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Utilization of broad- versus narrow-spectrum antibiotics for the treatment of outpatient community-acquired pneumonia among adults in the United States

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Abstract

Purpose: To characterize antibiotic utilization for outpatient community-acquired pneumonia (CAP) in the U.S.

Methods: We conducted a cohort study among adults 18–64 years diagnosed with outpatient CAP and a same-day guideline-recommended oral antibiotic fill in the MarketScan® Commercial Database (2008–2019). We excluded patients coded for chronic lung disease or immunosuppressive disease; recent hospitalization or frequent health care exposure (e.g., home wound care, patients with cancer); recent antibiotics; or recent infection. We characterized utilization of broad-spectrum antibiotics (respiratory fluoroquinolone, β-lactam + macrolide, β-lactam + doxycycline) versus narrow-spectrum antibiotics (macrolide, doxycycline) overall and by patient- and provider-level characteristics. Per 2007 IDSA/ATS guidelines, we stratified analyses by otherwise healthy patients and patients with comorbidities (coded for diabetes; chronic heart, liver, or renal disease; etc.).

Results: Among 263,914 otherwise healthy CAP patients, 35% received broad-spectrum antibiotics (not recommended); among 37,161 CAP patients with comorbidities, 44% received broad-spectrum antibiotics (recommended). Ten-day antibiotic treatment durations were the most common for all antibiotic classes except macrolides. From 2008–2019, broad-spectrum

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antibiotic use substantially decreased from 45% to 19% in otherwise healthy patients (average annual percentage change [AAPC], −7.5% [95% CI −9.2%, −5.9%]), and from 55% to 29% in patients with comorbidities (AAPC, −5.8% [95% CI −8.8%, −2.6%]). In subgroup analyses, broad-spectrum antibiotic use varied by age, geographic region, provider specialty, and provider location.

Conclusions: Real-world use of broad-spectrum antibiotics for outpatient CAP declined over time but remained common, irrespective of comorbidity status. Prolonged duration of therapy was common. Antimicrobial stewardship is needed to aid selection according to comorbidity status and to promote shorter courses.

Plain Language Summary

Community-acquired pneumonia (CAP) is a common indication for antibiotics in adults. We sought to describe antibiotic use for outpatient CAP among U.S. adults. Using national data from a health insurance claims database (2008–2019), we identified adults aged 18–64 years who were diagnosed with outpatient CAP and received a same-day guideline-recommended oral antibiotic. We summarized use of broad- versus narrow-spectrum antibiotics, overall and by patient- and provider-level characteristics. Since CAP treatment guidelines differ for otherwise healthy patients and patients with preexisting conditions (e.g., diabetes; chronic heart or liver disease), we reported findings separately for each group. Among otherwise healthy CAP patients, 35% received broad-spectrum antibiotics (not recommended); among CAP patients with preexisting conditions, 44% received broad-spectrum antibiotics (recommended). A ten-day antibiotic treatment duration was the most common duration for all antibiotic classes except macrolides. Use of broad-spectrum antibiotic use substantially declined from 2008–2019 in otherwise healthy patients (45% to 19%) and patients with preexisting conditions (55% to 29%). Broad-spectrum antibiotic use varied by age, geographic region, provider specialty, and provider location. Broad-spectrum antibiotic use and long duration of therapy were common among CAP patients. Antibiotic stewardship is needed to improve selection of antibiotic regimens and to promote shorter durations.

INTRODUCTION

Community-acquired pneumonia (CAP) is common, accounting for approximately 4.7 million ambulatory visits annually in the US.[1] Based on randomized clinical trials, experts and US clinical practice guidelines recommend several empiric antibiotic regimens for outpatient CAP treatment depending on patient comorbidity status and local rates of macrolide-resistant *Streptococcus pneumoniae*.[2–4] Adults with liver disease, renal disease, diabetes, alcoholism, perivascular disease, valvular disease, asplenia, malignancy, chronic lung disease, chronic heart disease, or an immune-suppressing condition, or adults who use an immunosuppressing drugs are classified as having a comorbidity according to the CAP treatment guidelines.[2] Narrow-spectrum regimens (i.e., macrolide, doxycycline) are recommended in otherwise healthy patients whereas broad-spectrum regimens (i.e., fluoroquinolone, β-lactam plus macrolide, β-lactam plus doxycycline) are recommended for patients with comorbidities.[2]

Understanding antibiotic utilization patterns is a public health priority because of the potential consequences of inappropriate antibiotic exposure including disruption of the

microbiome,[5] adverse drug events,[6–10] antibiotic-resistant infections,[11] and increased health care costs.[9,10] Yet, knowledge is limited about contemporary antibiotic utilization patterns of outpatient CAP treatment. The most recent studies evaluating outpatient CAP treatment patterns for US adults are restricted to data from 2008[12] or earlier.[13,14] Antibiotic prescribing patterns have likely changed given increasing prevalence of antibiotic resistance and recent antimicrobial stewardship efforts. We sought to characterize contemporary patterns of antibiotic use for outpatient CAP in a large population of commercially-insured US adults stratified by otherwise healthy patients and patients with comorbidities, in accordance with the 2007 Infectious Diseases Society of America / American Thoracic Society (IDSA/ATS) clinical practice guidelines. Specifically, we documented antibiotic utilization by subgroups defined by individual-level characteristics (age group and geographic region) as well as provider-level characteristics (provider type and location). We also evaluated temporal trends in broad-spectrum antibiotics over the study period (2008–2019).

