Antibiotic Overuse for Never-Appropriate Acute Respiratory Tract Infections Among Older Adults Presenting to United States Emergency Departments, 2013-2025: Interrupted Time Series Analysis Across National Stewardship MilestonesRunning head: ED antibiotic overuse and stewardship milestones

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During preparation of this work, the authors used OpenAI ChatGPT to support formatting and language editing. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the manuscript.

Author contributions

M.A.M.: Conceptualization, Methodology, Data curation, Formal analysis, Investigation, Writing - original draft, Writing - review and editing. K.A.: Conceptualization, Writing - review and editing. D.S.: Conceptualization, Methodology, Writing - review and editing. D.E.N.: Conceptualization, Writing - review and editing. C.N.: Conceptualization, Supervision, Writing - review and editing. All authors read and approved the final manuscript.

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Abstract

Background: Antibiotic overuse for acute respiratory tract infections (ARTIs) remains common in emergency departments (EDs), but national trends among older adults are not well described. **Methods:** We conducted a retrospective cohort study of US ED encounters in Epic Cosmos (January 2013-December 2025) among adults aged 65 years or older with never-appropriate ARTI diagnoses. Monthly antibiotic overuse (ED administration and/or discharge prescription) was evaluated with segmented regression around Centers for Disease Control and Prevention

(CDC) Core Elements (November 2016), The Joint Commission (TJC) ambulatory stewardship standard (January 2020), COVID-19 onset (March 2020), and Centers for Medicare & Medicaid Services (CMS) interpretive guidance (July 2022).

Results: Among 838,929 encounters, antibiotic overuse occurred in 38.5%. In the primary model, estimated 12-month changes were -5.0 percentage points (95% CI, -7.1 to -3.0; P < .001) around the CDC milestone and -15.7 percentage points (95% CI, -31.3 to -0.1; P = .049) around TJC. Estimates around COVID-19 and CMS were less stable.

Discussion: Declines were most consistent around the CDC milestone; later estimates were limited by closely spaced interruptions and pandemic disruption.

Conclusions: ED-focused outpatient stewardship remains needed for older adults with never-appropriate ARTIs.

Keywords: antibiotic stewardship; emergency department; acute respiratory tract infections; older adults; interrupted time series; antimicrobial resistance

Introduction

Antibiotic overuse for acute respiratory tract infections (ARTIs) remains an important driver of antimicrobial resistance and avoidable patient harm in the United States.[1] ARTIs are among the most common reasons for ambulatory evaluation, and antibiotics are frequently prescribed when they are not indicated.[2,3]

Older adults are particularly vulnerable to the consequences of unnecessary antibiotics, including adverse drug events that prompt emergency care and *Clostridioides difficile* infection.[4,5] These individual harms occur alongside population-level consequences of resistance, underscoring the importance of stewardship efforts to reduce low-value antibiotic exposure.[1]

The emergency department (ED) is a high-volume site of outpatient care where diagnostic uncertainty, time pressure, and limited longitudinal follow-up can promote antibiotic prescribing "just in case."[6-8] Antibiotic stewardship in EDs has therefore been identified as a priority, although implementation barriers differ from clinic-based and inpatient programs.[6] Observational work has documented persistent inappropriate antibiotic prescribing in EDs for low-value respiratory conditions and highlights patient experience and satisfaction as important influences on prescribing.[7,8] Evidence from standardized patient audit studies also suggests that patient cues/knowledge and clinician incentives can influence antibiotic prescribing decisions, underscoring behavioral and institutional drivers of overuse.[9,10] Accordingly, understanding how national policies and accreditation standards shape ED prescribing is relevant to policy design and to outpatient stewardship efforts.

Several national initiatives over the past decade have sought to standardize and accelerate outpatient stewardship, including the Centers for Disease Control and Prevention (CDC) outpatient stewardship core elements released in 2016,[11] The Joint Commission (TJC) antimicrobial stewardship expectations for ambulatory care (effective 2020),[12] and the Centers for Medicare & Medicaid Services (CMS) updated interpretive guidance for hospital infection prevention and antibiotic stewardship programs (July 2022).[13] These milestones did not uniformly or specifically target hospital EDs, but they provide useful temporal anchors for examining national prescribing patterns.

We therefore described national temporal trends in antibiotic overuse among older adults treated in US EDs for never-antibiotic-appropriate ARTIs and estimated whether level or slope changes coincided with selected stewardship milestones.

