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Trends and disparities of diverticular disease mortality in the United States before and during the COVID-19 era: estimates from the Centers for Disease Control WONDER database

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Abstract

Background Diverticular disease (DD) is a common gastrointestinal condition in the United States (US) associated with significant morbidity and mortality. The COVID-19 pandemic posed new challenges that might exacerbate DD-related outcomes. This study analyzed the trends in all-cause, digestive system (DGS), and cardiovascular system (CVS) mortality associated with DD from 1999-2020, focusing on the impact of COVID-19 on age-adjusted mortality rates (AAMRs) and disparities across demographics and geography.

Methods Data from adults aged ≥25 years were extracted from the Centers for Disease Control WONDER database. AAMRs per 100,000 people were standardized using the 2000 US census. AAMRs were assessed from 1999-2020 for context, while the primary comparative analysis focused on the pre-COVID-19 (2016-2019) and post-COVID-19 (2019-2022) periods using linear regression models. AAMRs were stratified by age, sex, race/ethnicity and geographic region. Note: 2021-2022 trends were extrapolated, as finalized mortality records were not available at the time of analysis.

Results Between 1999 and 2020, 115,009 DD-related deaths occurred (AAMR 2.4/100,000), including 70,648 DGS-related deaths (AAMR 1.5) and 17,405 CVS-related deaths (AAMR 0.4). Females (AAMR 2.6), elderly individuals (AAMR 11.1), and non-Hispanic whites (AAMR 2.5) had the highest mortality rates. Post-COVID-19, AAMRs increased from 1.8 to 2.0, with significant increases among rural populations. DGS-related deaths were most prevalent, particularly in non-metropolitan areas.

Conclusions DD-related mortality has increased in the post-COVID-19 period, especially in vulnerable populations, such as the elderly, rural residents and females. These findings highlight the need for equitable healthcare interventions and the continued monitoring of pandemic-era health disparities.

Keywords Diverticular disease, COVID-19, mortality trends, disparities, CDC WONDER

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Introduction

Diverticular disease (DD) is a prevalent gastrointestinal condition characterized by the formation of diverticula and small pouches in the colonic wall. Its incidence has notably increased in western countries, with studies indicating that the prevalence of diverticulosis ranges from 20-42% in Europe and North America [1]. Its prevalence has risen significantly over the past few decades, affecting an estimated 2.5 million individuals in the United States (US) alone, with substantial implications for healthcare systems owing to the associated morbidity and mortality. In the US, DD has become a leading cause of gastrointestinal-related hospital admissions, with an estimated 280,000 hospitalizations in 2009, incurring an aggregate cost of $2.7 billion [2].

While the majority of individuals with DD remain asymptomatic, an estimated 10-25% will go on to develop diverticulitis, a complication that can cause severe outcomes related to hospitalization and death, including perforation, abscess formation and peritonitis [1]. The management of DD and its complications have changed in recent years. Between 2002 and 2007, there was an increasing trend in the number of elective surgical resections performed for diverticulitis [3]. Mortality rates associated with DD have remained a critical public health concern, disproportionately affecting older adults, females, and non-Hispanic white populations. Despite improved diagnosis and management, disparities persist across demographic and geographical lines, suggesting inequities in access to care and health outcomes. Additionally, deaths related to DD are often complicated, with other systemic conditions complicating the clinical course, and major comorbidities of the digestive system (DGS) and cardiovascular system (CVS).

The COVID-19 pandemic has created unmatched disruptions in the provision of healthcare services worldwide, which in turn have adversely affected the management of many diseases, including DD, by delaying diagnosis and reducing the provision of routine medical care, all of which may contribute to a deterioration in outcomes from DD. There was a significant reduction in hospital admissions for diverticulitis during the pandemic, with more severe cases presenting to emergency departments [4]. Lockdowns and fear of the virus have caused further delays in presentations, possibly contributing to more complicated presentations of DD [5]. Emerging evidence suggests that COVID-19 may indirectly contribute to mortality through shared pathogenetic mechanisms, such as increased systemic inflammation and hypercoagulability. Moreover, rural and underserved regions have been disproportionately burdened by reduced healthcare infrastructure and resource constraints during the pandemic.

Accordingly, the present study aimed to conduct an in-depth analysis of trends in mortality due to DD in the period between 1999 and 2020 in the US. The current study evaluated demographic and geographic disparities in mortality rates from DD, with special attention paid to possible influences of the COVID-19 pandemic, using data extracted from the Centers for Disease Control and Prevention's Wide-ranging Online Data for Epidemiologic Research (CDC WONDER) database. This analysis aimed to explain the interaction between chronic disease management and pandemic-related challenges, inform strategies for equitable healthcare delivery, and improve patient outcomes.

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Materials and methods

Study design and data source

We used the National Vital Statistics System (NVSS), via the CDC WONDER platform, to obtain de-identified data on the estimated diverticular disease-related mortality in all individual US counties. The NVSS database registers more than 99% of deaths in the USA, and this study used data updated on January 22, 2022 [6]. The CDC WONDER's Underlying Cause of Death database captures a single underlying cause of death, as well as demographic data including age, sex, race/ethnicity, from death certificates for US residents [7]. The underlying causes of death were classified according to the International Classification of Diseases, 10th revision (ICD-10), and were based on the physician's entry in the cause of death section of the death certificate. When a physician entered more than 1 cause or condition, the underlying cause was determined by the sequence of conditions on the certificate, the provisions of the ICD, and the associated selection rules and modifications.

Each death certificate includes 1 underlying cause of death, defined as the disease or injury that initiated the sequence of events leading directly to death, as well as up to 20 additional contributing causes, which may include comorbidities or intermediate steps [6,7]. The CDC WONDER platform distinguishes between these categories using ICD-10 coding algorithms and selection rules [6,7]. For instance, if a death certificate listed both COVID-19 and DD, the CDC's ICD-10 algorithm would determine which condition was the primary underlying cause. Chronic conditions such as DD often appear only as contributing causes and may not be captured when analyzing underlying causes alone. Consequently, our analysis may underrepresent the broader burden of DD-related mortalities.

We obtained county-level all-cause (ICD-10 code K57), DGS-related (ICD-10 code K00-K92), and CVS-related mortality rates (ICD-10 code I00-I99) associated with DD from January 1, 1999, to December 31, 2020. County-level mortality data were aggregated between 1999 and 2020 to maximize the data available for the multivariable modeling. All deaths related to COVID-19 and DD were considered, and the causes of death were identified using ICD-10 code U07.1 for COVID-19. These codes were used to categorize deaths as contributing or underlying causes. Both terms were then queried to identify patients who had both COVID-19 and DD as contributing or underlying causes of death (all-cause, DGS, or CVS-related deaths).

We then performed linear regression analysis to determine mortality rates based on trends 3 years before (between 2016 and 2019) and after (between 2019 and 2022) COVID-19. Following CDC guidelines, county-level data representing fewer than 10 people were suppressed for confidentiality. We also censored counties reporting fewer than 20 deaths, because these mortality rates are unreliable [7]. A flowchart (Fig. 1) was constructed to illustrate the data selection and stratification process. Additionally, a conceptual diagram (Fig. 2) was developed to clarify the hypothesized relationships among COVID-19, demographic factors, healthcare access and DD-related mortality.

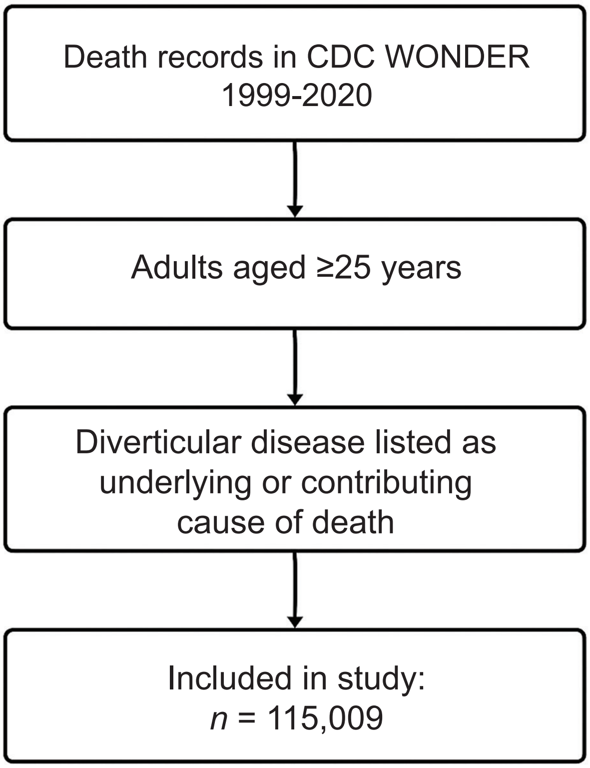

Figure 1 Study selection flowchart showing inclusion of death records from CDC WONDER for adults aged ≥25 years with diverticular disease listed as underlying or contributing cause of death (1999-2020)

