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Duration of outpatient antibiotic therapy for common outpatient infections, 2017

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Abstract

Our objective was to describe the duration of antibiotic therapy for the management of common outpatient conditions. The median duration of antibiotic courses for most common conditions, except acute cystitis, was 10 days, in many cases exceeding guideline-recommended durations.

Keywords

Antibiotics; Antibiotic Stewardship; Outpatient

Introduction

Using minimum effective antibiotic therapy durations is a component of antibiotic stewardship. Streptococcal pharyngitis, sinusitis, acute otitis media (AOM), community-acquired pneumonia (CAP), skin and soft tissues infection (SSTI), and acute cystitis are common bacterial infections leading to outpatient antibiotic prescriptions [1]. When antibiotics are indicated for these conditions, recommended therapy durations vary by syndrome (Table 1, Supplemental Table 1). Although unnecessary outpatient antibiotic prescribing is common [1], few studies have examined outpatient antibiotic course durations in the United States. The objective of this study is to describe the duration of antibiotic prescriptions for pharyngitis, sinusitis, AOM, CAP, SSTI, and acute cystitis in 2017 in U.S. outpatients.

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Methods

We identified antibiotic prescriptions associated with pharyngitis, sinusitis, AOM, CAP, SSTI (abscess and cellulitis), and acute cystitis from the National Disease and Therapeutic Index (NDTI; IQVIA, Plymouth Meeting, PA) 2017 dataset. NDTI is a two-stage stratified cluster sample of U.S. private-practice, office-based physicians reporting quarterly on all patient visits for two randomly-selected, consecutive workdays. Sampled visits can be projected using NDTI sampling weights to estimate all visits to private-practice, office-based physicians in specialties captured within NDTI.

In NDTI, diagnoses are recorded in a proprietary coding scheme (see Supplemental table 2 for included NDTI diagnosis codes). For AOM, we excluded prescriptions to adults, as only pediatric treatment guidelines are available. For acute cystitis, we only included prescriptions to females 12–64 years without pregnancy-related diagnoses to exclude populations for which duration recommendations do not exist or are unclear. We excluded CAP visits with ceftriaxone without another antibiotic as we could not ascertain if patients returned for further treatment.

We limited our study to oral and parenteral antibiotics prescribed or administered in office visits. We excluded observations with missing patient age or antibiotic duration. We also excluded prescriptions with durations >30 days (n=5) as these may represent prophylaxis or treatment of complex illness. We excluded hospital orders, previously initiated therapies, and reported replacement medications as true duration may be uncertain. To focus on cases not requiring specialty care, we limited our sample to prescriptions attributed to the following predefined NDTI physician specialties: emergency medicine, family practice, general practice, geriatrics, internal medicine (excluding infectious diseases), osteopathic medicine (excluding surgery and obstetrics/gynecology), and pediatrics (excluding neonatal-perinatal medicine). In NDTI, diagnoses are linked directly with medications; we excluded visits with antibiotic prescriptions for multiple conditions. For visits with multiple antibiotics for one condition, we used the longest duration to capture total antibiotic exposure. We excluded azithromycin prescriptions because of substantially different duration recommendations for azithromycin compared to other antibiotics based on its unique pharmacokinetics. Azithromycin is typically prescribed for ≤5-day courses; however, because of persistent drug tissue concentrations, true exposure is longer.

We used methods appropriate for complex samples and NDTI projection weights to estimate the number of antibiotic prescriptions, antibiotic therapy durations, and 95% confidence intervals (CI) from the sampled visits. We estimated the proportions of prescriptions by course duration and median duration and interquartile range (IQR) for each condition by age group. We categorized age group as children (<18 years) and adults (≥18 years) for all conditions except AOM and acute cystitis. For AOM, we categorized age as all children (<18 years), ≥2 years, and <2 years to align with guideline-recommended durations. We calculated potentially excessive antibiotic days by summing the number of days above minimum recommended duration by condition (Supplemental Table 3), accounting for sampling weights. For conditions with guideline-recommended durations provided as ranges

(e.g., sinusitis, abscess), we used the upper-bound value as the recommended duration. Analyses were conducted using SAS 9.4 (SAS Institute, Cary, NC).

Results

In 2017, there were 2,889 sampled antibiotic prescriptions from visits that met our inclusion criteria, translating to a national estimate of 31,548,464 (95% CI 29,833,606-33,263,322) antibiotic prescriptions from private-practice, office-based physicians in the included specialties. Eleven percent (95% CI 10–13%) of these estimated prescriptions were azithromycin, therefore excluded from our duration analyses, leaving 28,016,314 (95% CI 26,430,509-29,602,119) included antibiotic prescriptions.

