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Major Article

Antibiotic stewardship targets in the outpatient setting

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Key Words:

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Process improvement**Background:** Outpatient prescriptions comprise 60% of antibiotic use. This study prospectively identified inappropriate antibiotic use enabling a focused approach to outpatient antimicrobial stewardship.**Methods:** Outpatients at the Veterans Affairs Western New York Healthcare System were identified via an electronic antibiotic alert from June 2017 to September 2017. Descriptive statistics and multivariable logistic regression identified stewardship targets.**Results:** Of the 1,063 patients, 40% of antibiotic prescriptions were not indicated. Urinary tract infections (21%), bronchitis (20%), skin structure infections (17%), and sinusitis (10%) were common causes of inappropriate antibiotic use. Azithromycin (37%) was prescribed unnecessarily most often, followed by ciprofloxacin (16%), amoxicillin/clavulanate (13%), and cephalexin (12%). The correct drug was chosen in 52%, dose in 81%, and duration in 75% of patients. When the antibiotic was indicated, the correct drug was 2.9 times more likely to be prescribed and 2 times more likely to have the correct duration and receive care in the emergency room.**Discussion:** Focusing on 4 drugs; amoxicillin/clavulanate, azithromycin, ciprofloxacin, and cephalexin accounted for 80% of unnecessary drug use. This study provides a guide to concentrate efforts during implementation of an outpatient stewardship program.**Conclusions:** Poor antibiotic prescribing was found in the outpatient setting. This study identifies areas for improvement via stewardship.

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Improper use of antimicrobial agents has been associated with increased morbidity, costs, and the emergence of resistant bacteria.¹ Stewardship programs are common in the inpatient setting; however, the outpatient setting is largely uncharted, and best practices for antimicrobial stewardship in this setting remains unclear despite the Centers for Disease Control and Prevention's release of the Core Elements of Outpatient Antibiotic Stewardship that outlines the structure of their ideal outpatient stewardship program Srinivasan et al. The significance of this effort is exemplified by the Joint Commission,

who has begun to survey outpatient antimicrobial use since their standard published in January 2017.

A recent national study estimated 30% of outpatient, oral antibiotic prescriptions may have been inappropriate from 2010–2011.² Antibiotic trends were based on identified diagnosis, with the most common being sinusitis, followed by otitis media, then pharyngitis.² A retrospective analysis of outpatients treated for respiratory tract infections found the following factors significantly increased the likelihood of inappropriate prescribing: family medicine providers, patients of female sex, or patients of white or Hispanic race.³ Much of the literature focuses on interventions with respiratory tract infections and information detailing other infections is sparse.^{1,3}

Stewardship is optimized antibiotic use and comprises the concepts of the correct drug and dose for the proper duration; however, studies are lacking that focus on specific areas for intervention.⁴ There is limited health care resources and time, often making it impractical to review each prescription. The primary objective of this study was to identify the most commonly overused antimicrobial agents and their associated syndromes to enable a focused approach

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to maximize the return on stewardship effort. This study also investigated characteristics associated with inappropriate prescribing and identified potential stewardship targets so that resources can be optimized to reduce inappropriate prescribing in the outpatient setting.

METHODS

Study design

This was a prospective observational cohort study that identified patients in real-time via computerized alerts notifying the infectious disease pharmacist when one of the following target oral antibiotics were prescribed: amoxicillin, amoxicillin/clavulanate, azithromycin, cefdinir, cefpodoxime, cephalexin, ciprofloxacin, clindamycin, levofloxacin, moxifloxacin, or trimethoprim/sulfamethoxazole. Other antibiotics were reviewed, if they were prescribed along with one of the targeted antibiotics. A chart review was then performed to assess if the antibiotic prescription met criteria and each prescription was assessed for stewardship targets (drug choice, duration, and dosage). A formal protocol was not established at time of the study; thus, interventions were made only if it had the potential to harm a patient. Antibiotic order sets were in place during the entire study timeframe. The timeframe of the study ranged from June 2017 to September 2017. Patients were included if they received at least 1 of the earlier mentioned oral antibiotics and if they were at least aged 18 years or older. Patients were included if they were seen in the outpatient setting at the main campus or 1 of its 7 regional community-based outpatient clinics. Patients were excluded if they initially presented at non-Veterans Affairs Western New York Healthcare System institutions or had a physical exam performed by a non-Veterans Affairs Western New York Healthcare System provider because of the inability to access the full patient record. Patients were also excluded if the oral antibiotics were pre- or postoperative prophylaxis, orthopedic infection, urologic preprocedural, or if the oral antibiotics were prescribed on hospital discharge. Incomplete chart documentation lead to exclusion of the patient as there was insufficient information to assess for guideline compliance.