Methods

Study design and data source

We performed a retrospective cohort study (January 2013-December 2025) using deidentified electronic health record data from Epic Cosmos, a multi-institutional research platform that aggregates encounter-level data from participating US health systems and hospitals. We evaluated policy-related changes in the percentage of monthly antibiotic overuse using segmented regression interrupted time-series analysis.

Study population

We included US ED encounters among adults aged ≥65 years that met an encounter-level classification of never-antibiotic-appropriate acute respiratory tract infection (ARTI). Encounters were restricted to US locations, excluding US territories. We did not restrict the cohort based on whether the ED encounter subsequently resulted in hospital admission.

Never-antibiotic-appropriate ARTIs were identified using established diagnosis-based classification approaches that map International Classification of Diseases [Ninth Revision, Clinical Modification (ICD-9-CM) and Tenth Revision, Clinical Modification (ICD-10-CM) diagnosis codes] to tiers of antibiotic appropriateness used in prior outpatient research.[2,3] For each encounter, we used all encounter and billing final diagnoses linked to the visit to classify ARTI appropriateness, so classification was encounter-level rather than based on a single first-listed diagnosis code. Encounters with any non-ARTI diagnosis classified as always-antibiotic-appropriate were excluded; the remaining encounters were classified hierarchically as always, sometimes, or never antibiotic appropriate based on ARTI diagnoses present. In this framework, "never appropriate" diagnoses are those for which antibiotics are not recommended under national clinical guidelines (e.g., acute bronchitis [ICD-10-CM J20.x, including J20.8 and J20.9], viral upper respiratory infections [J00, J06.x], influenza [J09-J11], acute bronchiolitis [J21.x],

croup [J05.0], and nonsuppurative otitis media [H65.x]) (Supplementary Table S1). We did not add the ICD-10-CM COVID-19 diagnosis code (U07.1) to this denominator because it was introduced after the start of the study period and was not part of the published never-appropriate tiering framework used to define the cohort; instead, March 2020 was modeled as a separate interruption. Because this is a diagnosis-based measure, we refer to antibiotic use in these encounters as "overuse" rather than adjudicating appropriateness at the individual-patient level.

Outcome variable

The primary outcome was the monthly proportion of ED encounters with antibiotic overuse, defined as any antibiotic prescription and/or in-facility administration captured in the EHR during the classified encounter. Administration and prescription flags were retained separately in the analytic extract but were non-mutually exclusive, and the prespecified primary outcome used their union to capture any documented antibiotic exposure, consistent with prior work focused on potentially avoidable exposure.[2,3] Because documentation and transmission of medication administrations can vary across contributing systems and time, the outcome represents exposure captured in Cosmos and may underestimate in-ED administrations.

Policy interventions

We evaluated three stewardship-related milestones selected a priori as temporal anchors: publication of the CDC Core Elements of Outpatient Antibiotic Stewardship (November 2016),[11] implementation of antimicrobial stewardship standards by TJC for ambulatory care (January 2020),[12] and issuance of updated CMS interpretive guidance for hospital infection prevention and antibiotic stewardship programs (July 2022).[13] Because the coronavirus disease 2019 (COVID-19) pandemic substantially altered care-seeking and respiratory infection epidemiology, we included March 2020 as a separate interruption.

Covariates

Covariates included age, sex, race, ethnicity, insurance category, preexisting comorbidities (diabetes mellitus, chronic kidney disease, chronic liver disease, chronic obstructive pulmonary disease, congestive heart failure, and immunosuppression), and neighborhood-level social vulnerability. Social vulnerability was captured using the CDC/Agency for Toxic Substances and Disease Registry Social Vulnerability Index (SVI) variable provided in Cosmos at the ZIP Code level.[14] These EHR-derived covariates were used as represented in the analytic extract. Across the 13-year study period, the composition of participating systems, source-system mappings, and availability of historical EHR data could change; therefore, abrupt era differences in recorded comorbidity prevalence were interpreted cautiously and were not assumed to represent true population changes. Missingness for categorical covariates was handled by including an explicit missing/unknown category, and missingness was reported descriptively.

For descriptive analyses, the study period was divided into four eras: pre-CDC (<November 2016), CDC-to-pre-TJC (November 2016-December 2019), TJC-to-pre-CMS (January 2020-June 2022), and post-CMS (≥July 2022).

Statistical analysis

First, we summarized patient and encounter characteristics overall and by era using means with standard deviations (SDs) and medians with interquartile ranges (IQRs) for continuous variables and counts with percentages for categorical variables.

