

Factors Associated With Longer Than Recommended Durations of Antibiotic Therapy for Uncomplicated Ambulatory Infections in an Integrated Healthcare System

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Across the ambulatory care network of an integrated health care system, durations of antibiotic therapy prescribed for uncomplicated infections were longer than recommended in 39% of cases. By logistic regression, site of care, prescriber characteristics, and type of infection were independently associated with longer than recommended durations of therapy.

Keywords. health care epidemiology; outpatient antibiotic stewardship; outpatient infectious diseases; primary health care.

In the United States (US), at least 30% of antibiotic prescriptions are unnecessary or inappropriate [1]. The majority of national studies of outpatient antibiotic prescribing have focused on the appropriateness of the indication for the prescription or the spectrum of activity. Only recently have such studies evaluated the appropriateness of durations of therapy prescribed [2–4].

In a study from the United Kingdom, about 1.3 million antibiotic-days were in excess of the durations of therapy recommended for uncomplicated ambulatory infections [4]. In the US Veterans Affairs Health Care System, 13% of antibiotics prescribed in primary care were for a longer duration than recommended in national guidelines [3]. Specific conditions such as acute sinusitis, uncomplicated urinary tract infections, cellulitis, and cutaneous abscesses have been associated with

excessive durations of therapy [5–8]. Despite these studies, the extent and drivers of excessive durations of therapy in outpatient settings are incompletely understood. Our objectives were to describe durations of therapy prescribed for uncomplicated infections across the ambulatory care network of an integrated health care system and identify factors associated with longer than recommended durations.

METHODS

Setting and Population

This was a retrospective, cross-sectional evaluation conducted from 1 July 2018 to 30 June 2019 at Denver Health, an integrated health care system that serves as the primary safety net institution for the City and County of Denver, Colorado. We identified antibiotic prescriptions for patients ≥18 years of age presenting with an uncomplicated infection to an ambulatory care site in the network including 3 internal medicine clinics, 6 family medicine clinics, 2 urgent care centers, and the emergency department.

Data Collection

We identified potentially eligible antibiotic prescriptions linked to a visit with a primary *International Classification of Diseases, Tenth Revision (ICD-10)* diagnosis code for the following infections: acute cystitis, pyelonephritis, acute sinusitis, acute otitis media (AOM), community-acquired pneumonia, cellulitis, and cutaneous abscess (Supplementary Table 1). At Denver Health, institutional guidance for these typically uncomplicated infections is for 5 days or less of therapy [9]. Antibiotics prescribed for >5 days were defined as longer than recommended. The following prescriptions were excluded from the analysis: nonfluoroquinolone antibiotics for pyelonephritis, those prescribed for respiratory tract infections where antibiotics are not indicated (eg, acute bronchitis, nonspecific upper respiratory infection), those prescribed for bacterial infections that require >5 days of therapy (eg, group A streptococcal pharyngitis, *Helicobacter pylori* infection), and those intended for prophylaxis. Prescriptions for acute sinusitis were included since commonly used *ICD-10* codes do not distinguish between viral and bacterial sinusitis (Supplementary Table 1) and the vast majority of patients with acute sinusitis are treated with antibiotics [5, 7].

Analyses were based on the duration prescribed by the provider rather than patient adherence to the prescribed duration. Antibiotic prescriptions for a patient with a primary or secondary diagnosis with the same *ICD-10* code in the previous

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30 days were considered to potentially reflect a complicated infection and were excluded.

Statistical Analysis

Cellulitis and cutaneous abscesses were categorized as skin and soft tissue infections (SSTIs). Cystitis and pyelonephritis treated with a fluoroquinolone were categorized as urinary tract infections (UTIs). Multiple logistic regression was used to evaluate factors associated with longer than recommended duration of therapy. Factors with $P < .05$ by χ^2 test and $P < .2$ by univariate analysis were used to develop the multiple logistic regression model. All statistical analyses were performed using IBM SPSS Statistics, version 27.0 (IBM Corporation, Armonk, New York, USA).

Patient Consent Statement

This programmatic evaluation did not include factors necessitating patient consent and it was reviewed by the Quality Improvement Review Committee of Denver Health

and Hospital Authority and deemed not to constitute human subjects research.