The computerized patient record system was used to identify patients based on an alert for the target antibiotics that was generated at the time the prescription was signed by the provider. Baseline demographics collected included age, sex, race, serum creatinine, weight, height, estimated creatinine clearance (based on actual body weight), temperature, body mass index, antibiotic allergies, diagnosis of infection, and signs and symptoms. Laboratory data were included if it was collected within 6 months. Additional data collected included culture (if collected), antibiotic prescribed including dose and duration, the setting patient was seen in, ICD-10-CM code associated with the encounter, comorbid conditions including myocardial infarction, chronic heart failure, peripheral vascular disease, cerebral vascular accident/transient ischemic attack, dementia, chronic pulmonary disease (asthma/chronic obstructive pulmonary disease), connective tissue disease, peptic ulcer disease, liver disease, diabetes, hemiplegia, renal disease, tumor history, leukemia, lymphoma, and AIDS. A Charlson index score was calculated to provide a clinical picture of each patient's baseline comorbidities.⁵

Definitions. Appropriate treatment, drug, dose, and duration were evaluated based on criteria from the following guidance (Supplement 1):

- i **Centers for Disease Control and Prevention:** Bronchitis, sexually transmitted infections, epididymo-orchitis, and otitis media.^{6–8}
- ii **Infectious Disease Society of America:** Community-acquired pneumonia, prostatitis, sinusitis, pharyngitis, infectious diarrhea, uncomplicated cystitis, asymptomatic bacteriuria, diabetic foot infections, and skin and soft tissue infections.^{9–18}

- iii **Surgical Infection Society and the Infectious Disease Society of America:** Diverticulitis.¹⁹
- iv **Global Initiative for Chronic Obstructive Lung Disease (GOLD):** COPD Exacerbation.²⁰

Drug selection was defined as appropriate if the drug selected was first-line therapy or based on culture data when available. If the patient had a contraindication or allergy to receiving first-line therapy, then second-line therapy was considered appropriate. Prior antibiotic failures were considered when determining first-line therapy. Dose was considered inappropriate when the drug was improperly adjusted for renal function or when the dose varied from the guideline recommended dose. Duration was considered inappropriate if it was longer or shorter than guideline recommendations. Antibiotic was considered unnecessary if the guideline criteria for diagnosis of infection were not met.

Statistical analysis

The primary objective of this study was to identify the most commonly overused antimicrobial agents and their associated syndromes to enable a focused approach to maximize return on stewardship effort. Baseline characteristics, comorbidities, severity of illness, and risk factors were compared using a bivariate analysis for those who were considered appropriate to treat. The χ^2 test was used to analyze categorical data and the Student t test was used to analyze continuous data.

The secondary objective was to investigate characteristics associated with inappropriate prescribing patterns, which were analyzed using multivariable logistic regression. All significant factors were entered in the model and eliminated in a backward fashion until only significant factors predicting antibiotic use were included. Results from this analysis are presented as odds ratios with 95% confidence intervals (CI). Statistical analysis was performed using JMP software version 13. (SAS Corp, Cary, NC).

RESULTS

This study included 1,063 veterans, after 637 were excluded for reasons noted in Figure 1. Antibiotics were inappropriately prescribed in 40% of patients. The majority (90%) of the population was male, white (86%), and had an average age of 62 ± 16 years (Table 1). The majority had a Charlson index score of 0–4 (87%); the remaining had scores of 5–10. The Charlson score did not influence appropriateness of antibiotics. Nonsignificant factors of the population, in terms of appropriate antibiotic use, included chronic obstructive pulmonary disease (COPD) (22%), asthma (7%), myocardial infarction (6%), heart failure (6%), peripheral vascular diseases (14%), cerebrovascular accident (6%), dementia (2%), liver disease (7%), diabetes (28%), renal disease (12%), tumor (21%), and HIV/AIDS (0.3%). The emergency

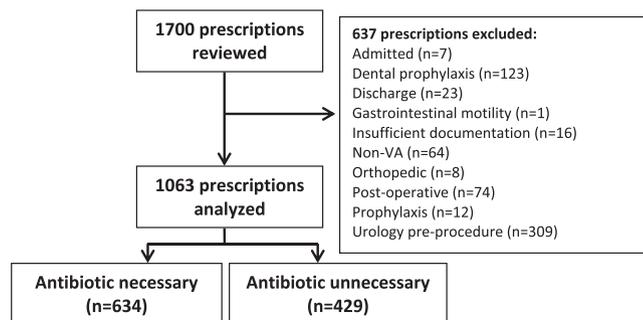


Fig 1. Schematic for patient inclusion.

