

Mortality trends and disparities in *Clostridioides difficile* infection with concurrent sepsis and acute kidney injury in the United States, 2000–2024

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Abstract

Background

Although overall *Clostridioides difficile* infection (CDI) burden declined before the COVID-19 pandemic, trends in deaths involving concurrent sepsis and acute kidney injury (AKI) are poorly characterized.

Objective

To characterize U.S. mortality in which CDI was the underlying cause and both sepsis and AKI were documented and assess variation across demographic and geographic groups.

Design

Serial cross-sectional study of 2000–2024 death certificate data from CDC WONDER. Joinpoint regression estimated annual percent changes (APCs), and parallelism tests compared subgroup trajectories.

Participants

U.S. resident decedents with CDI (ICD-10 A04.7) as the underlying cause and sepsis (A40–A41) and AKI (N17) among multiple causes.

Main Measures

Annual age-adjusted mortality rates (AAMRs) per 100,000 population nationally and by race, Hispanic ethnicity, and Census region, and age-specific rates among adults aged 55 years or older.

Key Results

During 2000–2024, 9,736 deaths met the case definition. Annual deaths increased from 39 to 543, and the national AAMR increased from 0.0076 to 0.1166 per 100,000. After declining during 2015–2019 (APC, – 15.38%; 95% CI, – 21.90% to – 9.45%), mortality increased during 2019–2024 (APC, + 10.14%; 95% CI, + 5.69% to + 18.31%). Recent increases occurred among adults aged 65–74 years (APC, + 7.49%; 95% CI, + 0.03% to + 28.12%) and were greatest among those aged 85 years or older (APC, + 21.64%; 95% CI, + 14.44% to + 30.11%). AAMRs also increased in recent segments among Black, White, Hispanic, and non-Hispanic populations. All four Census regions experienced recent increases (APCs, + 7.10% to + 19.83%), with significant regional heterogeneity.

Conclusions

Following several years of decline, U.S. mortality records identifying CDI as the underlying cause with concurrent sepsis and AKI increased after 2019, particularly among the oldest adults. This surveillance signal requires patient-level validation to distinguish changes in disease severity and vulnerability from changes in healthcare delivery or death certificate documentation.

Introduction

Clostridioides difficile infection (CDI) remains a major cause of healthcare- and community-associated illness in the United States. Population-based surveillance estimated approximately 453,000 infections and 29,300 deaths in 2011, with a disproportionate burden among adults aged 65 years or older [1]. After adjustment for changes in diagnostic testing, the estimated national burden declined by 24% from 2011 through 2017, driven largely by reductions in healthcare-associated CDI [2]. Hospitalization analyses similarly documented declining prevalence and mortality through 2019 or 2020, although some markers of severe disease increased [3, 4]. These trends show that progress in prevention has been substantial yet incomplete, and severe outcomes remain concentrated among older and medically-vulnerable populations.

Sepsis and AKI identify a clinically vulnerable subset of patients with CDI. Guidelines by the American College of Gastroenterology (ACG) and the Infectious Diseases Society of America (IDSA) incorporate creatinine evaluation into severe CDI classification and identify hypotension or shock as features of fulminant disease [5, 6]. In a multicenter cohort, the absolute creatinine threshold used in current severity classification was associated with inpatient mortality [7]. In another national propensity-matched study, hospitalized patients with concurrent CDI and AKI had an 18.2% mortality rate, and AKI remained associated with mortality after matching [8]. Among 497,489 Medicare beneficiaries with CDI, 41.0% developed sepsis during follow-up; 57.7% of those with sepsis died compared with 32.4% of those without sepsis [9]. These studies do not establish that CDI caused either organ dysfunction or sepsis, but they show that their co-occurrence identifies a high-risk population relevant to hospitalists, intensivists, general internists, gastroenterologists, and infection prevention programs.

Death certificates complement surveillance and hospitalization data by identifying conditions recorded in the causal chain leading to death. From 1999 through 2004, mortality records mentioning CDI increased rapidly, and septicemia and renal failure were recorded in 37% and 23% of those deaths, respectively [10]. More recent death certificate studies described an overall peak followed by declining CDI-related mortality through 2020 or 2023, but neither isolated deaths in which CDI was the underlying cause and both sepsis and AKI were also recorded [11, 12]. We therefore examined this narrowly defined mortality phenotype from 2000 through 2024 and tested whether its trajectory differed by age, race, Hispanic ethnicity, Census region, and county urbanization. We hypothesized that the national trend changed near 2020 and that recent patterns varied across demographic and geographic groups.

