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Original Research Article

Temporal trends in mortality from diverticular disease of the intestine with septicemia stratified by demographics: a retrospective study

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ABSTRACT

Background: Diverticular disease of the intestine is a major cause of mortality, and its association with septicemia remains underexplored. Understanding this relationship is essential to identify high-risk population and develop targeted public health interventions. The aim of the study is to analyze mortality trends and demographic disparities in diverticular disease of intestine with septicemia as a contributing cause using the CDC multiple causes of Death (MCD) database from 1999-2020.

Methods: A retrospective observational study was conducted using CDC MCD database to assess mortality trends in individuals aged 25 years and older in the United States From 1999-2000. The study included deaths where diverticular disease of intestine (ICD - 10: K57) was listed as the underlying cause and septicemia (ICD-10:A44) as a contributing cause. Data were analyzed by age, gender, race, geographic region, and place of death. Age- related mortality rates (AAMR) and annual percentage change (APC) were calculated.

Results: A total of 67310 Deaths were recorded. The AAMR for diverticular disease of intestine showed increase over time (APC). The highest mortality was observed in females, whites and temporal trends showed increase with disparities noted across demographic and geographic factors.

Conclusions: This study highlights significant mortality trends increasing in diverticular disease of intestine with septicemia, with disparities by gender, age and location. Findings underscore the need for targeted prevention strategies and improved healthcare success.

Keywords: Diverticular disease of intestine, Septicemia, Age-related mortality rate, Retrospective study, CDC MCD

INTRODUCTION

Diverticulosis is a common condition that can develop small pouches or pockets in the inside walls of the small intestine. They develop when the inside lining of the intestine pushes into weak spots in the outer wall. The term “diverticulosis” comes from the word “divert,” indicating that the path through your intestines is diverging into these side pockets. Several pouches are called “diverticula,” and

one pouch is called a “diverticulum”. They most commonly occur in the large intestine (colon), which is more likely to have denser food waste pushing against the weak spots, especially towards the sigmoid colon. If the infection develops and is left untreated for too long, it can lead to complications like sepsis, leading to frequent bleeding & could risk serious blood loss. The symptoms include lower abdominal pain or fever, and might have an infection (diverticulitis), irritable bowel syndrome (IBS) and constipation. Diverticular disease is a common

condition globally, especially in Western countries. Diverticulitis, Symptomatic, uncomplicated Diverticular disease, and Segmental Colitis associated with diverticula constitute diverticular disease. Although most patients with diverticula are asymptomatic, around 25% of patients will experience symptoms, whilst 5% of patients have an episode of acute diverticulitis.¹

The annual incidence of diverticulitis in the US is approximately 180 per 100,000 people, resulting in approximately 200,000 hospital admissions annually and an estimated health care expenditure of more than \$6.3 billion/year.² Incidence of diverticulitis is increasing. From 1980 to 2007, the incidence increased from 115 150 American Family Physician per 100,000 person-years to 188 per 100,000 person-years. The global Prevalence of diverticulitis is less than 10% in people older than 45 years vs. 80% in those older than 85 years. Only 1% to 4% of patients with diverticular disease will develop diverticulitis in their lifetime.³ In the U.S., 30% of people over 50, 50% of people over 60, and 75% of people over 80 have diverticulosis. Almost all of them have it in the last part of their colon (sigmoid colon). Diverticulosis is uncommon before the age of 40. It's also uncommon in parts of the world where the standard diet is less processed than in the West, such as Africa and Asia.⁴

Although diverticulosis is common, diverticular disease, in which there are clinical sequelae, is rare. This collective term includes diverticulitis, diverticular hemorrhage, and less well-defined entities such as segmental colitis associated with diverticulosis, and symptomatic, uncomplicated diverticular disease. The initial management includes antibiotics, with surgery reserved for complicated disease, although newer evidence questions the optimal role and timing of both interventions.⁵

Lower gastrointestinal hemorrhage can be seen in a smaller number of patients with colonic diverticulosis. Diverticulitis and non-complicated diverticulosis both have a tendency to bleed because the outpouchings, or diverticula, mainly appear where the vessels puncture the muscularis layer of the colonic wall.⁶ Diverticular bleeding is the source of 17 to 40 percent of lower gastrointestinal (GI) hemorrhage in adults, making it the most common cause of lower GI bleeding. In adults older than 65 years, diverticular hemorrhage can lead to significant morbidity, especially in those with hemodynamic instability and comorbid conditions.⁷

In the context of diverticulitis, sepsis typically develops when the infection in the colon wall breaks through, allowing bacteria to enter the bloodstream. Sepsis developing from diverticulitis is a serious, potentially fatal complication that requires immediate medical attention. When bacteria from an infected diverticulum escape into the bloodstream, body can launch an overwhelming inflammatory response that damages tissues, causes organ failure, and may lead to death if not promptly treated.