METHODS

Data Source

We used the Merative™ MarketScan® Commercial Database (2006–2019) which includes longitudinal, patient-level data on enrollment, adjudicated inpatient and outpatient medical insurance claims, and outpatient pharmacy-dispensed medications. The database primarily includes individuals with employer-sponsored commercial insurance and their spouses and dependents.[15] The Washington University School of Medicine institutional review board deemed this study exempt from human subjects review.

Study Design & Population

We identified a cohort of U.S. adults aged 18–64 years with an *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) or ICD-10-CM diagnosis code for pneumonia (eTable 1, ignoring diagnostic/rule-out claims) diagnosed in an outpatient setting from January 1, 2008 to October 1, 2019. We required treatment on the same day as the CAP diagnosis (index date) with a guideline-recommended oral antibiotic (see “Antibiotic Exposure” section) according to the 2007 IDSA/ATS CAP guidelines that were in place during the study period;[2] we did not include index events after the October 1, 2019 release of updated CAP guidelines.[3] We required continuous medical and prescription drug insurance enrollment during the 180-day baseline period before the index date.

To increase the likelihood that the pneumonia diagnosis was community-acquired, we excluded index events with risk factors for multidrug-resistant pathogens that can cause hospital-acquired pneumonia/healthcare-associated pneumonia (HCAP) or ventilator-associated pneumonia.[16] Risk factors for multidrug-resistant pathogens included index events with antimicrobial therapy ≤ 90 days before the index date (intravenous, intramuscular, oral); immunosuppressive disease (all-available lookback period before index) and/or immunosuppressive therapy (≤ 180 days before index; e.g., history of solid organ transplant, systemic steroids prescription); HCAP (i.e., hospitalization of ≥ 2 days, residence in a nursing home, home infusion therapy, or home wound care ≤ 90 days before

index); regular healthcare exposures (i.e., individuals with end-stage renal disease before index or cancer/leukemia ≤ 365 days before index); or mechanical ventilation ≤ 90 days before index (eTables 2–3). We excluded index events with chronic lung disease before the index date (all-available lookback period) because of the difficulty in distinguishing symptoms of pneumonia versus lung disease (eTable 3). We excluded index events with a non-CAP bacterial or viral infection ≤ 30 days before the index date,[17] influenza ≤ 21 days before index due to the risk of post-influenza bacterial pneumonia,[18] or any outpatient pneumonia diagnosis ≤ 90 days before the index date using a broader list of diagnosis codes than those qualifying as an index event (e.g., viral pneumonia, pneumonia with a rare organism not captured in routine testing; eTable 4). We restricted to standard antibiotic durations of 3 (azithromycin only), 5, 7, and 10 days, and excluded index events with >1 antibiotic within a class on the index date (e.g., azithromycin and clarithromycin) or >1 antibiotic class other than guideline-recommended β-lactam combinations (Table 1). Finally, we restricted the population to the first qualifying index event per adult (eFigure 1).

Antibiotic Exposure

Guideline-recommended oral antibiotics for outpatient CAP are reported in Table 1.[2] Macrolide and doxycycline antibiotic regimens were considered narrow-spectrum and recommended for healthy patients; respiratory fluoroquinolones and β-lactam plus macrolide or doxycycline were categorized as broad-spectrum and recommended for patients with comorbidities.[2] Antibiotic durations of 3 and 5 days were considered short, and 7 and 10 days were considered long durations.

Patient- and Provider-level Characteristics

Patient- and provider-level characteristics were assessed at index including age, sex, geographic region, urban residence (i.e., residence in a metropolitan statistical area),[19] provider specialty, and provider outpatient location (i.e., office, emergency department (ED), urgent care center, other). The number of ED encounters, physician office visits, and unique medication therapeutic groups were assessed during the 180-day baseline period. We used diagnosis codes for the comorbidities listed in the CAP treatment guidelines[2] to stratify adults into patients with comorbidities and otherwise healthy patients using an all-available lookback period on or before the index date (eTable 5). The comorbidities included were liver disease, renal disease, diabetes, alcoholism, perivascular disease, valvular disease, asplenia, and chronic heart disease (congestive heart failure, stroke/ transient ischemic attack, intermittent claudication, coronary artery disease); malignancy, chronic lung disease, and immune-suppressing condition/drug were not included because they were considered exclusions.

Statistical Analysis

We conducted all analyses separately by comorbidity status. We summarized baseline patient- and provider-level characteristics of each population by year. We plotted state-level maps of the proportion of broad-spectrum antibiotic prescriptions and long regimen durations, and temporal trends in the use of individual antibiotic regimens, broad- versus narrow-spectrum regimens, and antibiotic durations.

We used the Joinpoint Regression Program (version 4.9.1.0, NCI) to calculate the average annual percentage change (AAPC) in broad-spectrum antibiotic use over the study period.[20] The Joinpoint Program uses permutation tests to find a best fit regression model with the smallest number of "joinpoints" (distinct linear segments that differ statistically in their slopes).[21] We used multivariable logistic regression models to generate unadjusted and adjusted half-year estimates of the proportion of patients who used broad-spectrum antibiotic agents. Calendar time was considered a categorical variable to relax the assumption of linearity. We plotted the adjusted estimates for broad-spectrum antibiotic use, which were population marginal means that account for changes over time in patient-level (sex, age group, geographic region, urban residence) and provider-level (provider specialty, provider location) characteristics.[22] Trend lines were calculated as LOESS smoothed conditional means of the half-year adjusted estimates.[23] We also performed subgroup analyses by age group, geographic region, urban residence, provider specialty, and provider location.