Methods

Study Design and Data Source

We conducted a serial cross-sectional study using publicly available, deidentified, aggregate death certificate data from CDC WONDER [13]. Observations for 2000 through 2020 were obtained from the historical Multiple Cause of Death database, and observations for 2018 through 2024 were obtained

from the Multiple Cause of Death by Single Race database. Estimates from overlapping years were checked for consistency before the series was combined. The primary analysis began in 2000 as only 19 qualifying deaths were recorded in 1999, producing an unstable estimate. Provisional 2025 data were excluded. The analysis did not involve access to identifiable information or contact with human participants.

Outcome Definition

The outcome was a death among U.S. residents with CDI recorded as the underlying cause (ICD-10 code A04.7), sepsis recorded among multiple causes (A40–A41) and AKI recorded among multiple causes (N17). All three criteria were required. The underlying cause is the condition selected as initiating the sequence of events leading directly to the death, while multiple causes include other conditions reported on the death certificate. We use concurrent to describe co-documentation and do not infer a causal or temporal sequence among CDI, sepsis, and AKI.

Rates and Subgroup Analyses

Annual national rates and rates stratified by race, Hispanic ethnicity, and Census region were age standardized to the 2000 U.S. population and are reported per 100,000 population. Age analyses used crude age-specific rates for adults aged 55–64, 65–74, 75–84, and 85 years or older. Analytic periods reflected the complete, stable series available for each variable. Ethnicity summaries were calculated among deaths with stated Hispanic-origin classification. Race-specific models included Black or African American and White decedents because other groups had insufficient stable annual observations for trend modeling. CDC WONDER suppresses cells containing fewer than 10 deaths.

County urbanization was examined as a secondary analysis using the 2013 National Center for Health Statistics urban-rural classification scheme [14]. Large central and large fringe metropolitan counties were grouped as metropolitan, medium and small metropolitan counties as suburban, and micropolitan and noncore counties as rural. Urbanization rates were crude because age-adjusted rates were unavailable in CDC WONDER. This series ended in 2021 because population denominators were unavailable for 2022 through 2024.

Statistical Analysis

We modeled annual rates on the logarithmic scale using Joinpoint regression, with standard errors used for weighting. Candidate models allowed up to four joinpoints for the national analysis and up to three for subgroup analyses, subject to the number of observations. Final national, age, race, and Census region models used permutation test model selection. Ethnicity and urbanization models used weighted Bayesian information criterion selection. For each fitted segment, we report the annual percent change (APC), 95% confidence interval (CI), and two-sided P value. We also calculated full-period average annual

percent changes (AAPCs) and prespecified pre-2020 AAPCs over 2007–2019 for age and ethnicity, 2006–2019 for race and urbanization, and 2003–2019 for Census regions, reflecting dates with data suppression.

Pairwise parallelism test evaluated whether temporal slopes differed between subgroups. Coincidence tests were interpreted primarily when parallelism was not rejected. To address multiplicity, we used Bonferroni thresholds for approximately 0.0083 for the six Census region comparisons and 0.0167 for the three urbanization comparisons. Other tests used a two-sided alpha of 0.05. Analyses were performed with the National Cancer Institute Joinpoint Regression Program, version 6.1.0 [15, 16].

Results

National Trend

From 2000 through 2024, 9,736 deaths had CDI recorded as the underlying cause with both sepsis and AKI recorded among multiple causes. Annual deaths increased from 39 in 2000 to 543 in 2024. The national AAMR increased from 0.0076 to 0.1166 deaths per 100,000 population (Fig. 1). Joinpoints were identified as 2005, 2010, 2015, and 2019. Mortality increased steeply during 2000 through 2005 (APC, + 59.62%; 95% CI, + 45.27% to + 88.34%; $p = 0.001$), increased more slowly during 2005 through 2010 (APC, + 9.89%; 95% CI, + 5.56% to + 27.97%; $p = 0.001$), and was statistically stable during 2010 through 2015 (APC, – 2.34%; 95% CI, – 7.92% to + 3.12%; $p = 0.255$). The rate declined during 2015 through 2019 (APC, – 15.38%; 95% CI, – 21.90% to – 9.45%; $p = 0.022$) before increasing during 2019 through 2024 (APC, + 10.14%; 95% CI, + 5.69% to + 18.31%; $p = 0.004$). All segment-specific APCs can be visualized in Fig. 3 as discussed below.