Recognizing the early warning signs of sepsis can be lifesaving when one has diverticulitis.⁸

By understanding the severity of the above medical conditions, more information is required to predict warning signs, seek prompt medical care, and implement prevention strategies. Hence, it becomes the utmost priority to study and analyze diverticular disease using databases like CDC WONDER, where one can get updated statistics regarding the comprehensive evidence, multiple causes of death, mortality, etc.

Thus, this study is beneficial in understanding the underlying trends resulting in diverticular disease and septicemia, to improve diagnosis and care, timely information and advice about diagnosis and management.

The aim of this study is to evaluate long-term national trends in mortality associated with diverticular disease of the intestine and septicemia in the United States from 1999 to 2020. The objectives are to quantify annual mortality patterns, calculate crude and age-adjusted rates per 1,000,000 populations, assess demographic and geographic variations, and analyze temporal changes using joinpoint regression.

METHODS

This retrospective population-based study utilized mortality data from the Centers for Disease Control and Prevention's Wide-ranging Online Data for Epidemiologic Research (CDC WONDER) Multiple Cause of Death (MCD) database.⁹ The dataset includes national, de-identified death certificate information; therefore, institutional review board approval was not necessary.¹⁰ The study covered 1999–2020, providing 22 years to evaluate patterns in mortality associated with diverticular disease of the intestine and septicemia. Data were accessed through the CDC WONDER online query interface, which allows customized extraction by ICD-10 codes and demographic characteristics.

Deaths attributed to diverticular disease of the intestine were identified using ICD-10 code K57 as the underlying cause of death (UCD). The ICD-10 code A41, which is a multiple cause of death (MCD), was used to record septicemia. Extracted variables included age group (restricted to adults aged 25 years or older), sex, and race. Race categories followed CDC WONDER classifications: American Indian or Alaska Native, Asian or Pacific Islander, Black or African American, and White. Geographic context was determined using the National Center for Health Statistics (NCHS) urban–rural classification system, which categorizes counties as large central metro, large fringe metro, medium metro, small metro, micropolitan, or non-core rural.¹¹ Place of death was classified into five categories: medical facility, decedent's home, hospice facility, nursing home/long-term care, and other. Records lacking essential demographic or diagnostic information were excluded

from the analysis.¹² Mortality measures included annual death counts, crude mortality rates, and age-adjusted mortality rates per 1,000,000 populations. Age adjustment followed the direct standardization method using the U.S. 2000 Standard Population to allow comparison across groups and over time.¹³ Rate calculations and descriptive statistics were generated using built-in CDC WONDER functions.

Temporal patterns were evaluated using the Joinpoint Regression Program (version 5.0 or later).¹⁴ This statistical approach identifies significant inflection points in mortality trends and calculates the annual percent change (APC) for each segment, along with the average annual percent change (AAPC) for the entire study period. All estimates were presented with 95% confidence intervals, and significance was defined as $p < 0.05$. Comparative analyses were conducted across demographic groups and place-of-death categories to identify disparities and assess whether mortality trends associated with K57 and co-occurring A41 varied by age, sex, race, urbanization level, or location of death.

RESULTS

In the year, 1990-2020, the CDC multiple cause of death (MCD) database recorded 28320 deaths in the United States Among individuals aged 25 years and older. Among these, deaths where diverticular disease of intestine (ICD: K57) was listed as underlying cause of death and septicemia (ICD-10: A44) was recorded as a multiple cause of death were included in the study. The crude mortality rates for diverticular disease of intestine with septicemia as a contributing cause was 5.2 per 1,000,000 populations. Deaths due to causes other than criteria were excluded.

The genders included were male and female. Among the total deaths analyzed, males accounted for ($n=21995$, 32.6 %), females accounted for ($N=45328$, 67.4%). The

mortality rate for diverticular disease of intestine with septicemia as a contributing cause was higher in females compared to males, indicating a potential demographic disparity.