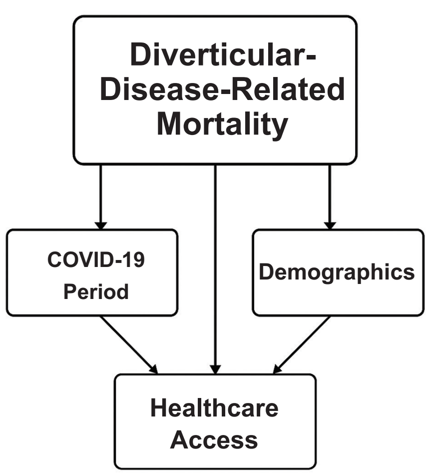

Figure 2 Conceptual model illustrating hypothesized impact of COVID-19 period, demographics, and healthcare access on diverticular disease-related mortality

Study population

To narrow the scope of our analysis to the adult population, our inclusion criteria focused on adults aged ≥25 years. Individuals younger than 25 years were excluded from the study. We also collected sociodemographic data for all 3 patient subgroups, including information on age, sex, race/ethnicity and region of residence. Patients were divided into 3 age groups: elderly (age ≥65 years), middle-aged adults (45-64 years), and young adults (25-44 years). Race/ethnicity was used to examine racial disparities. Based on the database, patients were divided into Hispanic, non-Hispanic black, non-Hispanic white, and non-Hispanic Asian groups. We also classified counties into urban (large metro [≥1 million], medium/small metro [50,000-999,999]) and rural (micropolitan and noncore [nonmetropolitan counties that did not qualify as micropolitan: <50,000]) counties. All covariates were obtained at the county level and linked with age-adjusted DD-related mortality rates to form the final dataset for analysis. All the data sources are presented in Tables 1-3 and Supplementary Tables 1-3.

To provide meaningful comparisons across demographic groups and over time, age-adjusted mortality rates (AAMR) were calculated and presented as deaths per 100,000 people, standardized to the 2000 US population. This adjustment accounted for variations in age distribution, enabling more accurate comparisons between the groups.

Statistical analysis

Age-adjusted mortality rates were obtained from CDC WONDER and calculated using the direct method, which applies age-specific death rates to the US standard population age distribution in 2000. This produced a weighted average of age-specific death rates, where the weight represented a fixed population by age, allowing the comparison of relative mortality risk across populations with different underlying age structures over time. According to the National Center for Health Statistics recommendations, 2000 was considered the reference year for the standard population [8]. We quantified the association between the pandemic and DD-related deaths by calculating the percentage difference between the projected and observed mortality rates. A stratified analysis was performed according to the strata of individual-level demographic characteristics: age, sex, race/ethnicity and county rurality. Linear regression models were then fitted to identify county-level factors associated with age-adjusted DD-related mortality. Finally, a sensitivity analysis was conducted to evaluate the potential time trends in the geographic disparity in DD-related mortality. First, the cohort was divided into 2 equal 4-year periods (2016-2019 and 2019-2022), and similar methods were applied to assess geographic disparities in age-adjusted mortality rates. To enrich for robustness, we performed a sensitivity analysis by setting DD as the underlying (primary) cause of death. Statistical analyses were performed using the CDC WONDER database (age standardization) and R version 4.0.2 (data cleaning and management, and graphic creation).

Ethical considerations

This study involved human subjects; however, as this cross-sectional study used de-identified publicly available data from the CDC WONDER platform, the Western Institutional Review Board provided a waiver to CDC WONDER in accordance

Table 1 Age-adjusted mortality rates per 100,000 for all causes of deaths associated with diverticular diseases (1999-2020)

Demographics	Deaths, n	Population, n	Age-adjusted mortality rate per 100,000 (95%CI)
Entire cohort	115,009	4,473,854,489	2.4 (2.4-2.4)
Sex			
Female	75,551	2,319,297,578	2.6 (2.6-2.6)
Male	39,458	2,154,556,911	2.1 (2.0-2.1)
Age groups			
Young adults (25-44 years)	965	1,851,376,757	0.1 (0.1-0.1)
Middle age (45-64 years)	11,287	1,694,001,067	0.6 (0.6-0.6)
Elderly (>65 years)	102,757	928,476,665	11.1 (11.1-11.2)
Ethnicity			
Hispanic	5,524	589,350,210	1.7 (1.7-1.8)
Not Hispanic	109,255	3,884,504,279	2.5 (2.4-2.5)
Race			
American Indian	442	49,853,431	1.4 (1.3-1.6)
Asian	1,372	245,576,124	0.8 (0.8-0.9)
Black	8,781	546,447,527	2.1 (2.1-2.1)
White	104,414	3,631,977,407	2.5 (2.5-2.5)
Census Regions			
Northeast	21,822	827,193,779	2.3 (2.2-2.3)
Midwest	27,977	969,567,311	2.6 (2.5-2.6)
South	39,173	1,652,256,217	2.3 (2.3-2.3)
West	26,037	1,024,837,182	2.6 (2.6-2.6)
2013 Urbanization			
Large Central Metro	29,546	1,364,782,777	2.3 (2.2-2.3)
Large Fringe Metro	24,625	1,107,354,420	2.2 (2.2-2.2)
Medium Metro	24,388	918,036,376	2.4 (2.4-2.4)
Small Metro	11,907	405,040,249	2.5 (2.5-2.6)
Micropolitan (Nonmetro)	13,885	392,223,879	2.9 (2.9-3.0)
NonCore (Nonmetro)	10,658	286,410,290	2.8 (2.8-2.9)

CI, confidence interval

with the Health Insurance Portability and Accountability Act (HIPAA) and applicable federal regulations, as it utilizes aggregate counts and there is no access to protected health information from the participating healthcare organizations. Thus, informed and written patient consent was not required or feasible, in accordance with the Common Rule. Moreover, CDC WONDER suppresses the number of patients to the nearest 10 for analytic purposes to fortify protected health information. This study followed the STROBE reporting guidelines [9]. The study was conducted in compliance with the ethical standards of the responsible institution on human subjects, as well as with the Helsinki Declaration.

Results

Overall mortality trends

From 1999-2020, 115,009 deaths (Table 1) in the USA were attributed to DD, resulting in an AAMR of 2.4 per 100,000 population. Among these, 70,648 deaths (Supplementary Table 1) were linked to DGS conditions (AAMR 1.5, 95% confidence interval [CI] 1.5-1.5), and 17,405 deaths (Supplementary Table 2) were associated with CVS conditions (AAMR 0.4, 95%CI 0.3-0.4). The mortality trends for DD were stable between 1999 and 2016, followed by a slight increase in AAMR from 2016-2020, with notable variations observed across the demographic and geographic categories.

It is important to interpret these mortality figures in light of the potential misclassification of the death certificate data. The reliance on the underlying cause of death may exclude cases where diverticular disease was a significant contributor, but not the coded primary cause. Conversely, COVID-19, when listed on the certificate, was coded as the underlying cause in the vast majority of cases (~95%), which may partially account for the rise in non-diverticular coded causes during the pandemic period.

Trends by sex

Mortality rates were consistently higher among females than among males across all categories. The AAMR for females was 2.6 (95%CI 2.6-2.6), compared to 2.1 (95%CI 2.0-2.1) in males (Fig. 3). Similarly, DGS-related deaths were more frequent among females (AAMR 1.6, 95%CI 1.6-1.7) compared to males (AAMR 1.2, 95%CI 1.2-1.2) (Supplementary Fig. 1). CVS-

Table 2 Age-adjusted mortality rates per 100,000 for all causes of deaths associated with diverticular diseases before (2016-2019) and after COVID-19 (2019-2022)