RESULTS

The final cohort included 301,075 adults with outpatient CAP; see flow chart eFigure 1 for a description of excluded index events. Mean age was 43 years among healthy patients and 52 years among patients with comorbidities (eTable 6). Family practice was the most common provider specialty (40%), and 77% of patients were seen in an office setting (eTables 6 and 7). In the most recent years, nurse practitioners / physician assistants accounted for a larger proportion of providers and urgent care centers became a more common provider location (eTable 7).

Antibiotic regimens

Of 263,914 otherwise healthy CAP patients, 35% received broad-spectrum antibiotics (32% respiratory fluoroquinolone, 2% β-lactam + macrolide, <1% β-lactam + doxycycline) and 65% received narrow-spectrum antibiotics (57% macrolide, 8% doxycycline; eFigure 2). Among healthy patients, use of respiratory fluoroquinolones decreased over the study period while doxycycline increased; macrolides remained the most common regimen throughout the study period (Figure 1A). Among 37,161 CAP patients with comorbidities, 44% received broad-spectrum antibiotics (41% respiratory fluoroquinolone, 3% β-lactam + macrolide, 1% β-lactam + doxycycline) and 56% received narrow-spectrum antibiotics (46% macrolide, 9% doxycycline; eFigure 2). Among patients with comorbidities, respiratory fluoroquinolones were the most common regimen until 2010, when macrolides became most common. Otherwise, trends were similar to healthy patients (Figure 1B).

From 2008 to 2019, broad-spectrum antibiotic use decreased from 45% to 19% in healthy patients (AAPC, −7.5% [95% CI −9.2%, −5.9%]), and from 55% to 29% in patients with comorbidities (AAPC, −5.8% [95% CI −8.8%, −2.6%]; Figure 2). Broad-spectrum antibiotic use varied by state. States in the South had more broad-spectrum antibiotic use, particularly in the earlier timeframe (2008–2011 versus 2016–2019; Figure 3).

In multivariable analyses, broad-spectrum antibiotic use increased with patient age in both healthy patients and those with comorbidities (Figure 4) and also varied by

provider specialty (Figure 5). Broad-spectrum antibiotic use was consistently lowest among encounters with nurse practitioners/physician assistants, as compared to other provider types. Broad-spectrum antibiotic use did not differ by rurality (eFigure 3) but varied by geographic region, with the highest proportion of broad-spectrum antibiotic use in the South (eFigure 4). In the first half of the study period, broad-spectrum antibiotic use was higher in urgent care settings compared to ED, office, and other provider locations (eFigure 5), though differences narrowed over time. For all subgroup analyses, unadjusted and adjusted estimates of broad-spectrum antibiotic use were similar.

Antibiotic duration

Among all patients treated for outpatient CAP, the most common antibiotic durations were 5- and 10-day prescriptions (eFigures 6–7). For both populations, the proportion of 5- and 7-day prescriptions increased over the study period, while 10-day prescriptions decreased (eFigures 6–7). For all patients, the most common duration for macrolides was 5 days, whereas the most common duration for other regimens was 10 days (Figure 6); the most common duration by antibiotic regimen was the same for all time periods (eTable 8). Prolonged antibiotic durations of 7- or 10-day prescriptions were most common in the South (eFigures 8).

DISCUSSION

We performed a large administrative claims database study to characterize contemporary real-world antibiotic utilization for the treatment of outpatient CAP among commercially-insured adults in the U.S. We observed similar patterns of broad-spectrum antibiotic use among otherwise healthy patients and patients with comorbidities, despite clinical guidelines for CAP in place during the study period that recommended broad-spectrum antibiotics only for patients with comorbidities.[2] We documented declines over time in broad-spectrum antibiotic use for all patients, irrespective of comorbidity status, driven by sharp decreases in fluoroquinolone prescriptions and increases in macrolide and doxycycline prescriptions. In subgroup analyses, broad-spectrum antibiotic use varied by individual-level characteristics (age group and geographic region) and as well as provider-level characteristics (provider type and location). In addition, 10-day prescriptions were the most common duration for all regimens except macrolide monotherapy, even though clinical guidelines for CAP state that 5-day durations should be appropriate for most patients. Over the study period, we observed declines in the proportion of 10-day prescriptions, with simultaneous increases in 5- and 7-day prescriptions.

The study-period guideline recommendations for outpatient CAP treatment are stratified into two patient populations, defined by the presence of certain comorbidities.[2] For example, narrow-spectrum regimens (i.e., macrolide, doxycycline) are indicated in otherwise healthy patients and broad-spectrum regimens (i.e., a fluoroquinolone, β-lactam plus macrolide, β-lactam plus doxycycline) are indicated in patients with comorbidities.[2] Yet, we documented relatively similar proportions and patterns of antibiotic utilization irrespective of comorbidities. In our study, approximately two-thirds of healthy CAP patients received a guideline-recommended narrow-spectrum antibiotic regimen. Most of these prescriptions

were for a macrolide (for which the 2007 guidelines gave a strong recommendation [level I evidence]), whereas a small proportion were for doxycycline (which had a weak recommendation [level III evidence]). Conversely, approximately one-third of the healthy CAP patients received a broad-spectrum antibiotic, primarily fluoroquinolones. The proportion of broad-spectrum antibiotics dispensed for outpatient CAP was <10 percentage-points different between patients with comorbidities and otherwise healthy patients, despite opposing guideline recommendations for these two groups. Similarly, the rank order of antibiotic regimen proportions was identical for both patient populations, with macrolides prescribed most commonly and β-lactam + doxycycline prescribed least commonly. These results suggest that healthcare providers often prescribe a "go-to" antibiotic based on personal preference and subjective assessment of patient severity of pneumonia presentation, rather than based on medical comorbidities, as recommended by guidelines. Our findings are consistent with a study examining outpatient CAP antibiotics in 2004, wherein macrolides and fluoroquinolones accounted for >80% of dispensed prescriptions regardless of comorbidity status.[14] Furthermore, our observation of non-guideline concordance for CAP-related antibiotic prescribing is consistent with previous literature documenting inappropriate antibiotic prescribing for a variety of infection types and patient populations.[9,10,24]