RESULTS

From July 2018 to June 2019, there were a total of 17775 antibiotic prescriptions for patients ≥ 18 years of age. Of these, 5331 prescriptions met inclusion criteria (Supplementary Figure 1). The duration of therapy was longer than recommended (>5 days) for 2100 (39%) prescriptions. The overall median duration of therapy was 5 days (interquartile range [IQR], 5–7 days). Median duration of therapy was 5 days (IQR, 5–7 days) for each type of infection, with the exception of acute sinusitis and AOM where the median was 7 days (IQR, 7–10 days). Prescribed durations varied significantly by ambulatory care site, sex of patient, provider type, and type of infection (Table 1). Of the 2100 longer than recommended prescriptions, urgent care centers accounted for 52.8%, followed by family medicine clinics (29%) and internal medicine clinics (11.4%). Acute sinusitis and AOM together accounted for 43.7% of all longer than recommended

Table 1. Antibiotic Duration of Therapy for Uncomplicated Outpatient Infections^a

| Factor | Guideline-Concordant Duration (≤ 5 Days) (n = 3231), No. (%) | Longer Than Recommended Duration (>5 Days) (n = 2100), No. (%) | P Value |
|---|--|---|---------|
| Age, y | | | |
| 18–49 | 1979 (61.2) | 1291 (61.5) | .420 |
| 50–64 | 840 (26) | 565 (26.9) | |
| ≥ 65 | 412 (12.8) | 244 (11.6) | |
| Race/ethnicity | | | |
| Hispanic/Latino | 1664 (51.5) | 1071 (51) | .427 |
| White | 1049 (32.5) | 697 (33.2) | |
| Black | 371 (11.5) | 254 (12.1) | |
| Other ^b | 147 (4.5) | 78 (3.7) | |
| Sex | | | |
| Female | 2299 (71.2) | 1279 (60.9) | $<.001$ |
| Male | 932 (28.8) | 821 (39.1) | |
| Provider type | | | |
| Physician | 1735 (53.7) | 1031 (49.1) | $<.001$ |
| Advanced practice provider ^c | 1496 (46.3) | 1069 (50.9) | |
| Site of care | | | |
| Adult urgent care center | 1740 (53.8) | 1109 (52.8) | $<.001$ |
| Family medicine clinic | 700 (21.7) | 609 (29) | |
| Emergency department | 424 (13.1) | 143 (6.8) | |
| Internal medicine clinic | 367 (11.4) | 239 (11.4) | |
| Infection | | | |
| Urinary tract infection ^d | 1541 (47.7) | 420 (20) | $<.001$ |
| Skin and soft tissue infection ^e | 800 (24.8) | 703 (33.5) | |
| Acute sinusitis | 493 (15.2) | 589 (28) | |
| Acute otitis media | 109 (3.4) | 327 (15.6) | |
| Community-acquired pneumonia | 288 (8.9) | 61 (2.9) | |

^aUncomplicated outpatient infections include purulent and nonpurulent skin cellulitis, cutaneous abscess, acute sinusitis, acute otitis media, community-acquired pneumonia, cystitis, and pyelonephritis treated with a fluoroquinolone.

^bAmerican Indian or Alaska Native, Asian, and unknown race/ethnicity.

^cPhysician assistant, nurse practitioner, and midwife.

^dPyelonephritis treated with a fluoroquinolone and cystitis.

^ePurulent and nonpurulent skin cellulitis and subcutaneous abscess.

prescriptions, followed by SSTIs (33.5%) and UTIs (20%). There was not an association between longer than recommended durations of therapy and patient age or race/ethnicity (Table 1).

Prescriptions by advanced practice providers were more likely to be for a longer than recommended duration than those by physicians (41.7% vs 37.3%, $P < .001$). Similarly, men were more likely than women to be prescribed a longer than recommended duration of therapy (46.8% vs 35.6%, $P < .001$). When stratifying by sex, 40.1% of men with a UTI received an antibiotic prescription for >5 days in comparison to only 19.2% of females (Supplementary Table 2). The association between men receiving longer durations of antibiotic therapy is driven due to a significant interaction between sex of patient and UTIs (Supplementary Table 3). In comparison with the emergency department, providers from the urgent care centers, family medicine clinics, and internal medicine clinics more often prescribed longer than recommended durations. Family medicine clinics had the highest proportion of longer than recommended durations (46%) (Supplementary Figure 2). For cellulitis, acute sinusitis, and AOM, the duration was longer than recommended in 50%, 54%, and 75% of cases, respectively (Supplementary Figure 3).

By logistic regression, factors independently associated with longer than recommended durations of therapy, after adjusting for the interaction between sex of patient and UTIs, included prescriptions by advanced practice providers (adjusted odds ratio [aOR], 1.24 [95% confidence interval {CI}, 1.09–1.41]), prescriptions in urgent care centers (aOR, 1.51 [95% CI, 1.20–1.89]) or family medicine clinics (aOR, 2.24 [95% CI, 1.76–2.86]), and prescriptions for SSTIs (aOR, 3.82 [95% CI, 2.84–5.14]), acute sinusitis (aOR, 4.66 [95% CI, 3.41–6.36]), and AOM (aOR, 12.41 [95% CI, 8.68–17.73]) (Table 2).