Demographics	Deaths, n	Population, n	Age-adjusted mortality rate per 100,000 (95%CI)
Entire cohort			
Before Covid-19	18,737	888,381,105	1.8 (1.8-1.9)
After Covid-19	21,713	909,363,191	2.0 (2.0-2.1)
Sex			
Female			
Before Covid-19	11,891	458,699,369	2.0 (1.9-2.0)
After Covid-19	13,670	467,150,152	2.2 (2.2-2.3)
Male			
Before Covid-19	6,846	429,681,736	1.6 (1.6-1.6)
After Covid-19	8,043	442,213,039	1.8 (1.7-1.8)
Age groups			
Young adults (25-44 years)			
Before Covid-19	164	345,940,568	0.1 (0.0-0.1)
After Covid-19	270	353,900,927	0.1 (0.0-0.1)
Middle age (45-64 years)			
Before Covid-19	2,186	335,848,207	0.6 (0.6-0.6)
After Covid-19	2,681	332,101,831	0.7 (0.7-0.7)
Elderly (≥65 years)			
Before Covid-19	16,387	206,592,330	8.3 (8.1-8.4)
After Covid-19	18,762	223,360,433	9.0 (8.9-9.1)
Ethnicity			
Hispanic			
Before Covid-19	1,179	135,408,977	1.4 (1.3-1.4)
After Covid-19	1,622	144,863,405	1.6 (1.5-1.7)
Not Hispanic			
Before Covid-19	17,520	752,972,128	1.9 (1.8-1.9)
After Covid-19	20,045	764,499,786	2.1 (2.0-2.1)
Race			
White			
Before Covid-19	16,837	704,362,641	1.9 (1.9-2.0)
After Covid-19	19,337	707,029,734	2.2 (2.1-2.2)
Black			
Before Covid-19	1,486	114,595,177	1.5 (1.5-1.6)
After Covid-19	1,800	116,036,895	1.7 (1.7-1.8)
Asian			
Before Covid-19	309	58,234,627	0.6 (0.6-0.7)
After Covid-19	336	57,109,536	0.6 (0.6-0.7)
American Indian			
Before Covid-19	105	11,188,660	1.3 (1.1-1.6)
After Covid-19	134	10,513,082	1.6 (1.3-1.9)
Census Regions			
Northeast			
Before Covid-19	3,396	157,160,688	1.7 (1.7-1.8)
After Covid-19	3,863	159,428,624	1.9 (1.8-2.0)
Midwest			
Before Covid-19	4,040	184,940,748	1.8 (1.8-1.9)
After Covid-19	4,567	187,430,429	2.0 (1.9-2.1)
South			
Before Covid-19	6,675	336,388,504	1.8 (1.7-1.8)
After Covid-19	7,981	347,122,925	2.0 (1.9-2.0)
West			
Before Covid-19	4,626	209,891,165	2.0 (2.0-2.1)
After Covid-19	5,302	215,381,213	2.2 (2.1-2.3)

(*Contd...*)

Table 2 (*Continued*)

Demographics	Deaths, n	Population, n	Age-adjusted mortality rate per 100,000 (95%CI)
2013 Urbanization			
Large Central Metro			
Before Covid-19	4,736	274,826,096	1.7 (1.6-1.7)
After Covid-19	Not applicable	Not applicable	Not applicable
Large Fringe Metro			
Before Covid-19	4,212	223,127,096	1.7 (1.7-1.8)
After Covid-19	Not applicable	Not applicable	Not applicable
Medium Metro			
Before Covid-19	4,163	183,451,888	1.9 (1.8-2.0)
After Covid-19	Not applicable	Not applicable	Not applicable
Small Metro			
Before Covid-19	1,993	79,654,684	2.0 (1.9-2.1)
After Covid-19	Not applicable	Not applicable	Not applicable
Micropolitan (Nonmetro)			
Before Covid-19	2,069	74,330,971	2.1 (2.1-2.2)
After Covid-19	Not applicable	Not applicable	Not applicable
NonCore (Nonmetro)			
Before Covid-19	1,564	52,990,370	2.1 (2.0-2.2)
After Covid-19	Not applicable	Not applicable	Not applicable

CI, confidence interval

Table 3 Age-adjusted mortality rates per 100,000 for digestive system related deaths associated with diverticular diseases before (2016-2019) and after COVID-19 (2019-2022)

Demographics	Deaths, n	Population, n	Age-adjusted mortality rate per 100,000 (95%CI)
Entire cohort			
Before Covid-19	12,242	888,381,105	1.2 (1.2-1.2)
After Covid-19	13,463	909,363,191	1.3 (1.2-1.3)
Gender			
Female			
Before Covid-19	8,010	458,699,369	1.3 (1.3-1.4)
After Covid-19	8,742	467,150,152	1.4 (1.4-1.5)
Male			
Before Covid-19	4,232	429,681,736	1.0 (1.0-1.0)
After Covid-19	4,721	442,213,039	1.0 (1.0-1.1)
Age groups			
Young adults (25-44 years)			
Before Covid-19	116	345,940,568	0.1 (0.0-0.1)
After Covid-19	188	353,900,927	0.1 (0.0-0.1)
Middle age (45-64 years)			
Before Covid-19	1,399	335,848,207	0.4 (0.3-0.4)
After Covid-19	1,677	332,101,831	0.4 (0.4-0.5)
Elderly (≥65 years)			
Before Covid-19	10,727	206,592,330	5.4 (5.3-5.5)
After Covid-19	11,598	223,360,433	5.6 (5.5-5.7)
Ethnicity			
Hispanic			
Before Covid-19	790	135,408,977	0.9 (0.9-1.0)
After Covid-19	998	144,863,405	1.0 (0.9-1.1)
Not Hispanic			
Before Covid-19	11,426	752,972,128	1.2 (1.2-1.3)
After Covid-19	12,439	764,499,786	1.3 (1.3-1.3)

(*Contd...*)

Table 3 (*Continued*)

Demographics	Deaths, n	Population, n	Age-adjusted mortality rate per 100,000 (95%CI)
Race			
American Indian			
Before Covid-19	71	11,188,660	0.9 (0.7-1.1)
After Covid-19	78	10,513,082	0.9 (0.7-1.2)
Asian			
Before Covid-19	211	58,234,627	0.4 (0.4-0.5)
After Covid-19	210	57,109,536	0.4 (0.4-0.5)
Black			
Before Covid-19	963	114,595,177	1.0 (0.9-1.1)
After Covid-19	1,106	116,036,895	1.0 (1.0-1.1)
White			
Before Covid-19	10,997	704,362,641	1.3 (1.3-1.3)
After Covid-19	12,011	707,029,734	1.3 (1.3-1.4)
Census Regions			
Northeast	2,313	157,160,688	1.2 (1.1-1.2)
Before Covid-19	2,470	159,428,624	1.2 (1.2-1.3)
After Covid-19			
Midwest	2,633	184,940,748	1.2 (1.1-1.2)
Before Covid-19	2,978	187,430,429	1.3 (1.3-1.3)
After Covid-19			
South	4,299	336,388,504	1.1 (1.1-1.2)
Before Covid-19	4,762	347,122,925	1.2 (1.2-1.2)
After Covid-19			
West	2,997	209,891,165	1.3 (1.3-1.4)
Before Covid-19	3,253	215,381,213	1.4 (1.3-1.4)
After Covid-19			
2013 Urbanization			
Large Central Metro			
Before Covid-19\	3,198	274,826,096	1.2 (1.1-1.2)
After Covid-19	Not applicable	Not applicable	Not applicable
Large Fringe Metro			
Before Covid-19	2,768	223,127,096	1.1 (1.1-1.1)
After Covid-19	Not applicable	Not applicable	Not applicable
Medium Metro			
Before Covid-19	2,688	183,451,888	1.2 (1.2-1.3)
After Covid-19	Not applicable	Not applicable	Not applicable
Small Metro			
Before Covid-19	1,241	79,654,684	1.3 (1.2-1.3)
After Covid-19	Not applicable	Not applicable	Not applicable
Micropolitan (Nonmetro)			
Before Covid-19	1,360	74,330,971	1.4 (1.3-1.5)
After Covid-19	Not applicable	Not applicable	Not applicable
NonCore (Nonmetro)			
Before Covid-19	987	52,990,370	1.3 (1.2-1.4)
After Covid-19	Not applicable	Not applicable	Not applicable

CI, confidence interval

related deaths also showed higher rates in females (AAMR 0.4, 95%CI 0.4-0.4) compared to males (AAMR 0.3, 95%CI 0.3-0.3) (Supplementary Table 2).

Trends by age group

The elderly population (≥65 years) exhibited the highest mortality rates across all cause categories, with an AAMR of 11.1 (95%CI 11.1-11.2) for all causes (Table 1; Fig. 3), 6.8 (95%CI 6.7-6.8) for DGS (Supplementary Table 1; Supplementary Fig. 1), and 1.7 (95%CI 1.7-1.8) for CVS-related deaths (Supplementary Table 2). Middle-aged adults (45-64 years) displayed lower mortality rates, with an AAMR of 0.6 (95%CI 0.6-0.6), while young adults (25-44 years) had the lowest AAMR at 0.1 (95%CI 0.1-0.1).