The decrease in broad-spectrum antibiotics for outpatient CAP from 2008 to 2019 was driven by a steep decline in fluoroquinolone use from 44% to 13% among healthy patients and from 54% to 21% among patients with comorbidities. This is in contrast to a prior study examining ED visits for CAP that reported a striking increase in the use of quinolones from 1993 to 2008 (0% to 39%).[12] The decrease in fluoroquinolone use during the timeframe of our study was likely due to recognition of adverse effects as reported by the US Food & Drug Administration warnings and labeling changes during the study period,[25] as well as antimicrobial stewardship efforts. Decreases in fluoroquinolone use have also been reported for other outpatient infections since FDA warnings to limit prescribing for uncomplicated urinary tract infections, sinusitis, bronchitis, and acute exacerbation of chronic obstructive pulmonary disease.[26,27]

For all CAP regimens besides macrolide monotherapy, initial antibiotic treatment with a 10-day course was the most common duration. These findings align with a report on common outpatient infections (i.e., Streptococcal pharyngitis, sinusitis, acute otitis media, CAP, skin and soft tissues infection, and acute cystitis), wherein the median antibiotic duration was 10 days for all common outpatient infections studied in both children and adults except acute cystitis.[28] CAP guidelines and expert opinion recommendations endorse antibiotic treatment for at least 5 days, with extension of treatment if patients do not meet clinical stability criteria, but note that 5-day durations should be appropriate for most patients.[2–4] Meta-analysis of randomized controlled trials evaluating short versus long course antibiotic regimens for CAP in both inpatients and outpatients have demonstrated similar clinical outcomes and fewer adverse effects with short course regimens.[29] Antimicrobial stewardship efforts implemented in hospitals with a focus on transition-of-care have demonstrated improvement in duration of therapy for patients with CAP.[30,31] Efforts to shorten antibiotic duration is important given that longer antibiotic courses have been associated with increased risk of adverse events[29,32] and antibiotic-resistant infections.[33] Our findings

suggest outpatient antimicrobial stewardship is needed for outpatients with CAP to reduce unnecessarily long durations of therapy.

An important consequence of the overuse of broad-spectrum agents is selection for antibiotic-resistant organisms, and subsequently, the need for broader spectrum antibiotics to treat common community-acquired bacterial infections. This phenomenon is reflected in current expert opinion recommendations, in which macrolide and amoxicillin combination therapy is endorsed for healthy patients.[4] The change in macrolide prescribing recommendations was based on studies of macrolide failure in patients with macrolide-resistant *S. pneumoniae*.[34,35] *S. pneumoniae* is the most common cause of CAP,[36] and essentially all regions of the United States have *S. pneumoniae* macrolide resistance rates of >30%, most of which is high-level resistance.[3,37–39] Thus, current recommendations would dictate that all patients, even healthy individuals, should receive a broad-spectrum antibiotic regimen in the form of two antibiotics or a respiratory fluoroquinolone. We anticipate that increased use of broad-spectrum antibiotics will further drive antibiotic resistance and increase the risk of antibiotic-associated adverse events. Evidence suggests that doxycycline efficacy is comparable to broad-spectrum antibiotics, such as fluoroquinolones, for mild-to-moderate CAP.[40] Doxycycline may be a good option for otherwise healthy patients to reduce broad-spectrum prescribing, however the original trials are outdated and contemporary studies of doxycycline effectiveness would be beneficial. Antimicrobial stewardship interventions to reduce unnecessary macrolide prescribing in community settings would likely result in lower macrolide resistance, thus allowing more narrow-spectrum antibiotic use in the future.

To ensure that the antibiotic was given for the indication of CAP, we restricted the list of antibiotic agents to those listed in the 2007 CAP guidelines.[2] Therefore, our study overestimated the proportion of guideline-concordant prescribing in outpatient CAP patients. If we had included other possible CAP treatments that are *not* included in the 2007 guidelines (i.e., β-lactam monotherapy, ciprofloxacin, cefadroxil, cefprozil, cephalexin, clindamycin, gatifloxacin, linezolid, metronidazole, minocycline, norfloxacin, ofloxacin, tedizolid, trimethoprim-sulfamethoxazole) our cohort would have increased by 10.4% (8.4% β-lactam monotherapy, 1.1% ciprofloxacin, 0.9% other antibiotic), all of which would have been considered non-guideline-concordant. Targeted antimicrobial stewardship interventions are needed to promote use of guideline-concordant regimens and durations to reduce antibiotic-related harms and unnecessary health care utilization and expenditures while offering the best treatment option to each CAP patient.