Age

Among adults aged 55 years or older in 2007 through 2024, the highest absolute rates occurred in the oldest age groups (Table 1 **and** Fig. 2). Before 2020, rates declined among adults aged 55–64 years (AAPC, – 2.51%; 95% CI, – 4.28% to – 0.47%) and adults aged 85 years or older (AAPC, – 6.30%; 95% CI, – 7.71% to – 5.15%). In the most recent segments, rates increased among adults aged 65–74 years during 2019 through 2024 (APC, + 7.49%; 95% CI, + 0.03% to + 28.12%; $p = 0.049$) and adults aged 85 years or older during 2020 through 2024 (APC, + 21.64%; 95% CI, + 14.44% to + 30.11%; $p < 0.001$). Recent changes were not statistically significant among adults aged 55–64 years or 75–84 years. Trajectories for adults aged 55–64 years and those aged 85 years or older were nonparallel ($p < 0.001$).

Table 1

Descriptive characteristics of deaths involving *Clostridioides difficile* with concurrent sepsis and acute kidney injury, United States. Percentages are calculated within each stratification-specific analytic cohort and therefore use different denominators because analysis periods and category eligibility differ across characteristics.

Characteristic	Deaths during Study Period, n (%)	First-year Rate†	Final-year Rate†	Absolute Rate Change
Age				
55–64 years	690 (8.32%)	0.0724	0.1056	+ 0.0332
65–74 years	1,711 (20.63%)	0.3046	0.3160	+ 0.0114
75–84 years	3,019 (36.41%)	1.0774	1.0777	+ 0.0004
≥ 85 years	2,872 (34.64%)	3.0757	2.5019	–0.5738
Race				
Black or African American	683 (7.90%) ¹	0.1040	0.1106	+ 0.0066
White	7,968 (92.10%) ²	0.1106	0.1182	+ 0.0076
Ethnicity				
Hispanic	605 (7.07%)	0.1302	0.0931	–0.0371
Non-Hispanic	7,953 (92.93%)	0.1244	0.1182	–0.0062
Census Region				
Midwest	2,031 (21.24%)	0.0416	0.1103	+ 0.0687
Northeast	1,699 (17.77%)	0.0455	0.1054	+ 0.0599
South	3,504 (36.64%)	0.0490	0.1152	+ 0.0662
West	2,329 (24.35%)	0.0434	0.1526	+ 0.1092
†Note: Rates are expressed per 100,000 population. Race, ethnicity, and Census region rates are age-adjusted to the 2000 U.S. standard population; age-group rates are age-specific crude mortality rates. Analysis periods were 2007–2024 for age, 2006–2024 for race, 2007–2024 for ethnicity, and 2003–2024 for Census region. ¹Percentages for race are calculated among deaths classified as Black or African American or White, the two racial groups included in the trend analysis. ²Percentages for ethnicity are calculated among deaths with stated Hispanic-origin classification included in the analysis.				

Race and Hispanic Ethnicity

Race-specific AAMRs declined during the prespecified pre-2020 period for both Black and White populations, followed by increases in the most recent segments (Table 2). Among Black decedents, the AAMR increased during 2019 through 2024 (APC, + 14.32%; 95% CI, + 4.84% to + 41.71%; $p = 0.004$). Among White decedents, AAMR increased during 2020 through 2024 (APC, + 14.53%; 95% CI, + 4.20% to + 36.85%; $p = 0.002$). Parallelism was not rejected ($p = 0.943$) and fitted curves were not statistically distinguishable by coincidence ($p = 0.253$).

Table 2

Joinpoint regression analysis of mortality trends by demographic and geographic characteristics. Age-specific analyses use crude age-specific mortality rates. Race, ethnicity, and Census region analyses use age-adjusted mortality rates. Urbanization analyses use crude mortality rates as age-adjusted rates are unavailable for county-level urbanization in CDC WONDER. Pre-2020 AAPCs correspond to the custom pre-pandemic ranges used for each analysis. Note: APC = annual percent change; AAPC = average annual percent change; CI = confidence interval.