Trends by race and ethnicity

Significant racial disparities in DD-related mortality (Table 1 and Supplementary Table 1 and 2; Fig. 3 and

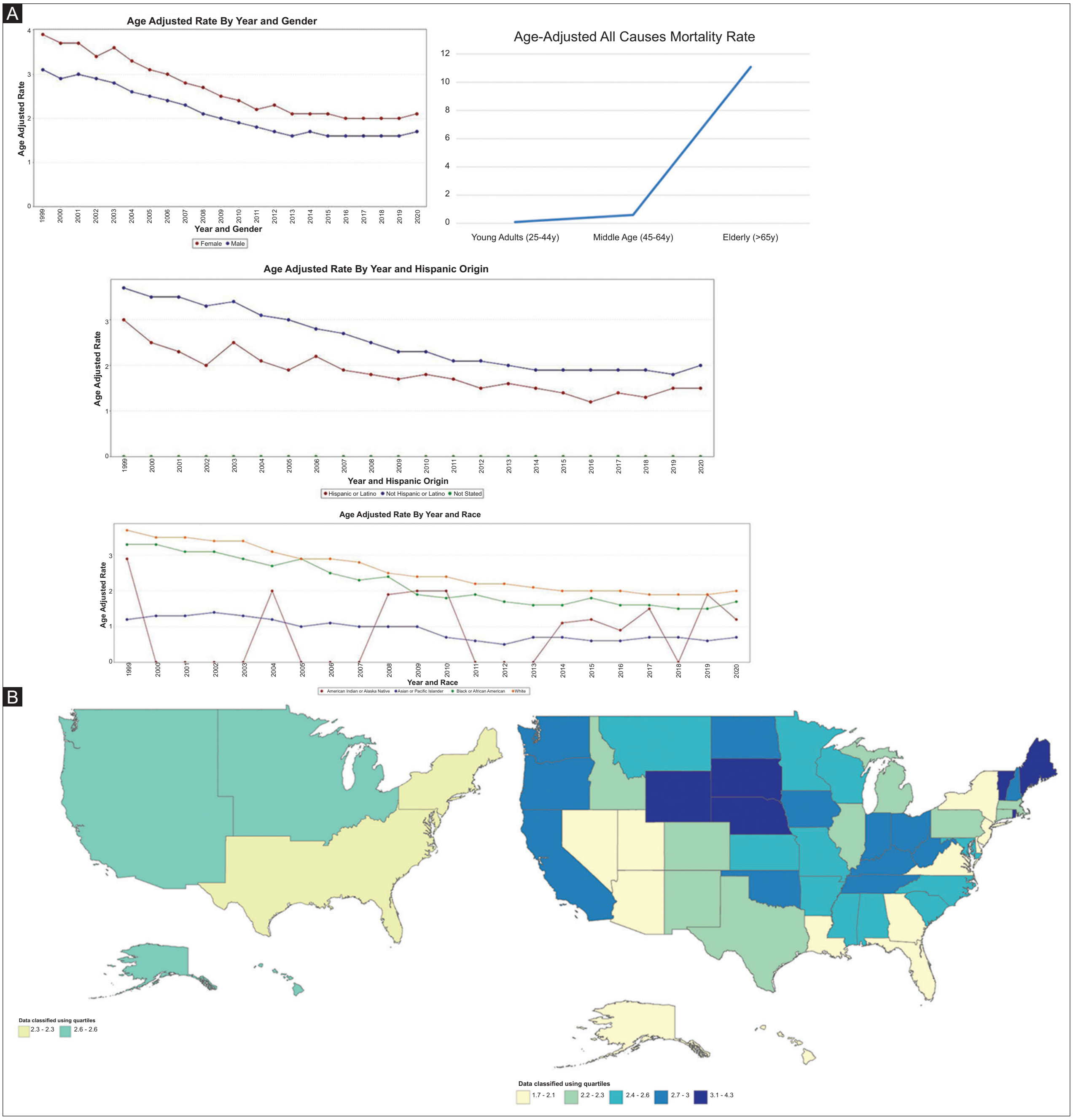

Figure 3 Age-adjusted mortality rate per 100,000 for all causes related deaths of diverticular disease (1999-2020) by: (A) sex, age categories, Hispanic/non-Hispanic origins, and race; (B) census regions and states within USA

Supplementary Fig. 1) were also observed. White individuals had the highest overall mortality rate (AAMR 2.5, 95%CI 2.5-2.5), followed by black individuals (AAMR 2.1, 95%CI 2.1-2.1). Hispanic populations exhibited lower overall mortality rates (AAMR 1.7, 95%CI 1.7-1.8) compared to non-Hispanic individuals (AAMR 2.5, 95%CI 2.4-2.5). Asian populations had the lowest mortality rates (AAMR 0.8, 95%CI 0.8-0.9), indicating significant interethnic variability (Fig. 3).

Geographic distribution

Geographic analysis revealed marked variations in the mortality rates (Table 1 and Supplementary Tables 1 and 2; Fig. 3 and Supplementary Fig. 1). The Midwest and West regions reported the highest overall AAMR (2.6, 95%CI 2.5-2.6), while the South and Northeast regions had slightly lower rates (AAMR 2.3, 95%CI 2.3-2.3). Regarding DGS-related deaths (Supplementary Table 1; Supplementary Fig. 1), the West exhibited the highest AAMR (1.6, 95%CI 1.6-1.7), followed by the Midwest. Rural areas, particularly non-metro-micropolitan regions, experienced the highest AAMR (2.9, 95%CI 2.9-3.0), whereas large central metropolitan areas reported lower rates (AAMR 2.3, 95%CI 2.2-2.3).

Pre- and post-COVID-19 trends

Temporal analysis comparing the pre-COVID-19 (2016-2019) and post-COVID-19 (2019-2022) periods demonstrated an increase in DD-related mortality (Table 2 and 3, Supplementary Table 3; Figs. 4 and 5, Supplementary Fig. 2,3). The overall AAMR rose from 1.8 (95%CI 1.8-1.9) in 2016-2019