Table 1
A comparison of characteristics of when an antibiotic was unnecessary versus necessary based on guidance

Variable	Total cohort N = 1063	Unnecessary antibiotic: N = 439 (40.4%)	Necessary antibiotic: N = 634 (59.6%)	P value
Duration	8.1 ± 4.9	7.7 ± 4.6	8.3 ± 5.1	.047
Correct drug for indication	554 (52.1%)	152 (35.4%)	402 (63.4%)	<.0001
Correct dose	864 (81.3%)	328 (76.5%)	536 (84.5%)	.0009
Correct duration	802 (75.4%)	282 (65.7%)	520 (82.0%)	<.0001
Age	62.4 ± 15.8	63.9 ± 15.4	61.4 ± 15.9	.011
Male	955 (89.8%)	392 (91.4%)	563 (88.8%)	.17
Temperature (F)	97.8 ± 0.9	97.8 ± 0.9	97.9 ± 0.9	.018
ICD-10-CM code related to infection	438 (41.2%)	124 (28.9%)	314 (49.5%)	<.0001
Indication				<.0001
Bronchitis	91 (8.6%)	89 (20.8%)	2 (0.3%)	
CAP	88 (8.3%)	15 (3.5%)	73 (11.5%)	
COPD exacerbation	70 (6.6%)	23 (5.4%)	47 (7.4%)	
Diabetic foot	8 (0.8%)	1 (0.2%)	7 (1.1%)	
Epididymitis	12 (1.1%)	2 (0.5%)	10 (1.6%)	
GI	28 (2.6%)	7 (1.6%)	21 (3.3%)	
Otitis media	57 (5.4%)	5 (1.2%)	52 (8.2%)	
Pharyngitis	34 (3.2%)	27 (6.3%)	7 (1.1%)	
Prostatitis	21 (2.0%)	16 (3.7%)	5 (0.8%)	
Sinusitis	127 (11.9%)	41 (9.6%)	86 (13.6%)	
SSTI	280 (26.3%)	73 (17.0%)	207 (32.7%)	
STI	12 (1.1%)	0	12 (1.9%)	
URI	42 (4.0%)	42 (9.8%)	0	
UTI	193 (18.2%)	88 (20.5%)	105 (16.6%)	
Antibiotic Rx				<.0001
Amoxicillin/clavulanate	167 (15.7%)	56 (13.1%)	111 (17.5%)	
Amoxicillin	67 (6.3%)	25 (5.8%)	42 (6.6%)	
Azithromycin	288 (27.1%)	159 (37.1%)	129 (20.4%)	
β-lactam + TMP/SMX	25 (2.4%)	1 (0.2%)	24 (3.8%)	
β-lactam + atypical*	5 (0.5%)	1 (0.2%)	4 (0.6%)	
Cefdinir/cefepodoxime	44 (4.1%)	21 (4.9%)	23 (3.6%)	
Cephalexin	140 (13.2%)	50 (11.7%)	90 (14.2%)	
Ciprofloxacin	138 (13.0%)	69 (16.1%)	69 (10.9%)	
Clindamycin	2 (0.2%)	0	2 (0.3%)	
FQ + metronidazole	15 (1.4%)	4 (0.9%)	11 (1.7%)	
Levofloxacin	33 (3.1%)	5 (1.2%)	28 (4.4%)	
Miscellaneous†	4 (0.4%)	0	4 (0.6%)	
Moxifloxacin	36 (3.4%)	11 (2.6%)	25 (3.9%)	
TMP/SMX	99 (9.3%)	27 (6.3%)	72 (11.4%)	
Emergency room versus clinic				<.0001
Clinic	730 (68.7%)	339 (79.0%)	391 (61.7%)	
Emergency room	333 (31.3%)	90 (21.0%)	243 (38.3%)	

CAP, community acquired pneumonia; COPD, chronic obstructive pulmonary disease; FQ, fluoroquinolone; GI, gastrointestinal; SSTI, skin and skin structure infection; STI, sexually transmitted infection; TMP/SMX, trimethoprim/sulfamethoxazole; URI, upper respiratory infection; UTI, urinary tract infection.