Characteristic	Analysis Period	Joinpoint Years	Full-period AAPC, % (95% CI)	Pre-2020 AAPC, % (95% CI)	Most recent segment Years	Recent APC, % (95% CI)	P value
Age							
55–64 years	2007–2024	2016, 2019, 2022	+ 2.46 (1.07, 3.90)	–2.51 (–4.28, – 0.47)	2022–2024	–6.27 (–18.64, 8.32)	0.285
65–74 years	2007–2024	2015, 2019	+ 0.18 (–1.33, 2.46)	–2.72 (–4.71, 0.97)	2019–2024	+ 7.49 (0.03, 28.12)	0.049
75–84 years	2007–2024	2013, 2019	–0.37 (–2.55, 2.66)	–4.03 (–6.86, 0.64)	2019–2024	+ 8.99 (–1.54, 40.77)	0.079
≥ 85 years	2007–2024	2010, 2015, 2020	–1.12 (–2.01, – 0.16)	–6.30 (–7.71, – 5.15)	2020–2024	+ 21.64 (14.44, 30.11)	< 0.001
Race							
Black or African American	2006–2024	2015, 2019	+ 0.16 (–1.43, 2.49)	–4.80 (–6.97, – 0.98)	2019–2024	+ 14.32 (4.84, 41.71)	0.004
White	2006–2024	2013, 2020	+ 0.32 (–1.06, 1.75)	–2.79 (–4.69, – 0.94)	2020–2024	+ 14.53 (4.20, 36.85)	0.002
Ethnicity							
Hispanic	2007–2024	2015, 2019	–1.14 (–2.99, 1.59)	–6.04 (–8.54, – 1.74)	2019–2024	+ 11.70 (1.49, 45.14)	0.028

Characteristic	Analysis Period	Joinpoint Years	Full-period AAPC, % (95% CI)	Pre-2020 AAPC, % (95% CI)	Most recent segment Years	Recent APC, % (95% CI)	P value
Age							
Non-Hispanic	2007–2024	2013, 2020	–0.19 (–1.48, 1.15)	–3.86 (–5.78, –2.13)	2020–2024	+ 14.95 (5.51, 33.52)	< 0.001
Census Region							
Midwest	2003–2024	2007, 2015, 2018	+ 4.42 (2.82, 8.08)	+ 2.61 (0.00, 7.15)	2018–2024	+ 10.45 (3.47, 38.14)	0.015
Northeast	2003–2024	2005, 2012, 2020	+ 4.62 (2.60, 7.50)	+ 2.22 (–0.40, 5.79)	2020–2024	+ 19.83 (6.44, 51.70)	0.001
South	2003–2024	2007, 2015, 2019	+ 4.01 (2.85, 5.90)	+ 3.07 (1.63, 5.78)	2019–2024	+ 7.10 (2.01, 17.28)	0.005
West	2003–2024	2012, 2020	+ 4.54 (2.88, 6.78)	+ 2.81 (0.51, 5.73)	2020–2024	+ 16.55 (3.35, 47.95)	0.012
Urbanization							
Metropolitan	2006–2021	2011	–2.45 (–5.12, 0.73)	–1.61 (–3.77, 1.96)	2011–2021	–7.77 (–13.27, –5.33)	< 0.001
Suburban	2006–2021	2015, 2019	–0.06 (–2.54, 1.70)	–1.97 (–4.21, 0.67)	2019–2021	+ 13.30 (–12.30, 34.30)	0.270
Rural	2006–2021	2014, 2019	+ 2.25 (0.96, 3.41)	+ 1.17 (0.01, 2.80)	2019–2021	+ 9.55 (–3.57, 20.18)	0.166

Ethnicity-specific AAMRs also declined before 2020 and increased in the most recent segments. The recent APC was + 11.70% (95% CI, + 1.49% to + 45.14%; p = 0.028) among Hispanic decedents during

2019 through 2024 and + 14.95% (95% CI, + 5.51% to + 33.52%; $p < 0.001$) among non-Hispanic decedents during 2020 through 2024. Parallelism was not rejected ($p = 0.912$) and the coincidence test did not identify a difference between fitted curves ($p = 0.351$).