Differences across policy eras were assessed using Kruskal-Wallis tests for continuous variables and chi-square tests for categorical variables; when expected cell counts were small, we used Fisher's exact test with Monte Carlo simulation to estimate exact P values.

Second, we used segmented regression interrupted time series methods at the encounter level.[15-17] We fitted linear probability models with month-of-year indicators to address seasonality and included department fixed effects to account for stable, time-invariant differences across ED sites. Linear probability models were chosen to facilitate interpretation of absolute changes in prescribing probability. Standard errors were clustered at the department level.[18] Policy effects were parameterized as a level change at each milestone and a change in slope thereafter. We report absolute probability differences at 12 months after each milestone, calculated as the sum of the level change and 12 times the post-milestone slope change, with 95% confidence intervals derived from the model variance-covariance matrix. Analyses were conducted using R statistical software (version 4.5.1; R Foundation for Statistical Computing, Vienna, Austria) and the fixest package for high-dimensional fixed-effects regression.

Sensitivity analyses

We conducted sensitivity analyses including (i) a monthly binomial interrupted time series model using aggregated counts of antibiotic use among never-appropriate ARTIs with Newey-West standard errors to account for autocorrelation; (ii) inverse probability of treatment weighting (IPTW) analyses restricted to symmetric windows around each milestone (±12, ±24, and ±36 months) to assess robustness to changes in case mix across eras; and (iii) an exploratory stratified analysis by neighborhood-level SVI comparing the highest and lowest quintiles (top 20% versus bottom 20%).

Ethics statement

Institutional review board approval was not required because the study used deidentified data and did not constitute human subjects research. Informed consent was not required for the same

reason. The study was conducted in accordance with institutional policies for research using deidentified or exempt data.

Results

Study cohort

The cohort included 838,929 ED encounters among adults aged ≥65 years with never-antibiotic-appropriate ARTIs. Antibiotics were administered or prescribed in 38.5% of encounters (Table 1). The mean age was 74.9 years (SD, 7.7), and 60.9% of encounters were among female patients. Most encounters were among patients recorded as White race (67.2%), followed by Black or African American race (19.1%). Ethnicity was recorded as not Hispanic or Latino in 83.3% of encounters, Hispanic or Latino in 6.6%, and missing/unknown in 10.1%. Medicare (43.8%) and Medicare Advantage (32.0%) accounted for three-quarters of encounters. Common chronic conditions included diabetes (28.7%), chronic obstructive pulmonary disease (20.6%), chronic kidney disease (15.0%), and congestive heart failure (14.5%). The mean SVI was 0.60 (SD, 0.28), with 1.4% missing.

Table 1. Overall and era-specific characteristics of never-appropriate ARTI ED encounters (US, adults aged ≥65 years).

Characteristic	Level	Overall	Pre-CDC (Before November 2016)	CDC-pre-TJC (2016 November-2019 December)	TJC-pre-CMS (2020 January-2022 June)	Post-CMS July 2022 onward)	P value
Encounters		838,929	121,799	192,513	126,260	398,357	
Age (years)	Mean (SD) Median [IQR]	74.87 (7.69) 73 [68, 80]	75.26 (8.05) 74 [68, 81]	75.02 (7.87) 73 [68, 80]	74.35 (7.54) 73 [68, 79]	74.85 (7.52) 74 [69, 80]	<.001
	Missing	0	0	0	0	0	
Social Vulnerability Index (SVI)	Mean (SD)	0.601 (0.279)	0.598 (0.283)	0.602 (0.280)	0.602 (0.278)	0.601 (0.278)	.005
	Median [IQR]	0.645 [0.372, 0.849]	0.642 [0.367, 0.852]	0.645 [0.373, 0.852]	0.648 [0.376, 0.848]	0.645 [0.372, 0.847]	
	Missing	11,480 (1.4%)	2,004 (1.6%)	2,732 (1.4%)	1,672 (1.3%)	5,072 (1.3%)	
Sex	Female	510,898 (60.9%)	75,131 (61.7%)	118,771 (61.7%)	75,731 (60.0%)	241,265 (60.6%)	<.001
	Male	327,994 (39.1%)	46,665 (38.3%)	73,734 (38.3%)	50,524 (40.0%)	157,071 (39.4%)	