*Atypical azithromycin or doxycycline.

†Nitrofurantoin, cefdinir + amoxicillin, ciprofloxacin + linezolid, ciprofloxacin + TMP/SMX.

department treated 31% of the cohort and the remaining patients were seen in clinics.

The non-first-line antibiotic, commensurate with guidelines, allergies, and prior antibiotics was chosen in 48% of cases. The duration of antibiotic prescribed was inappropriate in 25% of cases, and dosing was inappropriate in 19% of patients in this cohort. The most common indications resulting in unnecessary antibiotics, based on the targeted included antibiotics, were urinary tract infections (UTIs) (21%), bronchitis (20%), skin and skin structure infections (17%), and sinusitis (10%). ICD-10-CM codes were found to be unrelated to an infection in 58.8% of cases. The most common ICD-10-CM code used within our data was counseling, Z71.9. Patients with an ICD-10-CM code unrelated to infection were more likely to receive an antibiotic inappropriately (Table 2).

A subgroup analysis was performed of the most prevalent indications for antibiotics to identify the most common areas for intervention with each. Prescribing patterns associated with UTIs indicate that the correct drug was chosen in 54.9% of cases, the dose was correct in 70.5% of cases, the duration was correct in 52.9% of cases, and the antibiotic was prescribed for indication consistent with guideline diagnostic criteria in 54.4% of cases. Antibiotics were most commonly

prescribed for asymptomatic bacteriuria (n = 86); reasons included cloudy urine, positive urinalysis, foul smelling urine, and fatigue. Two patients were treated for altered mental status to determine if it would improve their dementia.

Prescribing patterns associated with skin and skin structure infections indicate that the correct drug was chosen in 58.2% of cases, the correct dose was used in 72.1% of cases, the duration was correct in 87.5% of cases, and the antibiotic was consistent with defined criteria in 73.9% of cases. Most common reasons for use of a non-first-line agent was that a patient would present with abscesses characteristic of community-acquired methicillin-resistant *Staphylococcus aureus* infection but were treated with amoxicillin/clavulanate. Other reasons included prophylaxis against cellulitis after various injuries and bilateral cellulitis associated with weight gain and diuretic noncompliance.

Finally, bronchitis (17.9%), community-acquired pneumonia (CAP) (17.3%), COPD (13.8%), otitis media (11.2%), pharyngitis (6.7%), sinusitis (25.0%), and upper respiratory tract infections (8.3%) were grouped and analyzed as respiratory infections/ear, nose, throat infections as a whole. The correct drug was chosen in 42.6% of cases, the correct dose was chosen in 88.4% of cases, duration was correct in 78.6% of

Table 2
ICD-10-CM information

Variable	Total cohort	Unnecessary antibiotic: 40.4% (429) N = 429 (40.4%)	Necessary antibiotic: 59.6% (634) N = 634 (59.6%)	P value
ICD-10-CM code				<.0001
Bacteriuria	1 (0.1%)	0	1 (0.2%)	
Bite	6 (0.6%)	2 (0.5%)	4 (0.6%)	
Bronchitis	47 (4.4%)	41 (9.6%)	6 (1.0%)	
Cat scratch	1 (0.1%)	0	1 (0.2%)	
COPD exacerbation	22 (2.1%)	10 (2.3%)	12 (1.9%)	
Cystitis	5 (0.5%)	3 (0.7%)	2 (0.3%)	
Diverticulitis	11 (1.0%)	1 (0.2%)	10 (1.6%)	
Epididymitis	3 (0.3%)	1 (0.2%)	2 (0.3%)	
Laryngitis	10 (0.9%)	9 (2.1%)	1 (0.2%)	
Lymphangitis	2 (0.2%)	0	2 (0.3%)	
Nasopharyngitis	2 (0.2%)	1 (0.2%)	1 (0.2%)	
None	615 (57.9%)	300 (69.9%)	315 (49.7%)	
Orchitis	3 (0.3%)	0	3 (0.5%)	
Osteomyelitis	1 (0.1%)	0	1 (0.2%)	
Otitis	23 (2.2%)	0	23 (3.6%)	
Pharyngitis	12 (1.1%)	7 (1.6%)	5 (0.8%)	
Pneumonia	36 (3.4%)	1 (0.2%)	35 (5.5%)	
Prostatitis	6 (0.6%)	3 (0.7%)	3 (0.5%)	
Rhinitis	8 (0.8%)	3 (0.7%)	5 (0.8%)	
Sinusitis	56 (5.3%)	17 (4.0%)	39 (6.2%)	
SSTI	123 (11.6%)	8 (1.9%)	115 (18.1%)	
STI	7 (0.7%)	0	7 (1.1%)	
UTI	63 (5.9%)	22 (5.1%)	41 (6.5%)	
ICD-10-CM related to infection	438 (41.2%)	124 (28.9%)	314 (49.5%)	<.0001