Our results are subject to several limitations. First, study eligibility criteria required a pharmacy claim for dispensation of an oral antibiotic. While a small proportion of patients likely paid out-of-pocket and thus would not be included in the study cohort, we do not anticipate differences related to payment via insurance benefit versus out-of-pocket. Second, diagnoses are not directly linked to prescription medication fills within insurance claims data, thus it is possible that the antibiotic we associated with CAP was prescribed for another condition. However, to minimize possible misclassification, we required a guideline-recommended antibiotic on the same day as the CAP diagnosis and excluded index events with another infection ≤ 30 days before the CAP diagnosis. Third, these data do not contain

complete information to optimally categorize antibiotic prescriptions as inappropriate versus appropriate. For example, clinical guidelines recommend broad-spectrum antibiotics among healthy patients living in areas of high prevalence of macrolide-resistant *S. pneumoniae*, however, we did not have information on local resistance. Fourth, diagnosis codes for pneumonia have not been validated in the outpatient setting; therefore it is possible that not all patients coded for CAP truly had pneumonia. However, we required an accompanying guideline-recommended antibiotic, which should increase the likelihood of CAP. Fifth, we did not have clinical information on patient factors such as vital signs or severity of illness (e.g., CURB-65 criteria) that may be associated with antibiotic prescribing practices. Lastly, the study was limited to non-elderly, privately-insured adults, thus results may not be generalizable to other populations such as uninsured adults or adults insured by Medicaid or Medicare. These limitations are counterbalanced by using a national commercial insurance database with a very large eligible cohort enabling novel characterization of antibiotic treatment patterns by regimen and duration within subgroups (e.g., age, region, specialty).

In summary, real-world use of broad-spectrum agents remained common among otherwise healthy adults in the U.S., particularly in certain subgroups. Use of broad-spectrum antibiotic regimens for outpatient CAP declined over time, which is encouraging from an antimicrobial stewardship standpoint. However, efforts are still needed to foster the optimal antibiotic choice for each CAP patient, including narrow-spectrum agents when possible and the shortest effective duration.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Key Findings

- Clinical practice guidelines for the outpatient treatment of CAP recommend narrow-spectrum antibiotic regimens for otherwise healthy adults and broad-spectrum regimens for adults with comorbidities, but knowledge is limited about utilization patterns.
- Use of longitudinal, patient-level, claims data allowed characterization of antibiotic utilization for outpatient CAP treatment in the U.S.
- Broad-spectrum antibiotics were commonly used to treat otherwise healthy CAP patients (35%; not recommended) and CAP patients with comorbidities (44%; recommended). Ten-day antibiotic durations were the most common duration.
- Broad-spectrum antibiotic use decreased over time and varied across subgroups.
- Antimicrobial stewardship is needed to improve selection according to comorbidity status and promote shorter courses.

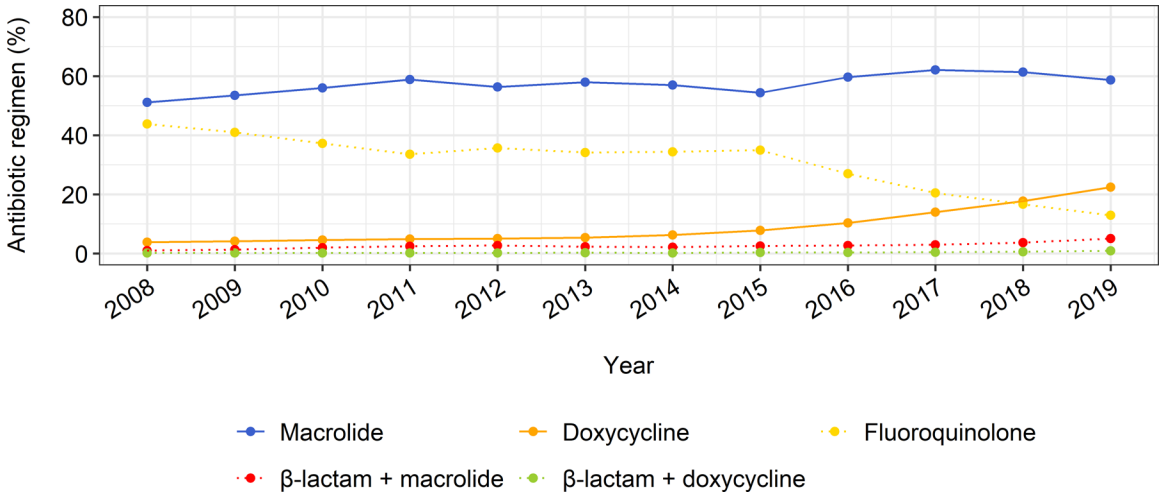

Figure 1A. Antibiotic Utilization for Outpatient Community-acquired Pneumonia by Year among Otherwise Healthy Patients

Footnote. Solid lines indicate a recommended regimen for otherwise healthy patients; dashed lines indicate a non-recommended regimen.

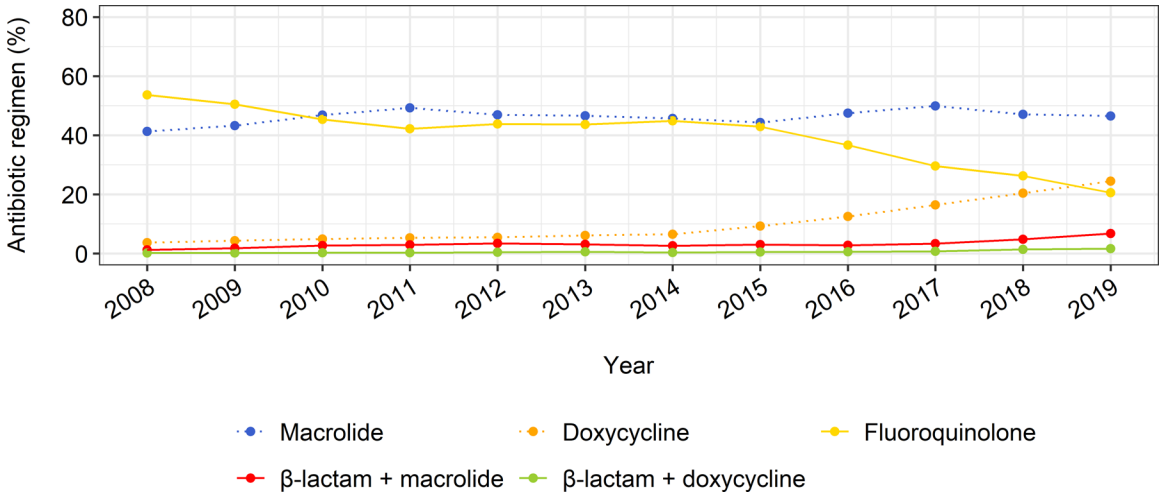

Figure 1B.