Characteristic	Level	Overall	Pre-CDC (Before November 2016)	CDC-pre-TJC (2016 November-2019 December)	TJC-pre-CMS (2020 January-2022 June)	Post-CMS July 2022 onward)	P value
	Missing/Unknown	33 (0.0%)	3 (0.0%)	8 (0.0%)	4 (0.0%)	18 (0.0%)	
	*Masked	4 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.0%)	3 (0.0%)	
Race	White	563,618 (67.2%)	84,297 (69.2%)	132,302 (68.7%)	87,182 (69.0%)	259,837 (65.2%)	<.001
	Black or African American	160,521 (19.1%)	24,065 (19.8%)	36,331 (18.9%)	22,498 (17.8%)	77,627 (19.5%)	
	Asian	20,015 (2.4%)	3,039 (2.5%)	4,598 (2.4%)	2,768 (2.2%)	9,610 (2.4%)	
	American Indian or Alaska Native	7,611 (0.9%)	847 (0.7%)	1,689 (0.9%)	1,185 (0.9%)	3,890 (1.0%)	
	Native Hawaiian or Other Pacific Islander	3,511 (0.4%)	631 (0.5%)	992 (0.5%)	442 (0.4%)	1,446 (0.4%)	
	Other race	21,570 (2.6%)	2,786 (2.3%)	4,922 (2.6%)	3,020 (2.4%)	10,842 (2.7%)	
	Missing/Unknown	62,083 (7.4%)	6,134 (5.0%)	11,679 (6.1%)	9,165 (7.3%)	35,105 (8.8%)	
Ethnicity	Not Hispanic or Latino	698,581 (83.3%)	104,710 (86.0%)	163,031 (84.7%)	105,592 (83.6%)	325,248 (81.6%)	<.001
	Hispanic or Latino	55,625 (6.6%)	7,198 (5.9%)	12,950 (6.7%)	8,249 (6.5%)	27,228 (6.8%)	
	Missing/Unknown	84,723 (10.1%)	9,891 (8.1%)	16,532 (8.6%)	12,419 (9.8%)	45,881 (11.5%)	
Payer group	Medicare	367,512 (43.8%)	58,741 (48.2%)	99,066 (51.5%)	56,353 (44.6%)	153,352 (38.5%)	<.001
	Medicare Advantage	268,659 (32.0%)	21,386 (17.6%)	46,166 (24.0%)	40,116 (31.8%)	160,991 (40.4%)	
	Commercial	65,701 (7.8%)	6,933 (5.7%)	13,219 (6.9%)	10,807 (8.6%)	34,742 (8.7%)	
	Medicaid	25,433 (3.0%)	2,731 (2.2%)	5,314 (2.8%)	4,075 (3.2%)	13,313 (3.3%)	
	Self-pay / No insurance	5,357 (0.6%)	608 (0.5%)	1,113 (0.6%)	807 (0.6%)	2,829 (0.7%)	
	Other / Unspecified	106,267 (12.7%)	31,400 (25.8%)	27,635 (14.4%)	14,102 (11.2%)	33,130 (8.3%)	
Comorbidities	Diabetes mellitus	240,406 (28.7%)	33,670 (27.6%)	57,496 (29.9%)	36,858 (29.2%)	112,382 (28.2%)	<.001
	Chronic kidney disease	126,116 (15.0%)	15,593 (12.8%)	27,757 (14.4%)	18,587 (14.7%)	64,179 (16.1%)	<.001
	Liver disease	37,261 (4.4%)	2,748 (2.3%)	7,743 (4.0%)	6,123 (4.8%)	20,647 (5.2%)	<.001
	COPD	172,814 (20.6%)	22,944 (18.8%)	42,856 (22.3%)	26,984 (21.4%)	80,030 (20.1%)	<.001
	Congestive heart failure	121,437 (14.5%)	16,257 (13.3%)	27,966 (14.5%)	17,747 (14.1%)	59,467 (14.9%)	<.001
	Immunosuppressed	90,806 (10.8%)	36,308 (29.8%)	11,889 (6.2%)	8,584 (6.8%)	34,025 (8.5%)	<.001

Notes: Values are n (%) unless otherwise specified. Overall antibiotic overuse occurred in 323,046/838,929 encounters (38.5%). P values compare distributions across eras using Kruskal-Wallis tests for continuous variables and chi-square tests for categorical variables. The number of contributing ED departments varied over time; month-to-month counts are shown in Supplementary Figure S2. SVI ranges from 0 (least vulnerable) to 1 (most vulnerable). The abrupt era difference in recorded immunosuppression may reflect changing site composition, source-system coding/mapping, or historical data capture and should not be interpreted as a clinical prevalence trend.