Census Region

Full-period AAPCs were positive in every Census region: +4.42% in the Midwest, + 4.62% in the Northeast, + 4.01% in the South, and + 4.54% in the West (all $p \leq 0.002$). Recent increases were observed in the Midwest during 2018 through 2024 (APC, + 10.45%; $p = 0.015$), Northeast during 2020 through 2024 (APC, + 19.83%; $p = 0.001$), South during 2019 through 2024 (APC, + 7.10%; $p = 0.005$) and West during 2020 through 2024 (APC, + 16.55%; $p = 0.012$). After Bonferroni correction, parallelism was rejected for the Midwest versus West ($p = 0.005$), Northeast versus South ($p = 0.001$), and Northeast versus West ($p = 0.008$), indicating regional heterogeneity in temporal shape.

County Urbanization

In the secondary crude-rate analysis for 2006 through 2021, metropolitan mortality declined during 2011 through 2021 (APC, - 7.77%; 95% CI, - 13.72% to - 5.33%; $p < 0.001$). Recent increases in suburban counties (2019 through 2021 APC, + 13.30%; $p = 0.270$) and rural counties (2019 through 2021 APC, + 9.55%; $p = 0.166$) were imprecise and not statistically significant. Metropolitan and rural trajectories were nonparallel ($p = 0.010$), meeting the Bonferroni threshold.

Discussion

In this national study, mortality records identifying CDI as the underlying cause with concurrent sepsis and AKI followed a multiphasic trajectory and increased by 10.14% per year after 2019. The reversal appeared in both modeled racial groups, both ethnicity groups, and all four Census regions. Adults aged 85 years or older had the clearest recent acceleration, with a 21.64% annual increase from 2020 through 2024. These findings extend prior CDI surveillance by identifying a severe recorded phenotype whose recent trajectory differs from the broad decline in CDI burden reported during much of the preceding decade.

The historical pattern is broadly consistent with previous national studies, but the endpoint is deliberately narrower. One study reported a 35% annual increase in deaths mentioning CDI from 1999 through 2004, while subsequent death certificate studies found declining overall CDI-related mortality after the national peak [10–12]. In contrast, the present endpoint began increasing in 2019. This divergence may indicate that trends in deaths accompanied by systemic illness and renal dysfunction can move differently from total CDI incidence or hospitalizations. It cannot demonstrate a rising case fatality rate as the number of diagnosed infections was unavailable.

The clinical literature supports the importance of the phenotype but not a single causal pathway. Creatinine elevation contributes to guideline-based severity classification, and AKI is associated with

mortality among hospitalized patients with CDI [5–8]. Sepsis likewise marks a large increase in mortality, intensive care use, length of hospitalization, and cost among older Medicare beneficiaries with CDI [9]. Nonetheless, ICD-10 N17 on a death certificate may represent hypovolemia from diarrheal losses, sepsis-associated organ dysfunction, medication effects, or preexisting renal susceptibility. Meanwhile, a sepsis code may reflect CDI, bacterial translocation, or a separate infection. However, selecting CDI as the underlying cause makes it more likely that CDI is considered the initiating disease, but it does not establish the chronology or mechanism connecting these diagnoses.

The recent increase overlaps the COVID-19 era, but the joinpoint was estimated at 2019 should not be interpreted as proof of a pandemic effect. In a national sample of U.S. hospitalizations, CDI prevalence decreased from the pre-pandemic to pandemic period while inpatient mortality increased from 5.5% to 7.4% [17]. A later nationwide study also found higher unadjusted mortality in CDI-associated hospitalizations during the pandemic [18]. Changes in the patients reaching hospitals, delayed care, antimicrobial exposure, diagnostics, infection prevention practices, staffing, and SARS-CoV-2 coinfection are plausible explanations, but the present data cannot quantify them. The finding is therefore best interpreted as a surveillance signal that warrants patient-level evaluation.

The acceleration among adults aged 85 years or older is clinically important because advanced age may combine greater healthcare and antimicrobial exposure with reduced reserve during diarrheal illness and systemic inflammation. Frailty may be more informative than age alone: one in population-based cohort of adults aged 60 years or older with CDI, 90-day mortality was 28% and a multidimensional frailty measure predicted mortality more accurately than age or CDI severity [19]. Our age-specific analysis could not measure frailty, skill nursing facility residence, functional status, or comorbidity. Even so, the nonparallel trajectories of adults aged 55–64 years and those aged 85 years or older argue against a uniform change across older adulthood.