COPD, chronic obstructive pulmonary disease; SSTI, skin and skin structure infection; STI, sexually transmitted infection; UTI, urinary tract infection.

cases, and the antibiotic was consistent with defined criteria in 52.5% of cases. The most common error in CAP prescribing was failure to account for comorbidities that place the patient at risk for drug-resistant *Streptococcus pneumoniae* (44.3%). Excessive durations of treatment for CAP was noted in 10%. Patients with otitis media received the incorrect drug in 44% of cases—the most commonly misused antibiotics included amoxicillin-clavulanate and ciprofloxacin. Patients with a diagnosis of sinusitis did not require an antibiotic in 32% of cases, as their symptoms were consistent with the common cold or did not meet Infectious Disease Society of America (IDSA) guideline criteria. The incorrect drug was chosen in 53% of patients with sinusitis—azithromycin in 64% of cases and amoxicillin in 19% of cases.

Azithromycin was the most commonly prescribed unnecessary antibiotic (37%) of our targeted agents, followed by ciprofloxacin (16%), amoxicillin/clavulanate (13%), and cephalexin (12%). Altogether, these 4 drugs accounted for nearly 80% of unnecessary drug use. Fifty-five percent of the 288 prescriptions for azithromycin were deemed unnecessary. It was the incorrect drug for the indication in 32% of cases azithromycin was prescribed for. Azithromycin was most commonly inappropriately used for bronchitis, sinusitis, upper respiratory tract infections, COPD, and CAP, in which the patient had comorbidities placing them at risk for drug-resistant *S pneumoniae*.

Ciprofloxacin (n = 138) was most commonly prescribed for UTI and prostatitis. Fifty percent of ciprofloxacin usage was unnecessary and was prescribed for asymptomatic bacteriuria or elevated prostate specific antigen. The dosage of ciprofloxacin was incorrect in 24% and the duration was incorrect in 52%

Amoxicillin/clavulanate was prescribed in 167 patients and was used most commonly for sinusitis, skin and soft tissue infections, and otitis media. It was prescribed unnecessarily in 33.5% of patients. Thirty percent of those prescribed amoxicillin/clavulanate for sinusitis lacked IDSA guideline-defined symptoms. Amoxicillin/clavulanate, for all indications, was the incorrect empirical choice in 45%, was prescribed at the incorrect dose in 28%, and for the incorrect duration in 35%.

A multivariable logistic regression was used to determine factors associated with inappropriate prescribing patterns. When the antibiotic

was needed, patients were 2.9 times more likely to receive the correct drug (95% CI, 2.2–3.8) and 2 times more likely to receive the correct duration (95% CI, 1.5–2.7). Additionally, patients seen in the emergency room were twice as likely to receive an antibiotic only when it was needed (95% CI, 1.5–2.7).

DISCUSSION

Inappropriate antimicrobial use in the outpatient setting is widespread, making it necessary to implement outpatient stewardship. In our study, 40% of antimicrobial use was unnecessary, which is higher than prior studies in which 30% of antimicrobial use was superfluous.² This higher rate of inappropriate use may be related to the subset of chosen outpatient antimicrobials, compared to Fleming-Dutra et al² who looked at all ambulatory visits with oral antibiotic prescriptions in the United States. With outpatient stewardship, the difficulty is finding ways to improve antimicrobial use before the patient is dispensed the prescription. Limited time and resources for an outpatient antimicrobial stewardship service can be challenging, given the plethora of infections and antibiotics used in the outpatient setting. Order sets were in place during the study period, however, they were used infrequently. Focusing on 4 drugs: amoxicillin/clavulanate, azithromycin, ciprofloxacin, and cephalexin, which accounted for 80% of unnecessary drug use, would provide the most opportunities for interventions.