Estimated prescription numbers, guideline-recommended durations and median antibiotic durations for each condition and age group are presented in the Table. Median duration was 10 days for every condition except acute cystitis, for which median duration was 7 days (IQR 5–7 days). Overall, 55% (95% CI 53–58%) of non-azithromycin antibiotic courses in our study exceeded guideline-recommended minimum effective durations, translating to up to 54,496,316 potentially excessive days of therapy. Among adults, 74% (95% CI 71–77%) of antibiotic courses exceeded minimum guideline-recommended durations, compared with 36% (95% CI 33–39%) in children. For pharyngitis, 85% (95% CI 79–90%; Supplemental Figure 1) of estimated antibiotic prescriptions in adults and 97% (95% CI 95–98%) in children were 10 days, the guideline-recommended duration. For sinusitis, among adults, 90% (95% CI 87–94%) of antibiotic prescriptions exceeded the guideline-recommended 5–7 days; 86% (95% CI 82–90%) of adult antibiotic courses for sinusitis were 10 days (Supplemental Figure 2). Almost all, 97% (95% CI 95–100%), antibiotic prescriptions for sinusitis in children were 10 days, in concordance with the guideline-recommendation of 10–14 days. For AOM in children <2 years, 96% (95% CI 93–99%) of prescriptions were for the recommended 10 days (Supplemental Figure 3). A similar proportion of 10-day courses was observed in children ≥2 years (95%, 95% CI 93–97%). Although courses of 5–7 days or 7 days are suggested for select children ≥2 years with AOM [2], only 5% (95% CI 2%–7%) of prescriptions for this population were 5–7 days. For CAP in adults, only 6% (95% CI 0–14%) of prescriptions were for 5 days, which is the appropriate duration for most patients, according to guidelines [3] (Supplemental Figure 4). For CAP in children, for which there is no recommended duration of antibiotic therapy, 93% (95% CI 84–100%) of prescriptions were for 10 days. For cellulitis, 99% (95% CI 97–100%) of prescriptions to adults and 93% (95% CI 85–100%) of prescriptions to children were for longer than 5 days, which is recommended for most patients demonstrating clinical improvement; the majority were for 10 days (Supplemental Figure 5). For abscess, 88% (95% CI 74–100%) of prescriptions in adults and 80% (95% CI 55–100%) of prescriptions in children were for guideline-recommended 5–10-day durations; all remaining antibiotic therapy durations for abscess were for ≥14 days (Supplemental Figure 6). For acute cystitis in females aged 12–64 years, duration distribution varied by agent (Supplemental Figure 7). At least 75% (95% CI 69–81%) of antibiotic prescriptions for acute cystitis had durations longer than guideline-recommended, accounting for antibiotic agent.

Discussion

In our study of systemic antibiotic therapy duration, we found that clinicians defaulted to 10-day courses for most conditions, regardless of guideline-recommendations. Median antibiotic course duration was 10 days for all conditions except acute cystitis. For some conditions and age groups, such as pharyngitis, pediatric sinusitis, and pediatric AOM, 10 days of antibiotic therapy aligns with guidelines. However, for many conditions, specifically sinusitis and CAP in adults and cellulitis, 10 days of antibiotic therapy is likely excessive for most patients based on guideline recommendations. Although median antibiotic therapy duration for acute cystitis was shorter, many course durations still exceeded guideline recommendations.

Recently, the body of evidence on minimum effective antibiotic therapy duration has grown and, consequently, guidelines recommend shorter antibiotic courses for acute uncomplicated cystitis in adult women [4], sinusitis in adults [5, 6], CAP in adults [3], and SSTI [7] and have suggested shorter courses may be appropriate for AOM in older children with mild or moderate disease [2]. Despite updated guideline recommendations for shorter courses, many outpatients are receiving antibiotic durations that exceed guideline recommendations, perhaps driven by clinician habit. Longer antibiotic courses have been associated with increased risks of adverse events [4, 8] and antibiotic-resistant infections [9, 10], putting patients at avoidable risk. Additionally, further research and stronger recommendations on minimum effective durations, especially in children, may be needed. For example, pediatric CAP guidelines do not provide definitive duration recommendations but note that 10-day courses are best studied, however shorter courses may be as effective [10]. Stronger evidence and explicit guidelines may empower clinicians to improve antibiotic therapy durations.

The Centers for Disease Control and Prevention's *Core Elements of Outpatient Antibiotic Stewardship* [11] provides a framework for improving antibiotic use, including duration, in outpatient settings. Particularly, clinical decision support shows promise in improving guideline-concordant antibiotic therapy duration in outpatient settings [12], perhaps by reinforcing recommended antibiotic therapy durations at the time of prescribing and changing clinician defaults.