Abbreviations: ARTI, acute respiratory tract infection; CDC, Centers for Disease Control and Prevention; CMS, Centers for Medicare & Medicaid Services; COPD, chronic obstructive pulmonary disease; ED, emergency department; IQR, interquartile range; SD, standard deviation; SVI, Social Vulnerability Index; TJC, The Joint Commission.

Characteristics by era

Across study eras, demographic characteristics, payer distribution, neighborhood social vulnerability, and comorbidity prevalence differed (Table 1). Given the large sample size, most comparisons were statistically significant; however, absolute differences across eras were

generally modest for core demographic variables. The largest absolute comorbidity difference involved recorded immunosuppression (29.8% pre-CDC vs 6.2%-8.5% in later eras). The magnitude and abruptness of this change suggest that at least part of the difference reflects changes in contributing-site mix, coding/mapping, or historical EHR capture rather than a true decrease in immunosuppression prevalence; we therefore interpreted early-versus-later comparisons cautiously.

Temporal trends and geographic variation

Monthly antibiotic overuse increased in the pre-CDC era, showed a visible level shift around late 2015 that was contemporaneous with the national ICD-10-CM transition, declined modestly through 2019, dropped sharply early in the COVID-19 period, and then gradually increased thereafter (Figure 1). The monthly denominator of eligible never-appropriate ARTI encounters was strongly seasonal and declined early in the COVID-19 period, while the number of contributing ED departments increased over the study period (Supplementary Figures S1 and S2). Average overuse varied across states (Figure 2), consistent with meaningful geographic heterogeneity in prescribing practices.