DISCUSSION

A recent national study by King and colleagues showed that for common outpatient infections, the median duration of therapy was 10 days and nearly three-quarters of prescriptions exceeded guideline-recommended durations [2]. Our findings differ from those by King and colleagues in that the overall median duration of therapy was 5 days and a substantially lower proportion of prescriptions (39%) were for longer than recommended durations. The shorter durations we observed may in part be the result of a long-standing antimicrobial stewardship program and the provision of syndrome-specific treatment guidance via a widely utilized smartphone application [9, 10]; however, there is still substantial opportunity to improve adherence to recommended treatment durations. Within our system, universal adherence to the recommended 5-day duration of therapy would have averted 6657 antibiotic-days over the 1-year period or 20% of the total antibiotic-days prescribed.

At a system level, excessive durations were common across all sites of care but particularly among the urgent care centers and family medicine clinics. Since the same prescribing guidance is available to all providers in our organization, there is a need to better understand why adherence is substantially better in some care locations than others. Although prescriptions by advanced practice providers were independently associated with longer than recommended durations, it is worth noting that excessive durations were common among physicians as well. Specific conditions including SSTIs, acute sinusitis, and AOM—among the most common indications for outpatient antibiotics [1]—were about 4, 5, and 12 times more likely, respectively, to be prescribed with excessive durations of therapy. This highlights the potential value of syndrome-specific antimicrobial stewardship interventions emphasizing appropriate durations of therapy.

Table 2. Logistic Regression Model of Factors Associated With Antibiotic Prescriptions for a Longer Than Recommended Duration of Therapy

| Variable | OR (95% CI) | Adjusted OR (95% CI) ^a |
|--|--------------------|-----------------------------------|
| Advanced practice provider ^b (vs physician) | 1.20 (1.08–1.34) | 1.24 (1.09–1.41) |
| Male patient (vs female) | 1.58 (1.41–1.78) | 1.07 (.92–1.25) |
| Site of care | | |
| Emergency department | | Reference |
| Family medicine clinic | 2.58 (2.07–3.21) | 2.24 (1.76–2.86) |
| Adult urgent care center | 1.89 (1.54–2.32) | 1.51 (1.20–1.89) |
| Internal medicine clinic | 1.93 (1.50–2.48) | 1.29 (.98–1.69) |
| Infection | | |
| Community-acquired pneumonia | | Reference |
| Acute otitis media | 14.16 (9.97–20.12) | 12.41 (8.68–17.73) |
| Acute sinusitis | 5.64 (4.17–7.62) | 4.66 (3.41–6.36) |
| Skin and soft tissue infection ^c | 4.15 (3.09–5.57) | 3.82 (2.84–5.14) |
| Urinary tract infection ^d | 1.29 (.96–1.73) | 0.97 (.70–1.33) |

Abbreviations: CI, confidence interval; OR, odds ratio.

^aMultiple logistic regression model is adjusted for the interaction between urinary tract infection diagnosis and sex of patient.

^bPhysician assistant, nurse practitioner, or nurse midwife.

^cCellulitis or cutaneous abscess.

^dPyelonephritis treated with a fluoroquinolone or cystitis.

For example, among older children with AOM, we were able to markedly increase adherence to 5-day durations of therapy with a multifaceted intervention [11].

This work has several limitations. First, these data are from a single health care system, and thus, the findings are not generalizable. However, based on national data, it may be that there is even greater opportunity to reduce excessive durations of therapy in other institutions [2]. Second, the use of *ICD-10* codes to identify conditions for which antibiotics were prescribed has inherent limitations including the potential for misclassification or miscoding of clinical conditions. Third, a large proportion of antibiotics prescribed were excluded from the analysis and antibiotics prescribed for concomitant infections were not evaluated. This is likely in large part due to the use of a limited set of *ICD-10* codes in an attempt to include only uncomplicated infections. Fourth, we did not evaluate clinical outcomes and were unable to assess whether longer than recommended durations impacted the likelihood of treatment success or antibiotic-related adverse events. Fifth, we did not evaluate the appropriateness of the duration prescribed in individual cases. However, given our large sample size, we suspect that the 5-day or less outcome measure was a reasonable surrogate for appropriateness in most cases. A strength is the inclusion of a wide breadth of ambulatory care sites that allowed us to assess variability in factors associated with longer durations of therapy across sites.

In summary, across the ambulatory care network of an integrated health care system, nearly 40% of antibiotic prescriptions for uncomplicated infections were for longer than recommended durations. Several system-level, provider-level, and patient-level factors were associated with longer than recommended durations of therapy. These data add to recent evidence that reducing excessive durations of therapy is an essential component of outpatient antimicrobial stewardship and highlight areas of focus that may be high yield.

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.

Notes

Potential conflicts of interest. All authors: No reported conflicts of interest.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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