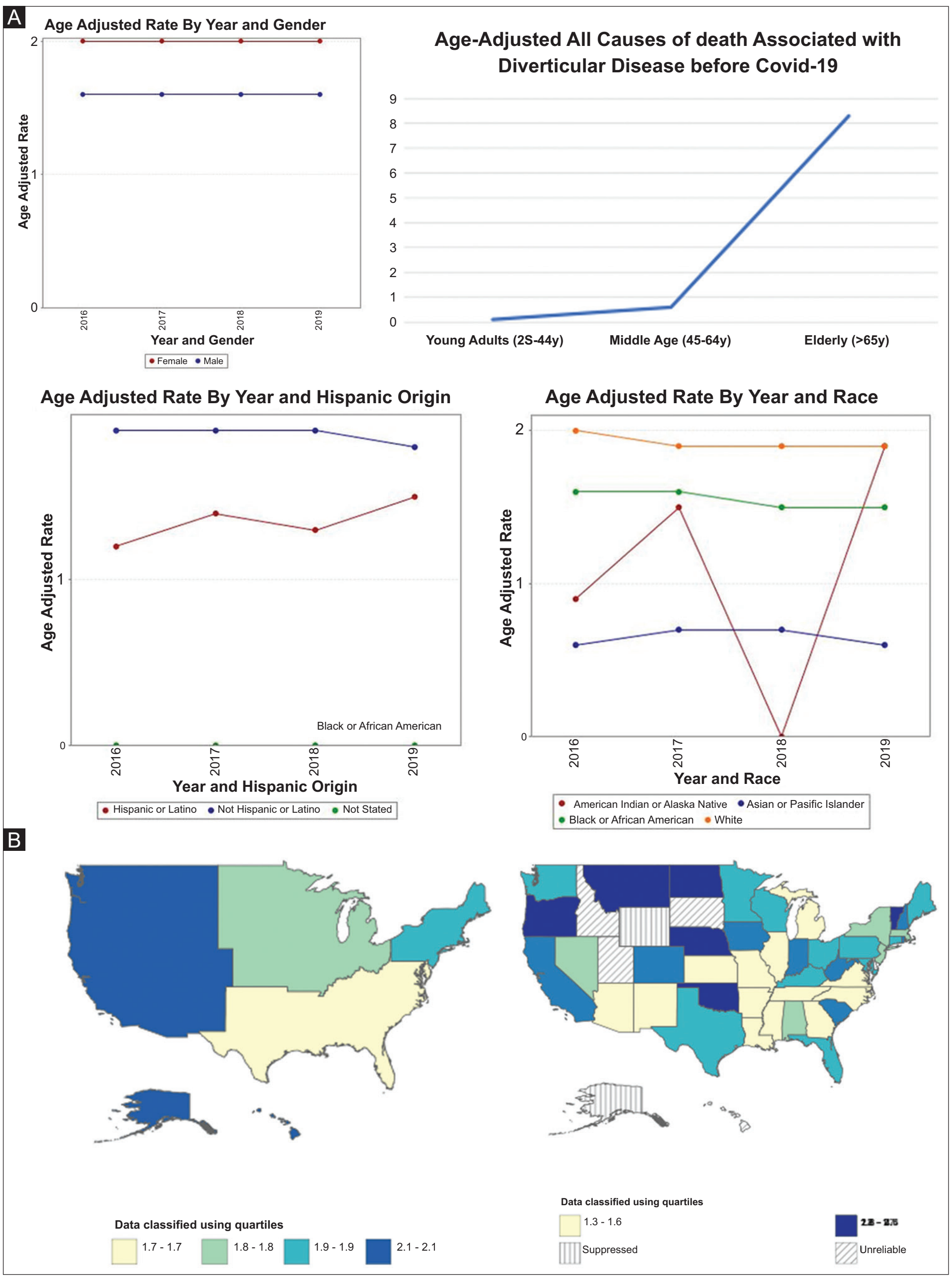

Figure 4 Age-adjusted mortality rate per 100,000 for all causes related deaths of diverticular disease before Covid-19 (2016-2019) by: (A) sex, age categories, Hispanic/non-Hispanic origins, and race; (B) census regions and states within USA

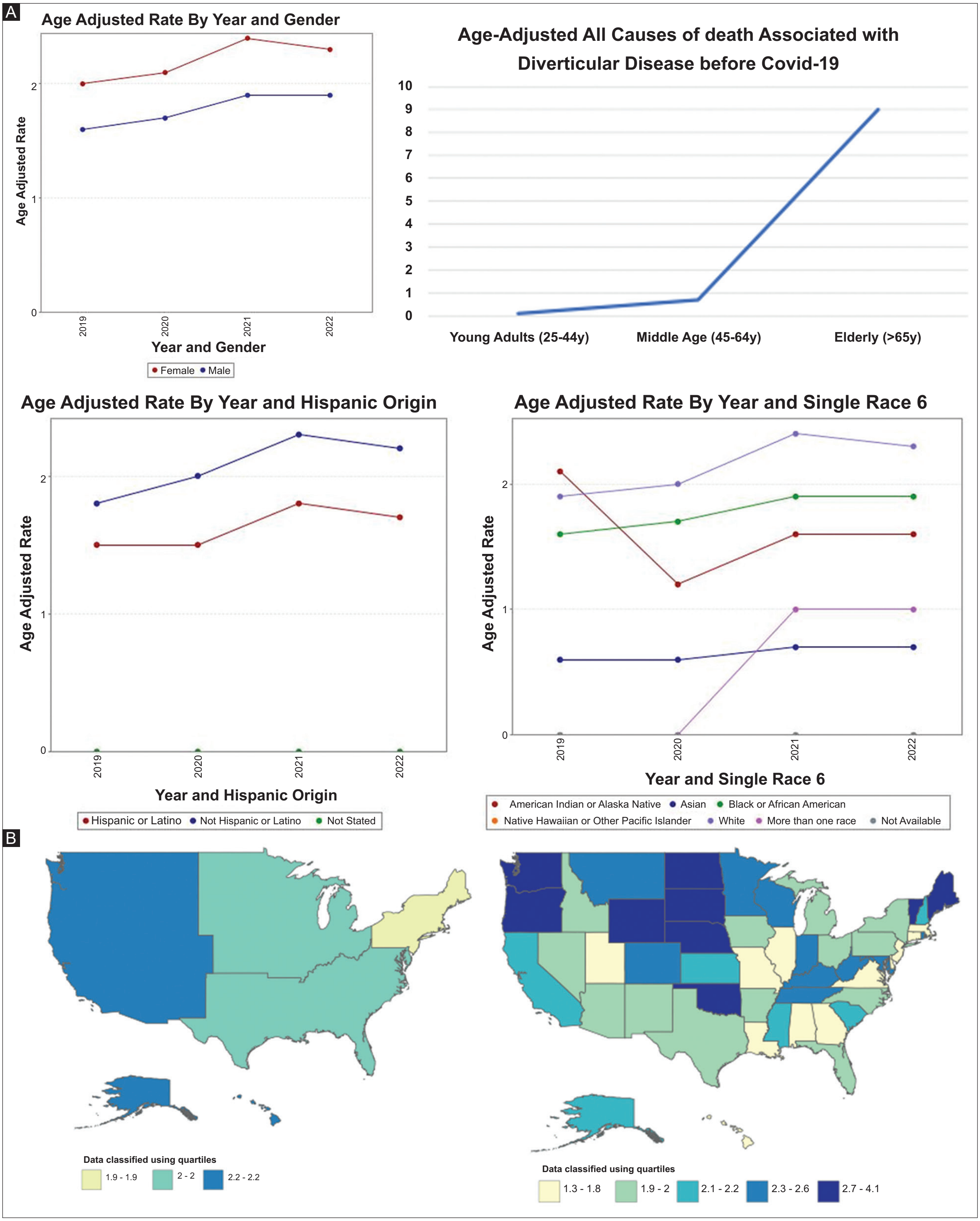

Figure 5 Age-adjusted mortality rate per 100,000 for all causes related deaths of diverticular disease after Covid-19 (2019-2022) by: (A) sex, age categories, Hispanic/non-Hispanic origins, and race; (B) census regions and states within USA

to 2.0 (95%CI 2.0-2.1) in 2019-2022. The increase was more pronounced in females (2.0-2.2) than in males (1.6-1.8). Elderly individuals experienced the largest post-pandemic increase in AAMR, rising from 8.3 (95%CI 8.1-8.4) to 9.0 (95%CI 8.9-9.1).

Digestive and circulatory system mortality

DGS-related mortality remained the predominant cause of death in patients with DD (Supplementary Table 1; Supplementary Fig. 1), with an AAMR of 1.5 (95%CI 1.5-1.5) across the study period. The AAMR for CVS-related deaths (Supplementary Table 2) was lower at 0.4 (95%CI 0.3-0.4). The Midwest and West regions had higher DGS-related mortality, with the highest AAMR reported in non-metropolitan areas (Fig. 5). Conversely, CVS-related mortality was highest in rural areas, particularly in non-core regions (Supplementary Table 2).

Discussion

This study provides a comprehensive analysis of the trends and disparities in DD-related mortality in the USA from 1999-2020, with a particular focus on the impact of the COVID-19 pandemic. The findings reveal significant demographic and geographic variations in DD-related mortality, underscoring persistent health inequities and the compounded challenges posed by the pandemic. Although the study includes mortality data from 2020, the primary pre- vs. post-COVID analysis utilizes trend comparisons from 2016-2019 and 2019-2022. Thus, we acknowledge that the effects beyond 2020 are only inferred from these modeled estimates, as full death certificate data for 2021-2022 were unavailable at the time of data extraction.

DD remains an important public health problem in the USA. Overall, from 1999-2020, the AAMR for deaths associated with DD was 2.4 per 100,000 individuals. Conditions related to DGS accounted for the majority of deaths. Deaths related to CVS are relatively rare but notable. This finding agrees with earlier research reporting on complications of DD, such as diverticulitis and diverticular bleeding, perforation and peritonitis, which have been identified as a leading cause of gastrointestinal-related admissions and mortality in DD patients, thus contributing to considerable healthcare costs and morbidity [2].

Sex-related mortality differences were present, with higher mortality rates among females than males. Our analysis showed that females had higher mortality rates due to DD than males (AAMR 2.6 vs. 2.1). This observation is in agreement with previous studies that reported approximately 70% of DD-related deaths in women [10]. The reasons for this have not yet been determined, but may include differences in biological (e.g., hormonal influence), behavioral and healthcare utilization factors. Females have been shown to experience more frequent complications such as chronic diverticulitis, and may thus be more likely to seek medical care, thereby increasing the likelihood of diagnosis and attribution to DD.

Age was confirmed as a strong predictor of mortality; for all causes studied, there was higher mortality among the elderly age group (≥65 years), with an AAMR for all causes of 11.1. This is not a surprising result, since the prevalence of diverticulosis and its complications increases with age. This result indicates that comorbid conditions add to the aggravating nature of aging in outcomes pertaining to DD. Studies have shown that the incidence of diverticulitis has increased over time, especially among older adults, leading to more hospitalizations and increased healthcare utilization [1]. Furthermore, the increased vulnerability of older adults to DGS and CVS complications underlines the need for targeted interventions, with particular emphasis on the management of comorbid conditions and timely care.