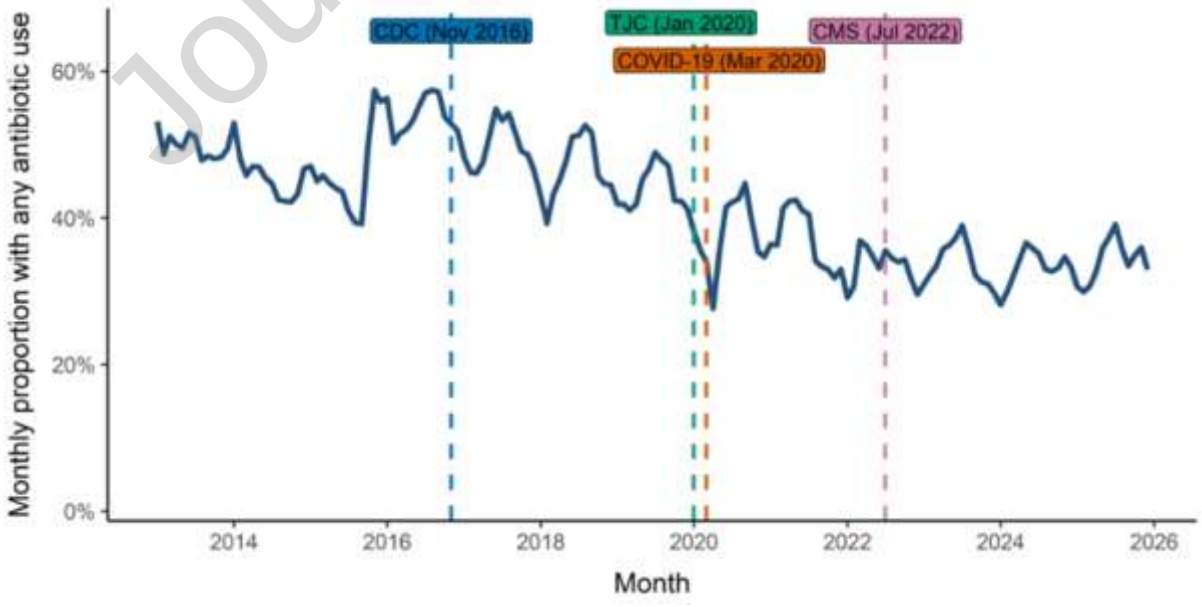

Figure 1. Monthly antibiotic overuse among emergency department (ED) encounters for never-antibiotic-appropriate acute respiratory tract infections (ARTIs) in adults aged ≥65 years in the Epic Cosmos network (United States), January 2013-December 2025. Notes: Plotted values (connected line) represent the unadjusted monthly proportion of eligible ED encounters with any antibiotic administered in the ED and/or prescribed at ED discharge; the monthly denominator is shown in Supplementary Figure S1. A visible level shift occurs in late 2015, contemporaneous with the ICD-10-CM transition. Vertical dashed lines indicate selected temporal milestones evaluated in segmented regression analyses: publication of the Centers for Disease Control and Prevention (CDC) Core Elements of Outpatient Antibiotic Stewardship (November 2016), implementation of The Joint Commission (TJC) ambulatory antimicrobial stewardship standard (January 2020), onset of the coronavirus disease 2019 (COVID-19) period (March 2020), and the Centers for Medicare & Medicaid Services (CMS) revised interpretive guidance for hospital infection prevention and antibiotic stewardship programs (July 2022). Abbreviations: ARTI, acute respiratory tract infection; CDC, Centers for Disease Control and Prevention; CMS, Centers for Medicare & Medicaid Services; COVID-19, coronavirus disease 2019; ED, emergency department; TJC, The Joint Commission.

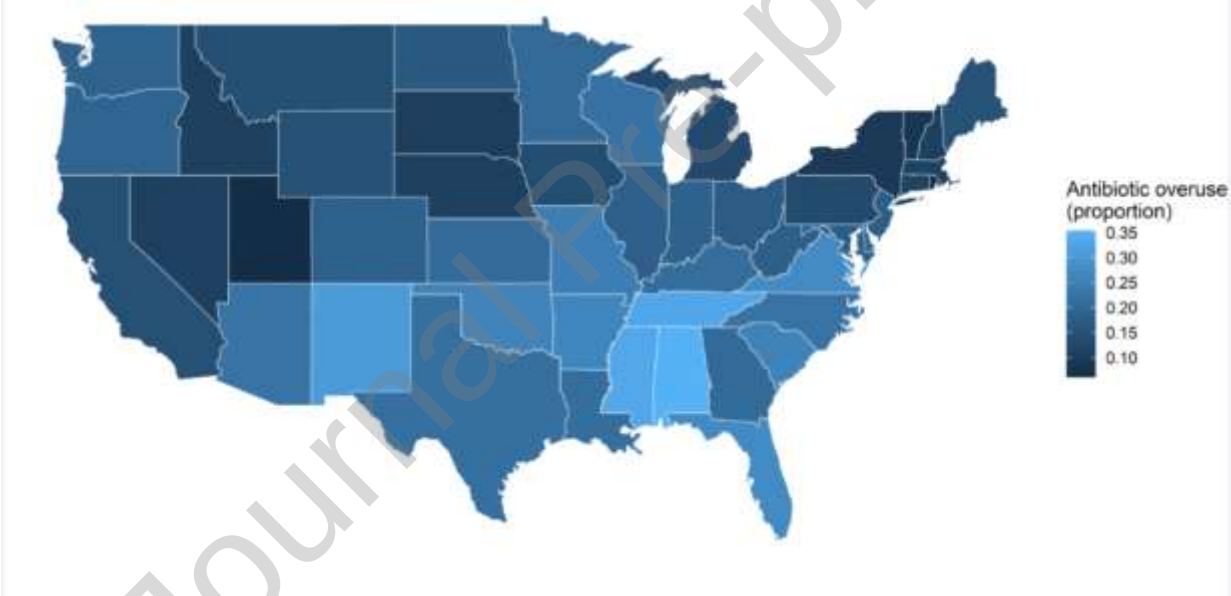

Figure 2. Geographic variation in antibiotic overuse among emergency department (ED) encounters for never-antibiotic-appropriate acute respiratory tract infections (ARTIs) in adults aged ≥65 years in the Epic Cosmos network (United States), January 2013-December 2025. Notes: For each state, antibiotic overuse was calculated as the proportion of eligible ED encounters in which any antibiotic was administered in the ED and/or prescribed at ED discharge; shading represents these state-level proportions averaged across the study period (see color bar). These state-level proportions are descriptive and unadjusted for patient or facility characteristics. State assignment was based on ED facility location when available and otherwise on patient state of residence. Map displays the contiguous United States; Alaska and Hawaii are not shown. Abbreviations: ARTI, acute respiratory tract infection; ED, emergency department.

Interrupted time series estimates

In segmented regression models (Table 2), the CDC milestone was associated with a 5.0-percentage point reduction in antibiotic overuse at 12 months (95% CI, -7.1 to -3.0; P < .001). The primary model also estimated a 15.7-percentage point reduction around the TJC milestone (95% CI, -31.3 to -0.1; P = .049). Changes around the COVID-19 period (+13.5 percentage points; 95% CI, -4.7 to 31.7; P = .15) and the July 2022 CMS update (+1.8 percentage points; 95% CI, 0.7 to 2.9; P = .001) were interpreted more cautiously because later interruptions were closely spaced, the TJC-to-COVID interval was only 2 months, and these later estimates were less stable in sensitivity analyses.