The subgroup findings require similarly cautious interpretation. National hospital data have identified differences in severe CDI and healthcare use by age, race, and Hispanic ethnicity [20]. Our failure to reject parallelism or coincidence does not establish equal burden or equal care, but rather only that fitted trajectories were not statistically distinguishable for the included groups. Regional differences may reflect population composition, healthcare and skilled nursing use, antimicrobial exposure, diagnostic and certification differences, or prevention practices.

For general internists, gastroenterologists, and infectious disease physicians, the main implication is not a new bedside rule but a need to connect population surveillance with clinical severity data. Healthcare systems already monitoring overall CDI incidence could also examine severe outcomes involving hemodynamic deterioration and renal dysfunction, particularly among the oldest adults. In the future, hospital discharge and electronic health record studies should test whether the post-2019 increase persists after adjustment for comorbidity and frailty and should distinguish community-associated from healthcare-associated infection, recurrent from initial CDI and CDI-attributable sepsis from other

sources. Linkage with death certificates would clarify how often this ICD-defined phenotype corresponds to clinically adjudicated severe or fulminant disease.

Conclusions

This study has several limitations. Death certificates are subject to underrecognition, diagnostic error, and variation in causal attribution. Validation studies have shown disagreement between death certificate classification and clinically adjudicated CDI-attributable mortality [21]. Requiring CDI as the underlying cause may improve specificity for deaths in which CDI was considered the initiating condition, but it excluded deaths in which CDI contributed without being selected as the underlying cause. Trends may also reflect changing recognition and ICD coding of CDI, sepsis, and AKI. Claims-based and clinical sepsis trends can diverge substantially, and the concurrent codes do not establish chronology, source of sepsis, clinical severity, or causality [22].

CDC WONDER provides aggregate data without laboratory results, recurrence status, treatment, antimicrobial exposure, comorbidities, frailty, hospitalization or intensive care course, or healthcare-associated disease. Subgroup periods differed because of data availability and estimate stability. Race and ethnicity reflect death certificate classification, and race-specific modeling included only Black and White groups, limiting generalizability. Sparse early counts produced wide confidence intervals and may make joinpoint locations sensitive to small changes. Urbanization rates were crude and ended in 2021, so age and other compositional differences may explain part of the observed pattern. Joinpoints are descriptive model features and need not represent discrete causal events. Although Bonferroni thresholds were applied to regional and urbanization comparisons, other multiple comparisons may increase false-positive findings. Finally, the national series combined two CDC WONDER products, in which overlapping estimates were checked, but residual differences in population denominators or classifications may remain.

U.S. mortality records identifying CDI as the underlying cause with concurrent sepsis and AKI increased after 2019 following several years of decline. The increase was broad but most pronounced among adults aged 85 years or older and varied across Census regions. Clinical validation is needed to determine whether this signal reflects changing disease severity, patient vulnerability, healthcare delivery, documentation, or a combination of these factors.

Declarations

Conflict of Interest

The authors declare they have no financial or non-financial conflicts of interest to disclose.

Human Ethics and Consent to Participate Declarations

Not applicable.

Clinical Trial Number

Not applicable.

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Author Contribution

MT conceived and designed the study, acquired and analyzed the data, interpreted the findings, prepared the tables and figures, and drafted the manuscript. JT and JR contributed the interpretation of the findings and critically reviewed and revised the manuscript for important intellectual content. All authors reviewed and approved the final manuscript and agreed to be accountable for the integrity of the work.

Data Availability

The data analyzed in this study are publicly available from the Centers for Disease Control and Prevention (CDC) WONDER Multiple Cause of Death database. Data can be accessed through the CDC WONDER platform at <https://wonder.cdc.gov/>. All data used in this study were derived from publicly available, deidentified, aggregate mortality records.