Antibiotic Utilization for Outpatient Community-acquired Pneumonia by Year among Patients with Comorbidities

Footnote. Solid lines indicate a recommended regimen for patients with comorbidities; dashed lines indicate a non-recommended regimen.

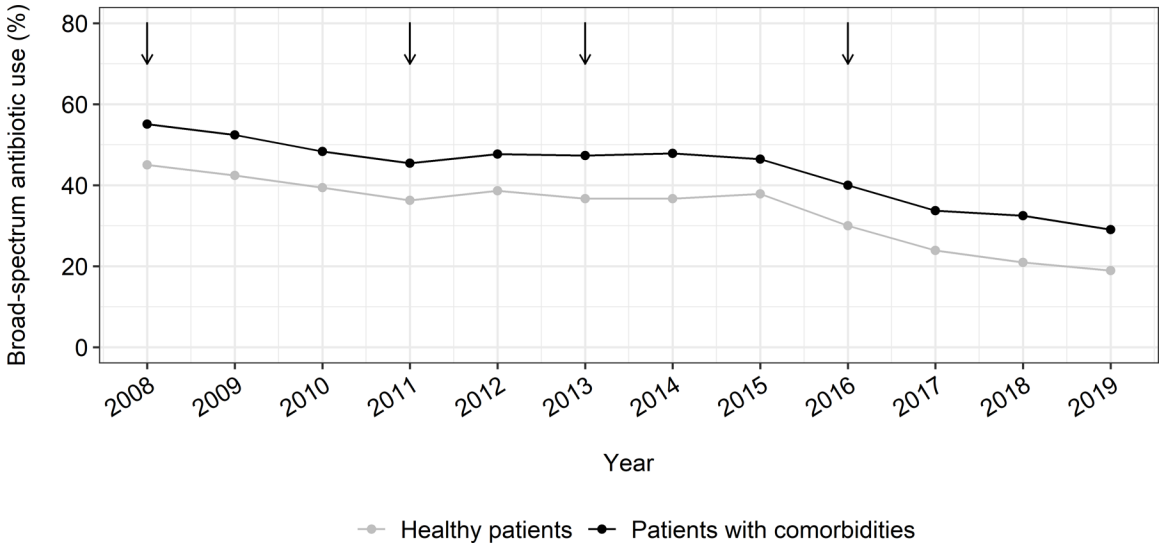

Figure 2. Broad-spectrum antibiotic use for outpatient community-acquired pneumonia by year and comorbidity status.

Footnote. Vertical arrows indicate timing of U.S. Food and Drug Administration (FDA) warnings and labeling changes for fluoroquinolones.

