and the frequency of vaccine-preventable infections may be declining, such that potentially inappropriate prescribing has declined. There may be demographic changes, such as fewer births, or changes in antibiotic marketing [30]. It is also possible that the period we studied does not reflect longer-term trends; therefore, continued tracking is warranted.

In this analysis, we also quantified the frequency with which individuals were receiving multiple prescriptions for antibiotics. Similar to the result from a nationwide study [31], we observed that more than three-quarters of people had either no antibiotic claims or 1 antibiotic claim per year. Furthermore, the frequency by age group was similar. However, we found dramatic geographic differences in antibiotic use rates within relatively small geographic areas, census tracts, and within the state. The availability of detailed, population-based rates of prescriptions will be helpful to facilities and providers in their antibiotic stewardship

efforts. Future analyses should explore sociodemographic and provider characteristics to understand local patterns of antibiotic use and perhaps target interventions.

The Centers for Medicare & Medicaid Services (CMS) Quality Innovation Network Quality Improvement Organizations (QIN-QIOs) and CDC use a community-based antibiotic stewardship approach described in Core Elements of Outpatient Antibiotic Stewardship [2]. Tracking and reporting are essential components of these core elements, and public health has oversight authority over licensed health care facilities to monitor infection and antibiotic use. Massachusetts was among the first states to require all hospitals to participate in the National Healthcare Safety Network (NHSN) to report health care-associated infections and monitors infections associated with resistant organisms mainly through this platform. In addition, there is a web-based infectious disease surveillance and case management system, which receives electronic laboratory reports of identifications of organisms of interest [32]. Although hospitals are encouraged to also use the NHSN antibiotic use module to monitor inpatient antibiotic use, there have been challenges with implementation. Public health monitoring of antibiotic use in outpatient care at the state and local levels is thus a novel and important element in antibiotic stewardship efforts.

Published studies of outpatient antibiotic prescribing have used costly private data sources [2, 33]. In addition to the cost, these sources use proprietary systems of classification of antibiotics, leaving a gap in applicability to other data sources. To our knowledge, Oregon is the only other state to use APCD to characterize local antibiotic prescribing for improvements in stewardship [34]. Our study confirms APCD as a valid source for population-based outpatient antibiotic surveillance. Our effort to share the methods developed could support their application by other public health authorities.

The strengths of our method include claims that are highly representative of health care utilization, including prescriptions without a clinical visit [25, 35] and data not subject to recall bias [25]. In addition, although claims data are de-identified, government users can de-duplicate unique members to measure individual utilization and link the prescription with a diagnosis.

The frequencies reported here follow the same rank order of antibiotic use as national findings, and the measurement of a decline in prescribing was also observed from independent data sources [21]. Our frequencies might overestimate prescriptions because the categorization of antibiotics for systemic use might include inhaled or injected formulations. However, frequencies might be conservative because several health care payment and service providers are not included in the Massachusetts APCD: Workers' Compensation, TRICARE and Veterans Health Administration, and the Federal Employees Health Benefit Plan. We excluded individuals aged 65 years and older because their claims were not part of the APCD. However, an analysis

of Medicare antibiotic prescribing indicated that Massachusetts was among the states with lowest rates of prescribing during the same years as this study [22]. Finally, data presented here are from 2011 to 2015; delays in processing limit the availability of claims for timely analysis and dissemination of rates.

Massachusetts is 1 of 16 states with APCD databases. In the 2016 *Gobeille v. Liberty Mutual Insurance Company* decision, the US Supreme Court held that states could not mandate reporting from "self-insured" employer plans under the Employee Retirement Income Security Act of 1974 (ERISA) [36]. The effect this might have on our ability to conduct surveillance related to infectious diseases and prescribing patterns in the future is unclear.

Building on this analysis, we plan to apply these findings by sharing results with providers and the community through online reports. Prescriber-specific audit and feedback may not be ideal from this database due to delays in data availability. Instead, annual and more detailed analyses of populations and provider groups with higher prescribing rates will be evaluated by prescription indication to understand whether some antibiotics might be unnecessary. Ongoing monitoring will be useful to evaluate stewardship effects.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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