There were significant racial and ethnic disparities in DD-related mortality, with white individuals having the highest mortality rate (AAMR 2.5), followed by black individuals (AAMR 2.1), whereas Asian populations had the lowest mortality rates. Hispanic populations also had lower AAMRs than non-Hispanic populations. These findings agree with those of other studies that have shown higher complication rates and mortality from DD among whites, possibly as a result of genetic predisposition, dietary patterns and healthcare access. These disparities may be related to underlying socioeconomic status, access to healthcare, dietary habits and prevalence of comorbid conditions. To reduce these disparities, focused public health interventions are required to increase access to care and to foster health equity. However, mortality rates in minority ethnic groups may be underestimated because of deficiencies in health care and diagnostics. The persistence of disparities in outcomes between Hispanic and non-Hispanic groups requires further investigation to uncover possible barriers to equal care.

Geographically, DD mortality also showed deep disparities. Our geographic analysis identified the Midwest and West regions bearing the highest overall AAMRs of 2.6, while rural areas, and specifically the non-metropolitan-micropolitan areas, had the highest AAMR (2.9), indicating the highest mortality burden. These findings suggest that access to health care and resource availability in rural areas may contribute to greater mortality rates. This may be partly due to limited access to specialized care, delayed diagnoses and constraints on healthcare resources in rural settings. Previous studies have also reported higher rates of advanced complications related to DD in rural areas, and improving infrastructure and access to healthcare in these areas is crucial for reducing these disparities.

The COVID-19 pandemic has brought about unprecedented challenges in DD management, exacerbating the massive burden of healthcare delivery. Our study demonstrated an increasing trend in mortality due to DDs in the post-COVID period: AAMRs increased from 1.8 to 2.0. This rise was more evident among older age groups and rural populations, possibly due to reduced access to healthcare services during the pandemic. A substantial reduction in the hospitalization of patients with diverticulitis during the pandemic has been observed, with increasing severity among cases presenting to emergency departments, according to previous studies [4]. Moreover, routine healthcare utilization was reduced during the pandemic, and delays in seeking medical care due to lockdowns and fear of contracting the virus probably further worsened the severity of DD presentations and may have resulted in more complicated presentations of DD [5]. Moreover, the proinflammatory and hypercoagulable states associated with COVID-19 might have contributed to worse outcomes in patients with DD.

The present study took advantage of strong national data from the CDC WONDER database, which has guaranteed comprehensive coverage of DD-related mortality trends over a period of 2 decades. The use of AAMRs has allowed for meaningful comparisons across diverse demographic and geographic regions. The major strength of our study is the comprehensive analysis of national mortality data over an extended period, which allowed us to assess long-term trends in mortality rates and the impact of the COVID-19 pandemic.

This study had several limitations. The analysis was based on death certificates, which may introduce misclassification bias, since DD-related deaths may be underreported or attributed to other causes—particularly when other acute conditions such as sepsis or cardiovascular events are present. Our reliance on administrative cause-of-death data from death certificates is a recognized limitation, and we urge cautious interpretation of causal attributions. In addition, the analysis did not account for potential confounders, including individual-level factors such as socioeconomic status, healthcare access or dietary patterns, which could influence mortality trends. Although the post-COVID-19 period was defined as 2019-2022, our dataset contained finalized mortality records only up to 2020. Therefore, our interpretations of post-COVID trends are partly extrapolative and should be treated with caution. We also recognize that our dataset cannot fully disentangle deaths primarily caused by DD from those in which it was a contributing factor, particularly when COVID-19 was also involved. While we included both underlying and contributing causes where possible, the CDC guidelines designate only 1 underlying cause per death, potentially underestimating the burden of comorbid conditions.

Despite advances in diagnosis and management, mortality rates for DD remain disproportionately high among elderly, female and non-Hispanic white populations, with significant geographic disparities. The COVID-19 pandemic has further amplified these inequities, underscoring the importance of targeted public health efforts to address the unique needs of the vulnerable populations. Therefore, future research should focus on identifying modifiable risk factors and developing strategies to enhance early detection, optimize management, and promote equitable access to care for all patients with DD across demographic and geographic settings. Future research should also consider leveraging multiple cause-of-death data and clinical linkage studies to better capture the full scope of DD mortality, particularly in the context of co-occurring infections, such as COVID-19.

Summary Box

What is already known:

- Diverticular disease (DD) is a common gastrointestinal condition associated with significant morbidity and mortality, particularly among older adults
- The prevalence of DD has been rising in the United States, with substantial healthcare costs due to hospitalizations and complications, such as diverticulitis
- Prior studies have identified demographic disparities in DD-related outcomes, with higher mortality observed in females, the elderly, and non-Hispanic white populations
- The COVID-19 pandemic has disrupted routine healthcare services, potentially worsening chronic disease outcomes, including those related to DD

What the new findings are:

- Despite overall medical advances, DD-related mortality has increased in the post-COVID-19 era, particularly among elderly, female and rural populations
- Rural and non-metropolitan regions experienced significantly higher age-adjusted mortality rates, highlighting geographic disparities in access to care
- COVID-19-related disruptions appear to have exacerbated the existing demographic and geographic inequities in DD-related deaths, with notable increases in digestive and circulatory system-related mortality
- This study offers a comprehensive, national-level analysis over 2 decades using CDC WONDER data, underscoring the urgent need for targeted interventions to mitigate disparities in DD outcomes

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Supplementary material

Supplementary Table 1 Age-adjusted mortality rates per 100,000 for digestive system related deaths associated with diverticular diseases (1999-2020)

Demographics	Deaths, n	Population, n	Age-adjusted mortality rate per 100,000 (95%CI)
Entire cohort	70,648	4,473,854,489	1.5 (1.5-1.5)
Sex			
Female	47,432	2,319,297,578	1.6 (1.6-1.7)
Male	23,216	2,154,556,911	1.2 (1.2-1.2)
Age groups			
Young adults (25-44 years)	717	1,851,376,757	0.1 (0.1-0.1)
Middle age (45-64 years)	7,349	1,694,001,067	0.4 (0.4-0.4)
Elderly (>65 years)	62,582	928,476,665	6.8 (6.7-6.8)
Ethnicity			
Hispanic	3,611	589,350,210	1.1 (1.1-1.1)
Not Hispanic	66,902	3,884,504,279	1.5 (1.5-1.5)
Race			
American Indian	278	49,853,431	0.9 (0.8-1.0)
Asian	849	245,576,124	0.5 (0.5-0.5)
Black	5,237	546,447,527	1.2 (1.2-1.3)
White	64,284	3,631,977,407	1.6 (1.5-1.6)
Census Regions			
Northeast	13,400	827,193,779	1.4 (1.4-1.4)
Midwest	16,605	969,567,311	1.5 (1.5-1.6)
South	24,142	1,652,256,217	1.4 (1.4-1.4)
West	16,501	1,024,837,182	1.6 (1.6-1.7)
2013 Urbanization			
Large Central Metro	18,651	1,364,782,777	1.4 (1.4-1.4)
Large Fringe Metro	15,099	1,107,354,420	1.4 (1.3-1.4)
Medium Metro	15,007	918,036,376	1.5 (1.5-1.5)
Small Metro	7,175	405,040,249	1.5 (1.5-1.6)
Micropolitan (Nonmetro)	8,200	392,223,879	1.8 (1.7-1.8)
NonCore (Nonmetro)	6,516	286,410,290	1.7 (1.7-1.8)

CI, confidence interval

Supplementary Table 2 Age-adjusted mortality rates per 100,000 for circulatory system related deaths associated with diverticular diseases (1999-2020)

Demographics	Deaths, n	Population, n	Age-adjusted mortality rate per 100,000 (95%CI)
Entire cohort	17,405	4,473,854,489	0.4 (0.3-0.4)
Sex			
Female	11,398	2,319,297,578	0.4 (0.4-0.4)
Male	6,007	2,154,556,911	0.3 (0.3-0.3)
Age groups	90	1,851,376,757	0.0 (0.0-0.0)
Young adults (25-44 years)	1,150	1,694,001,067	0.0 (0.0-0.0)
Middle age (45-64 years)	16,165	928,476,665	1.7 (1.7-1.8)
Elderly (>65 years)			
Ethnicity	716	589,350,210	0.2 (0.2-0.3)
Hispanic	16,659	3,884,504,279	0.4 (0.4-0.4)
Not Hispanic			
Race	52	49,853,431	0.2 (0.1-0.2)
American Indian	226	245,576,124	0.1 (0.1-0.1)
Asian	1,531	546,447,527	0.4 (0.3-0.4)
Black	15,596	3,631,977,407	0.4 (0.4-0.4)
White			
Census Regions	3,308	827,193,779	0.3 (0.3-0.3)
Northeast	4,543	969,567,311	0.4 (0.4-0.4)
Midwest	5,776	1,652,256,217	0.3 (0.3-0.3)
South	3,778	1,024,837,182	0.4 (0.4-0.4)
West			
2013 Urbanization			
Large Central Metro	4,484	1,364,782,777	0.3 (0.3-0.3)
Large Fringe Metro	3,615	1,107,354,420	0.3 (0.3-0.3)
Medium Metro	3,513	918,036,376	0.3 (0.3-0.3)
Small Metro	1,845	405,040,249	0.4 (0.4-0.4)
Micropolitan (Nonmetro)	2,315	392,223,879	0.5 (0.5-0.5)
NonCore (Nonmetro)	1,633	286,410,290	0.4 (0.4-0.4)