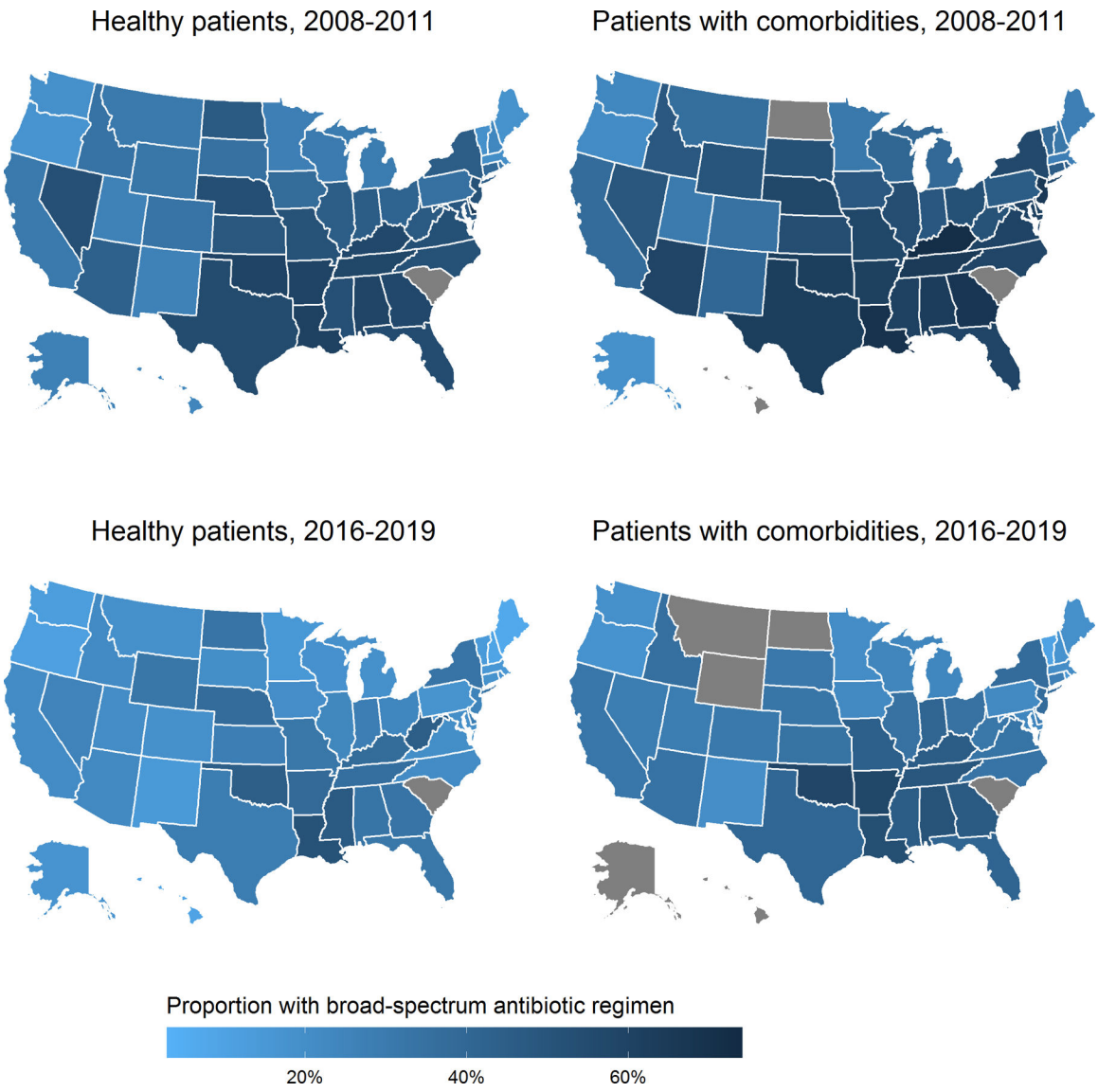

Figure 3. Broad-spectrum antibiotic use for outpatient community-acquired pneumonia by state and comorbidity status in 2008–2011 and 2016–2019.

Footnote. Results are unadjusted and are not presented for grey states due to small numbers (<11 community-acquired pneumonia cases in a state) and/or a data use agreement with Merative.

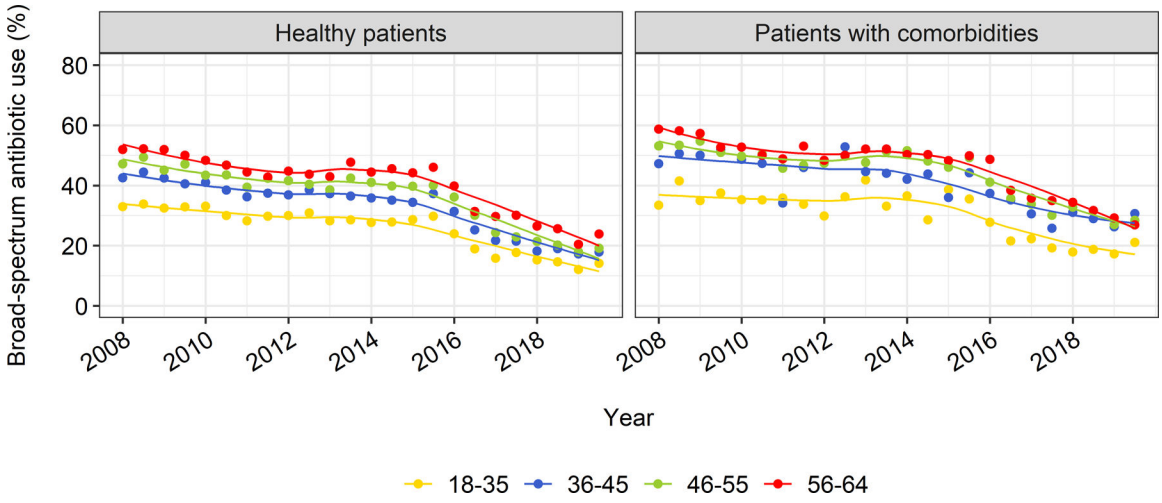

Figure 4. Broad-spectrum antibiotic use for outpatient community-acquired pneumonia by year and comorbidity status, stratified by age.

Footnote. Multivariable logistic regression models were used to generate adjusted half-year estimates of broad-spectrum antibiotic use. Calendar time was considered a categorical variable, and models were adjusted for sex, geographic region, urban residence, provider specialty, and provider location. Trend lines represent smoothed conditional means.

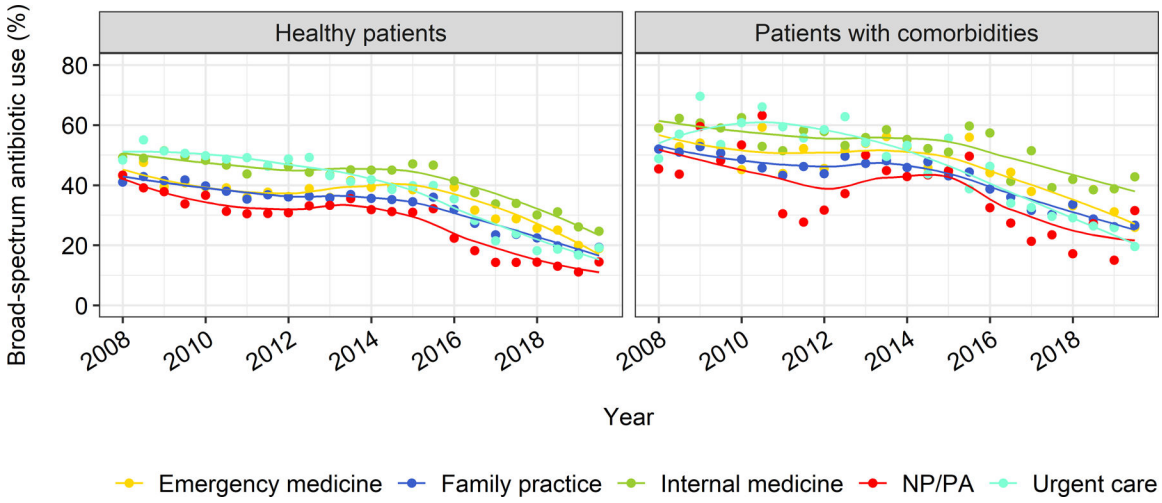

Figure 5. Broad-spectrum antibiotic use for outpatient community-acquired pneumonia by year and comorbidity status, stratified by provider specialty.