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Figures

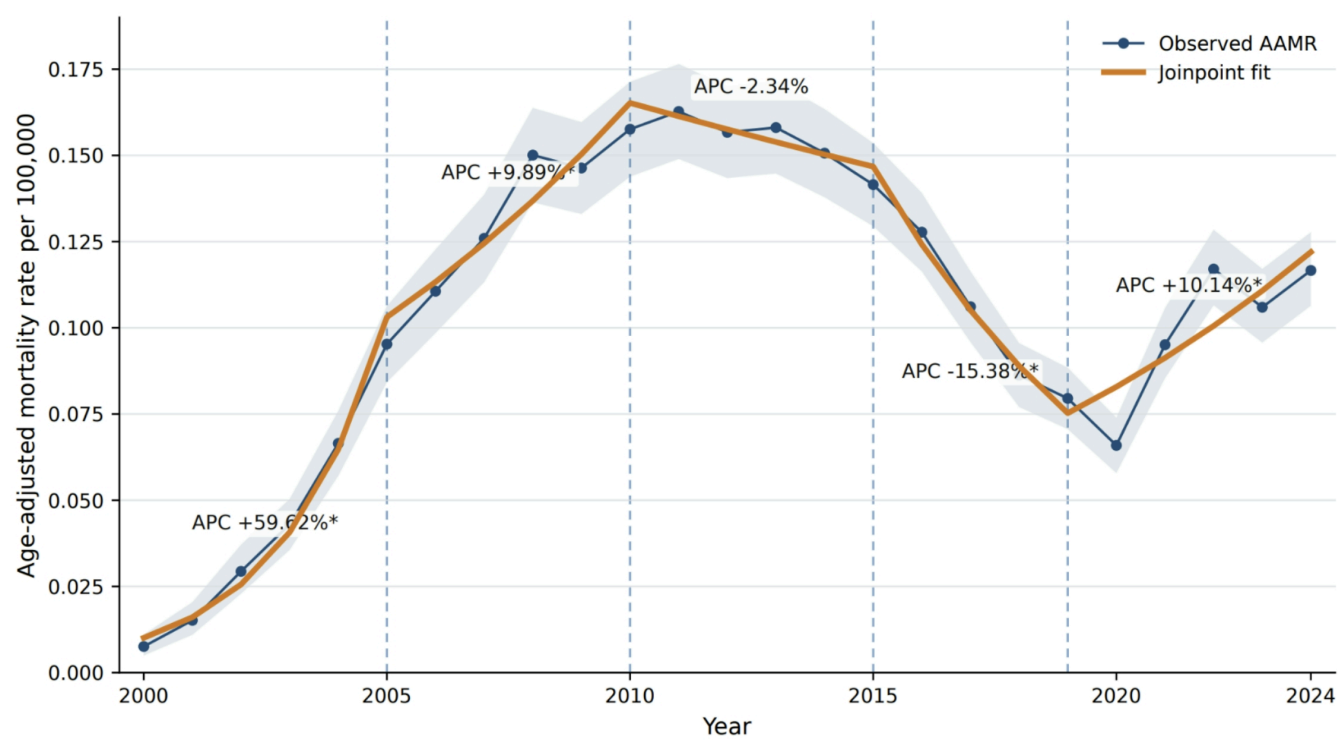


Figure 1

Overall national mortality trend for *Clostridioides difficile* infection with concurrent sepsis and acute kidney injury, United States, 2000–2024. Points and the thin line represent observed annual age-adjusted mortality rates, with the shaded band indicating 95% confidence intervals. The bold line represents the fitted log-linear Joinpoint model. Vertical dashed lines identify joinpoints in 2005, 2010, 2015, and 2019. Labels report the annual percent change for each segment; an asterisk indicates $p<0.05$. Rates are reported per 100,000 population and were age-adjusted to the 2000 U.S. standard population. *Note:* APC = annual percent change; AAMR = age-adjusted mortality rate.