Table 2. Estimated 12-month changes in antibiotic overuse around selected stewardship milestones (linear probability model).

Policy	12-month effect (percentage points)	95% CI (percentage points)	P value
CDC Core Elements (November 2016)	-5.03	-7.09 to -2.97	<.001
TJC antibiotic stewardship standard (January 2020)	-15.67	-31.25 to -0.09	.049
COVID-19 period (March 2020)	13.49	-4.71 to 31.69	.146
CMS interpretive guidance update (July 2022)	1.82	0.70 to 2.94	.001

Notes: Effects are absolute changes in the probability of receiving an antibiotic for never-appropriate ARTI diagnoses (percentage points), computed as step + 12*slope. Positive values indicate higher antibiotic overuse. Estimates around later milestones should be interpreted cautiously because of closely spaced interruptions.

Abbreviations: CDC, Centers for Disease Control and Prevention; CI, confidence interval; CMS, Centers for Medicare & Medicaid Services; COVID-19, coronavirus disease 2019; TJC, The Joint Commission.

Sensitivity analyses

In a monthly aggregated binomial interrupted time series model, estimates were directionally consistent but less precise; only the CDC milestone remained statistically significant (Supplementary Table S2). In inverse probability of treatment weighting analyses restricted to symmetric windows around each milestone (±12, ±24, and ±36 months), effect directions were generally consistent with the primary analysis, except for the narrowest CDC window, which was direction-inconsistent and imprecise; magnitude and statistical significance varied by

window length (Supplementary Table S3). In exploratory stratified analyses comparing encounters from the highest and lowest SVI quintiles, the CDC milestone was associated with reductions in both strata (high SVI: -6.1 percentage points; low SVI: -3.9 percentage points), whereas later milestone estimates were imprecise and did not show a consistent differential pattern (Supplementary Table S4).

Discussion

Among adults aged ≥65 years presenting to US EDs with ARTI diagnoses for which antibiotics are never recommended, more than one-third of encounters involved antibiotic exposure. Overuse declined over the 2013-2025 period but remained common and geographically heterogeneous. In the primary segmented models, the clearest reduction occurred around the 2016 CDC outpatient stewardship milestone, whereas estimates around the 2020 TJC, March 2020 COVID-19, and July 2022 CMS markers were less stable and should be interpreted cautiously.

The magnitude of overuse in this older adult ED cohort is consistent with national estimates showing that unnecessary antibiotic prescribing remains frequent in outpatient care, particularly for respiratory conditions.[1,2] In older adults, avoidable antibiotic exposure is especially concerning because antibiotic-associated adverse drug events and *Clostridioides difficile* infection occur more often and carry greater morbidity.[4,5] The persistence of prescribing for never-appropriate respiratory diagnoses likely reflects the diagnostic and communication challenges of ED care, where clinicians must make rapid decisions amid uncertainty and may prescribe “just in case” when follow-up is limited.[6-8,19]

The CDC-associated change is clinically plausible. The Core Elements provided a widely disseminated framework for outpatient stewardship, and prior implementation studies in

ED/urgent care networks as well as Veterans Health Administration ED and primary care settings have shown improved ARTI prescribing after multifaceted interventions aligned with these principles.[20,21] At the same time, our design cannot isolate the CDC milestone from concurrent secular trends in outpatient stewardship, local audit-feedback efforts, clinical decision support, or broader changes in prescribing culture, so these estimates should not be interpreted as causal effects of any single policy.

We are particularly cautious about interpreting the TJC and CMS markers. The TJC standard evaluated here was an ambulatory care standard, not an ED-specific hospital standard, and its January 2020 effective date preceded the COVID-19 disruption by only 2 months.[12] Any effect on ED prescribing would therefore most plausibly reflect indirect spillover from broader health-system stewardship efforts rather than a direct ED-targeted mandate. Likewise, the July 2022 CMS update emphasized hospital stewardship expectations rather than ED-specific outpatient prescribing.[13] These later markers are therefore best viewed as contextual anchors rather than direct ED-targeted interventions, and the absence of a robust TJC-specific pattern may reflect both the short pre-COVID interval and the mismatch between the targeted settings and ED care.