CI, confidence interval

Supplementary Table 3 Age-adjusted mortality rates per 100,000 for circulatory system related deaths associated with diverticular diseases before (2016-2019) and after COVID-19 (2019-2022)

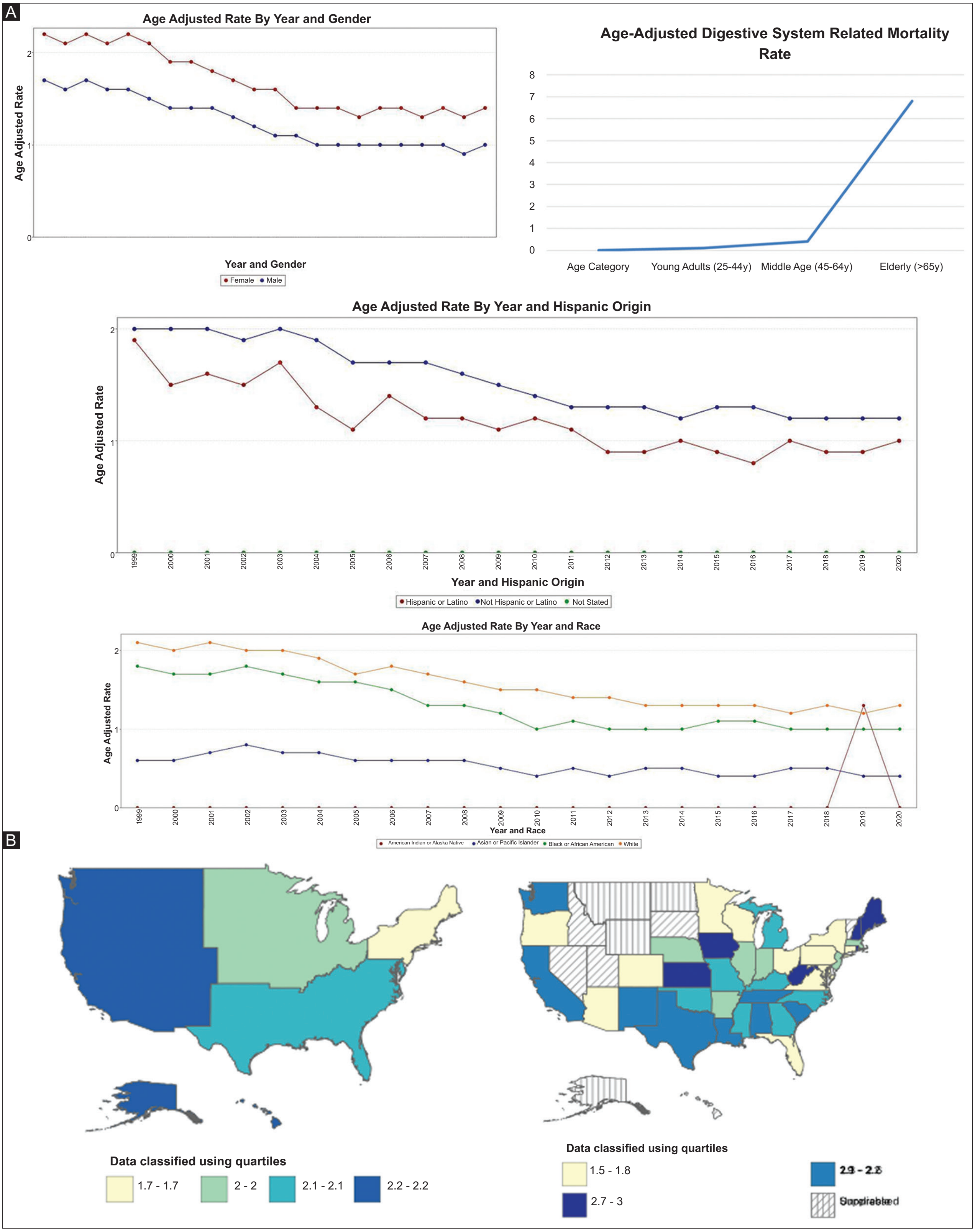
Demographics	Deaths, n	Population, n	Age-adjusted mortality rate per 100,000 (95%CI)
Entire cohort			
Before Covid-19	4,759	888,381,105	0.5 (0.5-0.5)
After Covid-19	5,437	909,363,191	0.5 (0.5-0.5)
Sex			
Female			
Before Covid-19	3,023	458,699,369	0.5 (0.5-0.5)
After Covid-19	3,412	467,150,152	0.6 (0.5-0.6)
Male			
Before Covid-19	1,736	429,681,736	0.4 (0.4-0.4)
After Covid-19	2,025	442,213,039	0.4 (0.4-0.5)
Age groups			
Young adults (25-44 years)			
Before Covid-19	-	-	-
After Covid-19	44	353,900,927	0.0 (0.0-0.0)
Middle age (45-64 years)			
Before Covid-19	453	335,848,207	0.1 (0.1-0.2)
After Covid-19	590	332,101,831	0.2 (0.2-0.2)
Elderly (≥65 years)			
Before Covid-19	4,268	206,592,330	2.2 (2.1-2.2)
After Covid-19	4,803	223,360,433	2.3 (2.2-2.4)
Ethnicity			
Hispanic			
Before Covid-19	338	135,408,977	0.4 (0.4-0.4)
After Covid-19	399	144,863,405	0.4 (0.4-0.4)
Not Hispanic			
Before Covid-19	4,412	752,972,128	0.5 (0.5-0.5)
After Covid-19	5,026	764,499,786	0.5 (0.5-0.5)
Race			
American Indian			
Before Covid-19	24	11,188,660	0.3 (0.2-0.5)
After Covid-19	23	10,513,082	0.3 (0.2-0.5)
Asian			
Before Covid-19	91	58,234,627	0.2 (0.1-0.2)
After Covid-19	90	57,109,536	0.2 (0.1-0.2)
Black			
Before Covid-19:	411	114,595,177	0.4 (0.4-0.5)
After Covid-19:	490	116,036,895	0.5 (0.4-0.5)
White			
Before Covid-19	4,233	704,362,641	0.5 (0.5-0.5)
After Covid-19	4,807	707,029,734	0.5 (0.5-0.6)
Census Regions			
Northeast			
Before Covid-19	943	157,160,688	0.5 (0.5-0.5)
After Covid-19	1,035	159,428,624	0.5 (0.5-0.5)
Midwest			
Before Covid-19	957	184,940,748	0.4 (0.4-0.5)
After Covid-19	1,109	187,430,429	0.5 (0.5-0.5)
South			
Before Covid-19	1,576	336,388,504	0.4 (0.4-0.4)
After Covid-19	1,857	347,122,925	0.5 (0.4-0.5)
West			
Before Covid-19	1,283	209,891,165	0.6 (0.5-0.6)
After Covid-19	1,436	215,381,213	0.6 (0.6-0.6)

(*Contd...*)