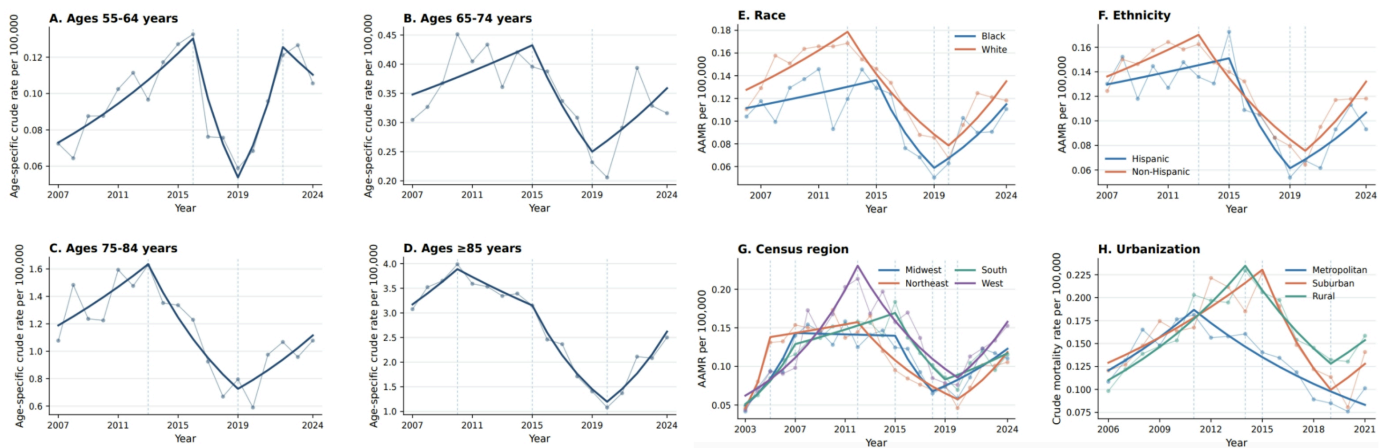


Figure 2

Observed and fitted mortality trends for *Clostridioides difficile* infection with concurrent sepsis and acute kidney injury by demographic and geographic subgroup. Panels A–D show crude age-specific mortality rates among adults aged 55–64 years, 65–74 years, 75–84 years, and 85 years or older, respectively. Panels E–G show age-adjusted mortality rates by race, Hispanic ethnicity, and Census region, respectively. Panel H shows crude mortality rates by county urbanization category. Thin lines and markers represent observed annual rates, bold lines represent fitted Joinpoint trends, and vertical dashed lines mark subgroup-specific joinpoints. Rates are reported per 100,000 population. Analysis periods were 2007–2024 for age and ethnicity, 2006–2024 for race, 2003–2024 for Census region, and 2006–2021 for urbanization. The urbanization analysis ended in 2021 because population denominators were unavailable for 2022–2024. *Note:* AAMR = age-adjusted mortality rate.

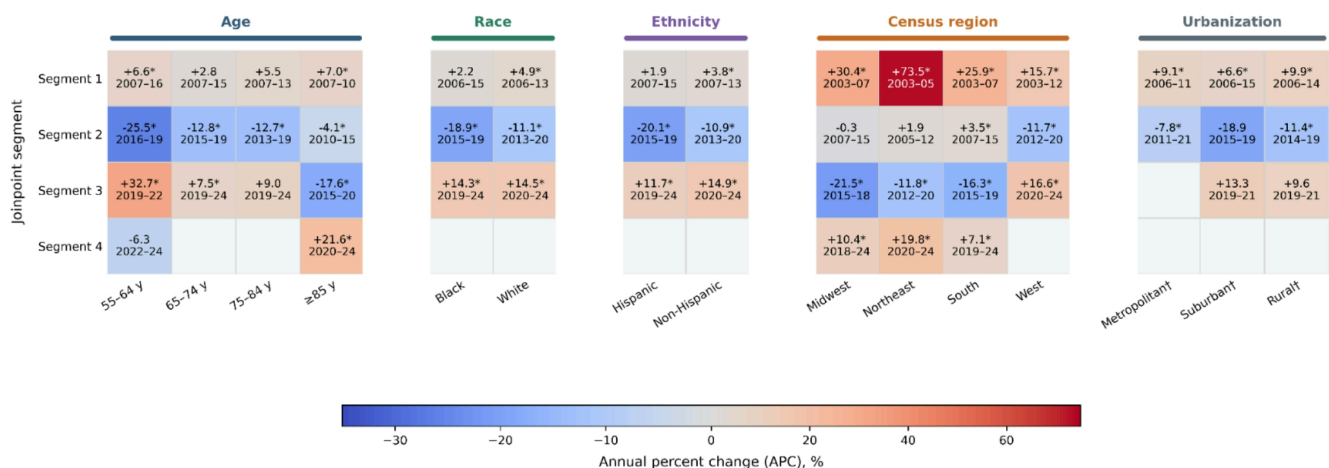


Figure 3

Segment-specific annual percent changes in mortality with *Clostridoides difficile* infection as the underlying cause and concurrent sepsis and acute kidney injury by subgroup. Cells report the annual percent change and corresponding years for each subgroup-specific Joinpoint segment. Warm colors indicate increasing, cool colors indicate decreasing rates, and an asterisk denotes $p<0.05$. Light-gray cells indicate no additional segment. Age and urbanization analyses used crude rates[†]; all other analyses used age-adjusted mortality rates. *Note:* APC = annual percent change.