We also observed substantial geographic variation in average ED antibiotic overuse across states, consistent with prior outpatient studies showing heterogeneous prescribing practices by region.[22] Visual inspection suggested higher average overuse in several Southern, Southeastern, and Southwestern states than in many Northern and Northeastern states. Potential explanations include regional prescribing norms and patient expectations, access to longitudinal primary care and follow-up, rurality and clinician availability, socioeconomic context and health literacy, and differences in local stewardship infrastructure.[7-10,22] These explanations are hypothesis-generating: the state estimates were descriptive and unadjusted, participating facilities and

patient mix varied by state and over time, and the extract did not include harmonized measures of rurality, income, or health literacy. From a benchmarking perspective, ED outpatient stewardship still lacks some of the infrastructure available for inpatient antimicrobial use monitoring: NHSN accepts antimicrobial use data from outpatient ED locations, but outpatient locations are excluded from the FacWideIN SAAR framework, limiting ED-specific external comparison.[23]

In exploratory SVI-stratified analyses, CDC-associated declines were present in both lower- and higher-vulnerability strata, but later milestone estimates were imprecise. These analyses were not designed to establish differential policy effects and should be viewed as hypothesis generating.

Strengths of this analysis include the large, multi-institutional sample of 838,929 older-adult ED encounters, the focus on diagnoses for which antibiotics are never recommended, and the use of an interrupted time series framework with department fixed effects and multiple sensitivity analyses. The scale and breadth of Cosmos enabled long-horizon descriptions of US prescribing patterns, state-level assessment of geographic heterogeneity, and analyses that would be difficult within a single health system. Although sample size cannot correct systematic measurement error, it reduces random imprecision for estimates of overall burden and broad temporal patterns.

Limitations should be considered. First, this is a diagnosis-based measure of overuse rather than individual adjudication of prescribing appropriateness. Encounters were classified using all encounter and billing final diagnoses linked to the visit, but diagnostic coding may shift over time. In particular, the national transition from ICD-9-CM to ICD-10-CM in late 2015 and selective coding of bacterial diagnoses when antibiotics are prescribed could move visits out of the never-appropriate denominator and bias temporal comparisons.[3,21] This limitation underscores the need for feasible, consistently implemented encounter-level stewardship

measures that incorporate clinical context rather than billing diagnoses alone. Second, we did not exclude ED encounters that subsequently resulted in hospital admission, so some clinically complex visits may remain in the cohort. Third, the primary outcome combined in-ED administration and discharge prescribing. The component flags were non-mutually exclusive and were not modeled separately; medication administration capture may also be incomplete or vary across Cosmos contributors. Consequently, in-ED administrations and total documented overuse may be undercounted, particularly when no discharge prescription is captured, and we could not examine antibiotic class or duration. Fourth, covariate definitions and completeness may not be stable over time. The abrupt difference between the pre-CDC era and later eras in recorded immunosuppression likely reflects, at least partly, changes in site composition, coding/mapping, or historical EHR capture rather than a true clinical shift. Explicit missing categories and covariate adjustment do not eliminate this measurement error, and department fixed effects account only for stable, time-invariant site differences. Fifth, we did not have a harmonized rural/urban measure in the deidentified extract and lacked state-level measures of income and health literacy, limiting geographic contextualization beyond ZIP-code-level SVI. Finally, the selected milestones overlapped with other stewardship efforts and secular changes. Later milestones, especially TJC versus COVID-19, occurred close together, site participation in Cosmos changed over time, and residual case-mix differences may persist despite adjustment, limiting causal attribution to any single national initiative.

In conclusion, among older adults treated in US EDs for never-antibiotic-appropriate ARTIs, antibiotic overuse remained common but declined over time. Changes were most consistent around the 2016 CDC outpatient stewardship milestone, whereas estimates around later national

milestones were less robust. ED-specific outpatient stewardship strategies and benchmarking infrastructure remain needed.

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Conflicts of interest

The authors report no conflicts of interest relevant to this article.

Data availability

The deidentified Epic Cosmos data used for this analysis are not publicly available and are accessible only through Epic Cosmos under applicable data-use terms.

Declaration of generative AI and AI-assisted technologies in manuscript preparation

During preparation of this work, the authors used OpenAI ChatGPT to support formatting and language editing. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the manuscript.

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Highlights

- Antibiotic overuse occurred in 38.5% of older-adult ED ARTI visits
- Declines were most consistent around the 2016 CDC stewardship milestone
- Later TJC, COVID-19, and CMS estimates were less stable
- State-level patterns showed geographic heterogeneity in ED antibiotic overuse