Our study has several limitations. First, we were unable to account for underlying conditions, previous treatment failures, and other factors that might warrant longer durations. Second, we limited our analysis to antibiotic duration and assumed all antibiotics prescribed were warranted, which is unlikely [1]. Third, the NDTI dataset uses proprietary methodology to estimate prescription weights and may not be nationally representative. Fourth, the NDTI dataset does not include non-private-practice physician outpatient settings, including urgent care clinics and emergency departments, where antibiotic duration patterns may vary.

We found that clinicians frequently defaulted to 10-day durations even when guidelines recommend shorter durations, potentially exposing patients to unnecessarily long antibiotic therapy durations for many common conditions. Specifically, compliance with recommended duration of antibiotic therapy could be improved for sinusitis and CAP in

adults, cellulitis in all ages, and acute cystitis in women 12–64 years. Increased focus on appropriate duration of antibiotic therapy for these common conditions could reduce unnecessary outpatient antibiotic use.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table.

Median duration of estimated non-azithromycin antibiotics prescribed for common outpatient conditions by condition and population, National Disease and Therapeutic Index (NDTI), 2017

Condition	Population	Guideline-recommended duration of oral antibiotic therapy[A]	Estimated no. non-azithromycin antibiotic courses (95% CI)[B]	Median course duration in days (IQR)
Pharyngitis	Adult	10 days [13]	2,116,517 (1,762,606–2,470,428)	10 (10–10)
	Pediatric	10 days [13]	4,774,913 (4,263,388–5,286,438)	10 (10–10)
Sinusitis	Adult	5–7 days[C] [5]	5,739,038 (5,065,041– 6,413,035)	10 (10–10)
	Pediatric	10–14 days [5]	1,478,820 (1,182,136–1,775,504)	10 (10–10)
Acute otitis media	Pediatric, all	10 days[D] [2]	6,252,288 (5,648,066–6,856,510)	10 (10–10)
	Pediatric, <2 years	10 days[D] [2]	1,822,027 (1,524,067–2,119,987)	10 (10–10)
	Pediatric, ≥2 years	10 days, shorter courses (5–7 days) may be appropriate for select older children[D] [2]	4,430,261 (3,959,364–4,901,158)	10 (10–10)
Community-acquired pneumonia	Adult	≥5 days; 5 days appropriate for most patients[E] [3]	563,790 (394,691–732,889)	10 (7–10)
	Pediatric	No recommendation[F] [10]	323,798 (204,637–442,959)	10 (10–10)
Cellulitis	Adult	5 days[G] [7]	2,471,967 (2,098,246–2,845,688)	10 (7–10)
	Pediatric	5 days[G] [7]	621,688 (466,009–777,367)	10 (10–10)
Abscess	Adult	5–10 days [7]	244,791 (137,974–351,608)	10 (7–10)
	Pediatric	5–10 days [7]	86,799 (28,731–144,867)	10 (10–10)
Acute cystitis	Females 12–64 years	Varies by agent; 1–7 days [4]	3,341,905 (2,879,353–3,804,457)	7 (5–7)

No. – Number; IQR – Interquartile Range; CI – Confidence Intervals

[A] See Supplemental table 1 for full recommendations.

[B] Estimates and 95% confidence intervals estimated using methods appropriate for complex samples.

[C] Per guidelines from the Infectious Diseases Society of America, 5–7 days is recommended for patients with uncomplicated acute bacterial sinusitis without risk factors for resistance and with initial improvement after 3–5 days [5]. The American Academy of Otolaryngology-Head and Neck Surgery Foundation recommends 5–10 days of antibiotic therapy but notes that 5–7 days may be as effective with fewer side effects compared with longer courses [6].

[D] Guidelines note 7 days likely effective for children 2–5 years with mild or moderate AOM and 5–7 days likely effective for children 6 years and older with mild or moderate AOM [2].

[E] Guidelines recommend that antibiotic therapy should be continued until the patient achieves stability, for at least 5 days, with longer durations recommended for pneumonia complicated by meningitis, endocarditis, and other infection or pneumonia due to less-common pathogens (e.g., *Burkholderia pseudomallei*, *Mycobacterium tuberculosis* or endemic fungi) [3].

[F] No duration recommendation. Guidelines note: "Treatment courses of 10 days have been best studied, although shorter courses may be just as effective, particularly for more mild disease managed on an outpatient basis" [10].

[G] With possible extension of antibiotic therapy duration based on symptom improvement [7].