This was a summertime cohort leading to variation in the typical respiratory infections seen in outpatient stewardship studies. UTIs (21%), bronchitis (20%), skin structure infections (17%), and sinusitis (10%) accounted for most of the inappropriate prescribing.²¹

Patients who met qualifications for receiving an antibiotic were more likely to be prescribed the correct drug for the correct duration. There may be pressure for patient satisfaction scores, whereas the provider appeases the patient with an antimicrobial agent, albeit an incorrect one.^{2,4}

A unique finding of our study is that emergency department patients were twice as likely to only receive an antibiotic when it was

needed compared with those seen in clinics. We hypothesize that patients in the emergency department may have a higher acuity of illness requiring urgent antibiotics, or there may be less of a patient-provider relationship, and thus, less of a pressure or expectation to prescribe antibiotics.^{1,22} Additionally, another study concluded that patient satisfaction scores were lower when antibiotics were not prescribed for acute sinusitis encounters.²³ These factors may influence providers to prescribe antibiotics with less accuracy in drug and duration choice.

Current literature recommends implementing and measuring the impact of outpatient antibiotic stewardship programs, based on disease state-specific targets and use of the Centers for Disease Control and Prevention's Core Elements for Outpatient Antibiotic Stewardship.²⁴ Other studies have evaluated interventions to decrease prescriptions for upper respiratory tract infections, which are commonly viral in nature and require no antibiotic use in most cases.^{1,3} These studies relied on ICD coding to identify their targets for intervention and were focused on a handful of outpatient disease states, rather than the entire outpatient population who received oral antibiotics.²⁵ In our study, ICD-10-CM codes were unreliable and were not associated with an infection in 60% of the population.

A systemic review found that most outpatient stewardship programs focus on respiratory infections. Although these interventions decrease antimicrobial use without adversely impacting patients' outcomes, much of the data are of low-quality.²⁶ Although antibiotics were overused in respiratory infections, especially bronchitis, antibiotics were also heavily overused in urinary tract and skin and soft tissue infections. Results may have varied if the timeframe of our study was extended.

There were challenges to implementation of this stewardship alert-based model. The range of clinics included spanned 100 miles, which required the stewardship team to rely on chart documentation as the team was not able to be physically present at each location. Occasionally, notes were not entered before the prescription was dispensed, thus limiting efficacy. In the absence of a formal antimicrobial stewardship program, interventions were not consistently made. However, this process did unveil some systems-based problems in which antibiotics were overused. Some examples include the use of antibiotics for treatment of pyuria when the urinalysis was done as part of diabetes care. Antibiotics were frequently prescribed for bronchitis or the common cold. Some system-based policies included treating an elevated prostate specific antigen for at least 28 days with antibiotics prior to urology consultation. A second policy identified was the need to obtain a urinalysis and treat any positive urinalysis prior to dementia consultations. These system-based problems promote inappropriate use of antimicrobials and could be potentially harmful as they delay workup of the abnormal finding.

There were limitations to this study. It was a prospective observational cohort study that relied on proper documentation in the electronic medical record as the stewardship team was not present for visits. It is possible that the chart did not contain documentation of all symptoms, or appropriate description of all symptoms, which may have impacted the appropriateness of the antibiotics. This study was geographically limited to western New York, a single locality, although there were multiple different study sites included. The study was limited to primarily white male veterans, so results may not be generalizable to the average adult population. Because there was a predominance of males in the study, nitrofurantoin was excluded. The data were also collected during the summer months, and winter months would be expected to have increased frequency of respiratory infections. Finally, this study was not all-encompassing of every oral antibiotic because we identified patients based on selected common oral antibiotics. Antibiotics such as doxycycline were excluded owing to the multitude of dermatologic conditions it is often prescribed for.

CONCLUSIONS

Antibiotics are overused in the outpatient setting. Alerts when an antimicrobial is prescribed may be an effective way to begin an outpatient stewardship program. The Veterans Affairs Western New York Healthcare System is unique in that these prescriptions can be intervened on before the patient leaves the building as the pharmacy is located at the site of care. Alerts potentially allow for real-time interventions before the patient leaves the office. Education should start with the patient regarding when an antibiotic is not needed and the harmful effects that can result when used inappropriately. This may decrease the feeling that the provider needs to appease the patient with an antibiotic, even when they know it is not truly indicated. We recommend beginning a stewardship program with alerts when azithromycin, amoxicillin/clavulanate, ciprofloxacin, and cephalexin are prescribed to capture maximal interventions and expand from there.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.ajic.2019.01.027>.

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