Abbreviation: NP/PA, nurse practitioner/physician assistant.

Footnote. Multivariable logistic regression models were used to generate adjusted half-year estimates of broad-spectrum antibiotic use. Calendar time was considered a categorical variable, and models were adjusted for sex, age group, geographic region, urban residence, and provider location. Trend lines represent smoothed conditional means. Provider specialties of MD/DO not elsewhere classified, other/missing, and unknown provider- other facility are not shown for simplicity.

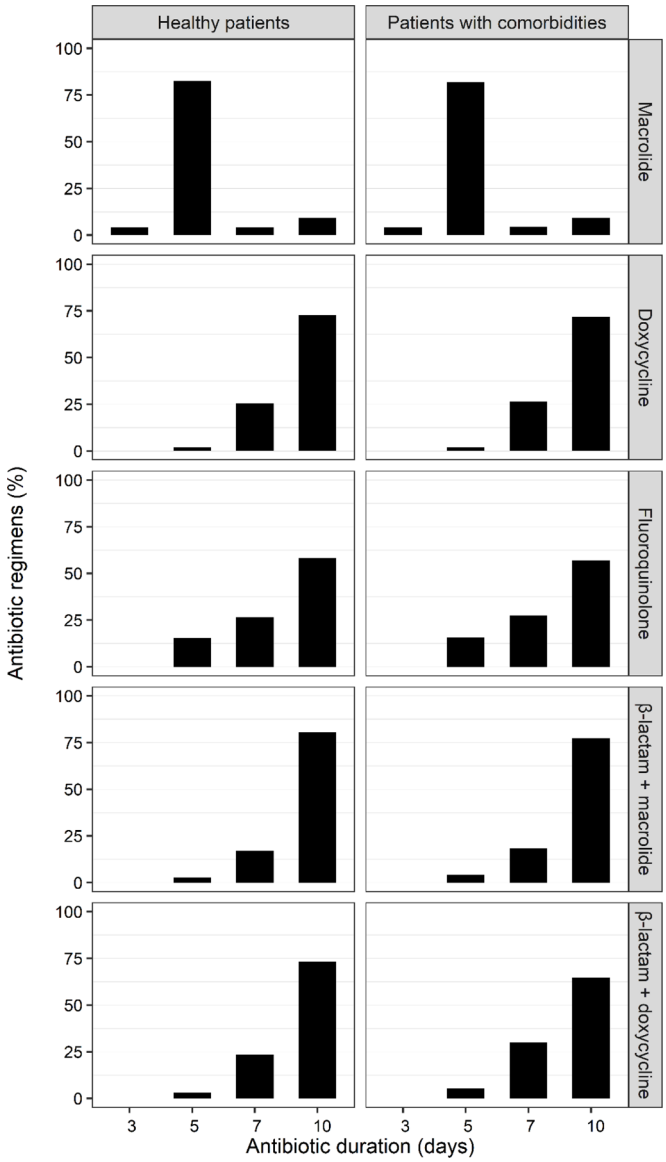

Figure 6. Duration of index antibiotic for outpatient community-acquired pneumonia by antibiotic regimen and comorbidity status.

Footnote. Cohort sizes for healthy patients as follows: 150,428 macrolide, 21,036 doxycycline, 85,226 fluoroquinolone, 6,417 β-lactam plus macrolide, 807 β-lactam plus doxycycline. Cohort sizes for patients with comorbidities as follows: 17,213 macrolide, 3,510 doxycycline, 15,066 fluoroquinolone, 1,165 β-lactam plus macrolide, 207 β-lactam plus doxycycline.

Table 1.

2007 Infectious Diseases Society of America / American Thoracic Society (IDSA/ATS) Guideline-recommended Antibiotic Regimens for the Treatment of Community-acquired Pneumonia

Antibiotic coverage[a]	**Antibiotic regimen**	**Antibiotic generic name**[b]
Narrow-spectrum	Macrolide	azithromycin, clarithromycin, erythromycin
	Doxycycline	doxycycline
Broad-spectrum	Respiratory fluoroquinolone	moxifloxacin, gemifloxacin, levofloxacin
	β-lactam plus a macrolide	β-lactam (amoxicillin, amoxicillin-clavulanate, ampicillin, cefdinir, cefditoren, cefixime, cefpodoxime, ceftibuten, cefuroxime) plus a macrolide (azithromycin, clarithromycin, erythromycin)
	β-lactam plus doxycycline	β-lactam (amoxicillin, amoxicillin-clavulanate, ampicillin, cefdinir, cefditoren, cefixime, cefpodoxime, ceftibuten, cefuroxime) plus doxycycline

Abbreviations: HCPCS, Healthcare Common Procedure Coding System.

[a] 2007 Infectious Diseases Society of America / American Thoracic Society guidelines recommend narrow-spectrum antibiotic regimens for otherwise healthy patients and broad-spectrum antibiotic regimens for patient with comorbidities and patients who live in areas with high rates of infection with macrolide-resistant *Streptococcus pneumoniae*.

[b] Healthcare Common Procedure Coding System (HCPCS) codes were also used for macrolides (Q0144) and β-lactam antibiotics (G9313–G9315).