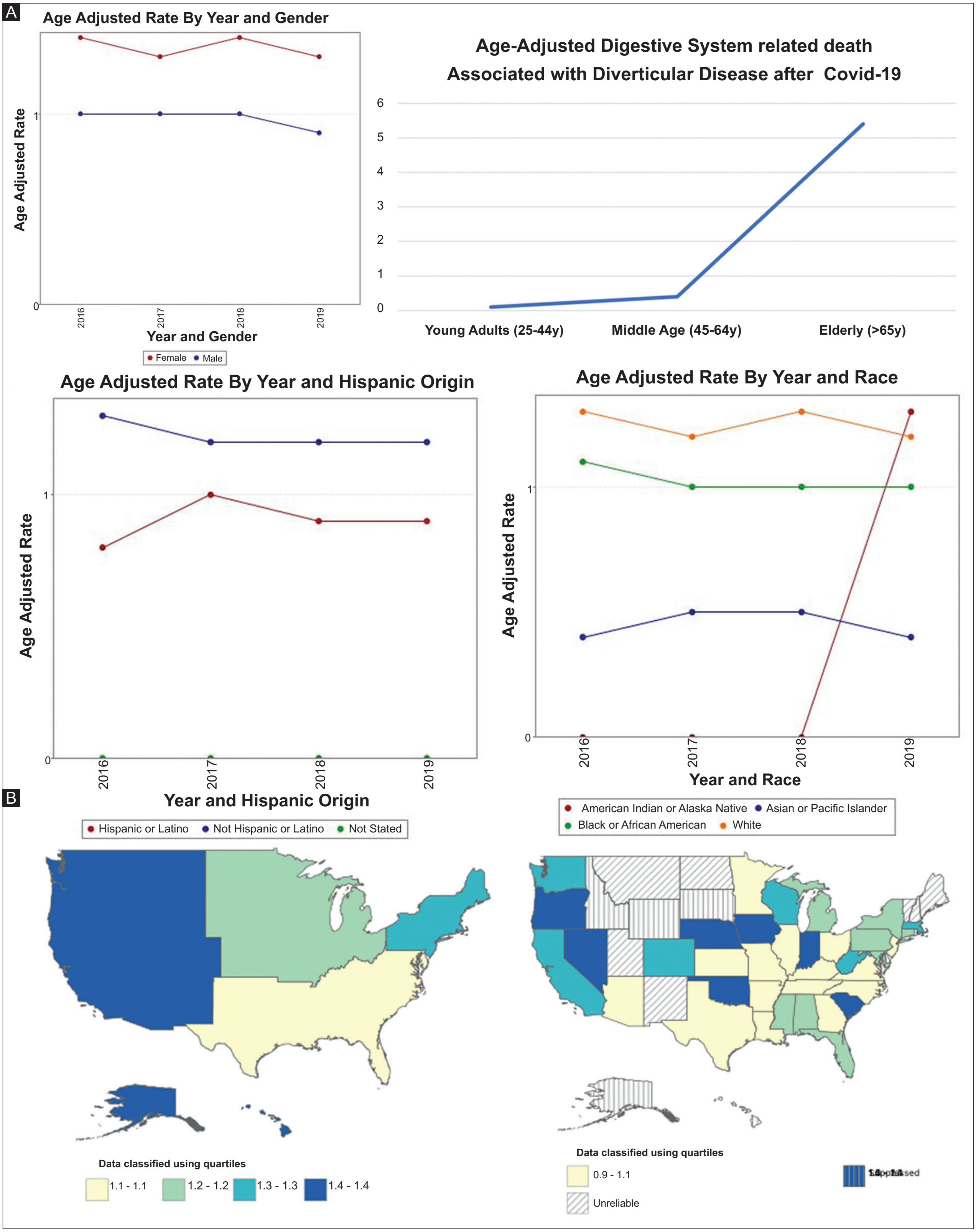
Supplementary Table 3 (*Continued*)

Demographics	Deaths, n	Population, n	Age-adjusted mortality rate per 100,000 (95%CI)
2013 Urbanization			
Large Central Metro			
Before Covid-19	1,339	274,826,096	0.5 (0.4-0.5)
After Covid-19	Not applicable	Not applicable	Not applicable
Large Fringe Metro			
Before Covid-19	1,035	223,127,096	0.4 (0.4-0.4)
After Covid-19	Not applicable	Not applicable	Not applicable
Medium Metro			
Before Covid-19	998	183,451,888	0.5 (0.4-0.5)
After Covid-19	Not applicable	Not applicable	Not applicable
Small Metro			
Before Covid-19	481	79,654,684	0.5 (0.4-0.5)
After Covid-19	Not applicable	Not applicable	Not applicable
Micropolitan (Nonmetro)			
Before Covid-19	540	74,330,971	0.6 (0.5-0.6)
After Covid-19	Not applicable	Not applicable	Not applicable
NonCore (Nonmetro)			
Before Covid-19	366	52,990,370	0.5 (0.4-0.5)
After Covid-19s	Not applicable	Not applicable	Not applicable

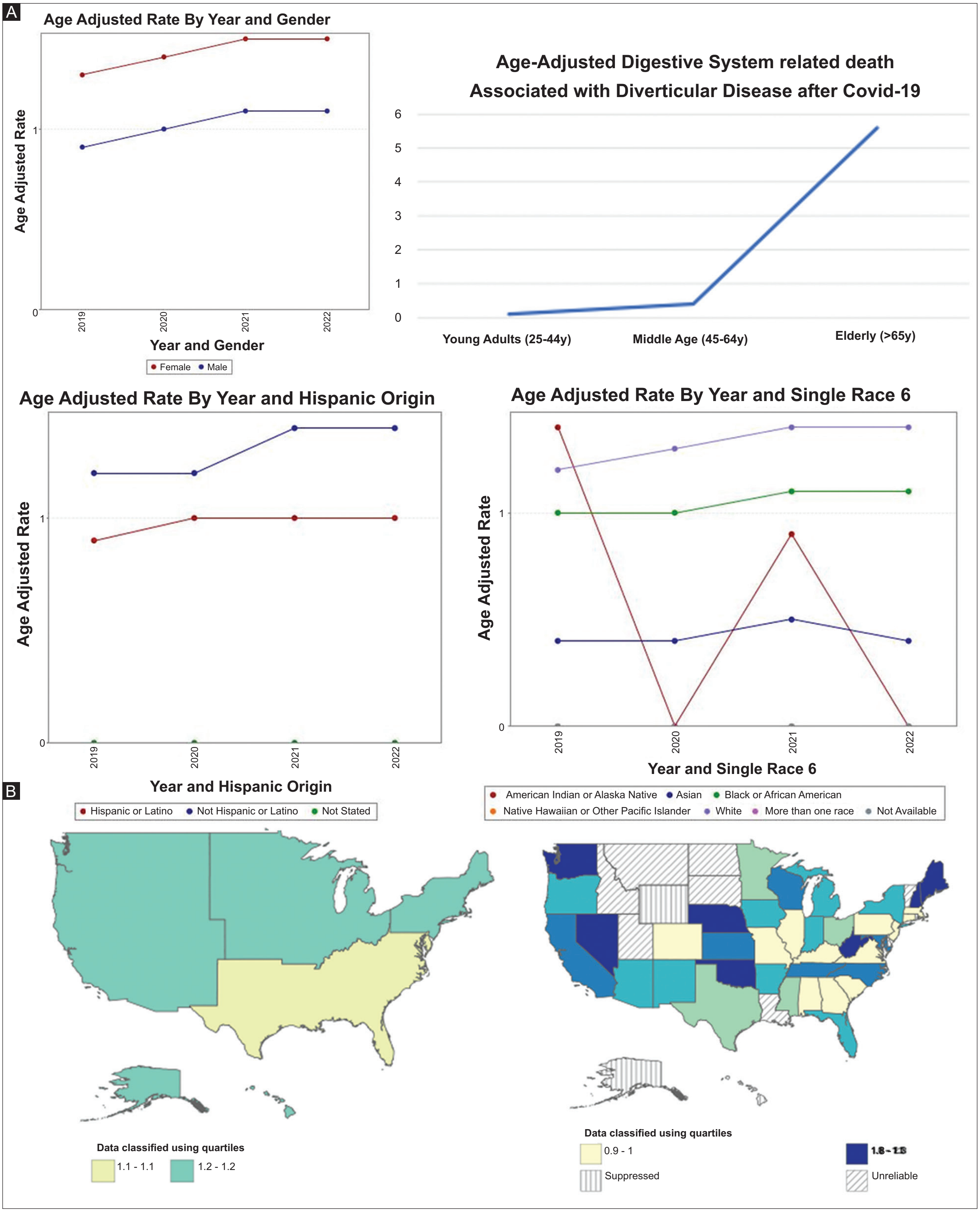
CI, confidence interval



Supplementary Figure 1 Age-adjusted mortality rate per 100,000 for digestive system-related deaths of diverticular disease (1999-2020) by: (A) sex, age categories, Hispanic/non-Hispanic origins, and race; (B) census regions and states within USA



Supplementary Figure 2 Age-adjusted mortality rate per 100,000 for digestive system related deaths of diverticular disease before Covid-19 (2016-2019) by: (A) sex, age categories, Hispanic/non-Hispanic origins, and race; (B) census regions and states within USA



Supplementary Figure 3 Age-adjusted mortality rate per 100,000 for digestive system related deaths of diverticular disease after Covid-19 (2019-2022) by: (A) sex, age categories, Hispanic/non-Hispanic origins, and race; (B) census regions and states within USA