The races included were American Indian, Asian or Pacific Islander, black or African American, white. Regarding racial distribution, the highest proportion of deaths occurred among white individuals ($n=61240$, 91%), followed by black or African Americans individuals ($n=4978$, 7.4%), Asian or Pacific Islander individuals ($n=813$, 1.2%), and American Indian or Alaska Native individuals ($n=252$, 0.4%). The mortality burden was highest among whites, highlighting racial disparities in mortality trends related to diverticular disease of intestine and septicemia.

Mortality based on urbanization was taken into account, including metropolitan and non-metropolitan areas, a majority of deaths occurred in metropolitan areas ($n=53294$, 79.3), while non-metropolitan areas accounted for ($n=13989$, 20.8 %) of deaths. Mortality based on place of death was also taken into account, for eg., medical facilities, decedent's home, nursing homes, and hospice facilities. Regarding the place of death, most deaths occurred in medical facilities ($n=47695$, 70.9%), followed by decedents' homes ($n=5502$, 11.6 %), nursing homes or long-term care facilities ($n=7817$, 8.2%) and hospice facilities ($n=2839$, 4.2%).

Overall temporal trends: The age-adjusted mortality rate (AAMR) for diverticular disease of intestine with septicemia as a contributing cause found that the mortality rates declined significantly from 1999 to 2011, followed by a period of stagnation from 2011 to 2020. The APC was -2.61 from 1999 to 2006 a significant decline; -4.88 from 2006 to 2011 the steepest and most declined; and -0.42 from 2011 to 2020 mortality rates plateaued, with a non-significant decline as represented in the figure 1.

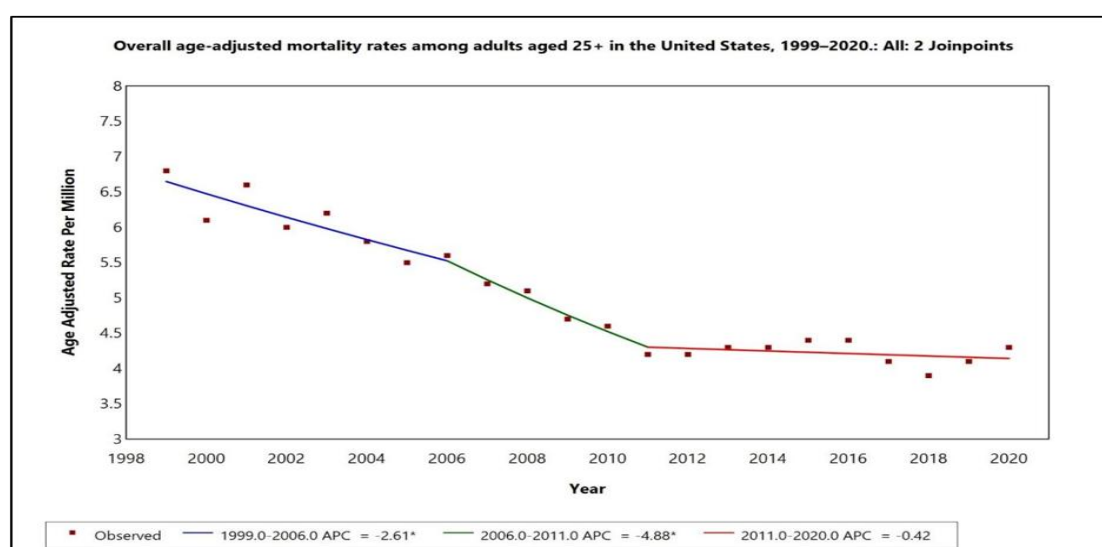


Figure 1: Overall age-adjusted mortality rates among adults aged 25+ in the United States, 1999–2020.

*Indicates that the Annual Percentage Change (APC) is significantly different from zero at $\alpha=0.05$ level.

Gender specific trends: Mortality declined significantly in both sexes from 1999 to approximately 2011, with steeper reductions in males, followed by a plateau in both groups and a persistent female mortality excess. The APC for females is -1.84 from 1999 to 2003 non-significant decline, for females is -1.84 from 1999 to 2003 non-significant decline,

-3.90 from 2003 to 2011 significant decline, -0.22 from 2011 to 2020 non-significant change. The APC for males is -3.08 from 1999 to 2008 the significant decline, -7.07 from 2008 to 2011 mortality declined most steeply and -0.23 from 2011 to 2020 with no significant change as represented in figure 2.

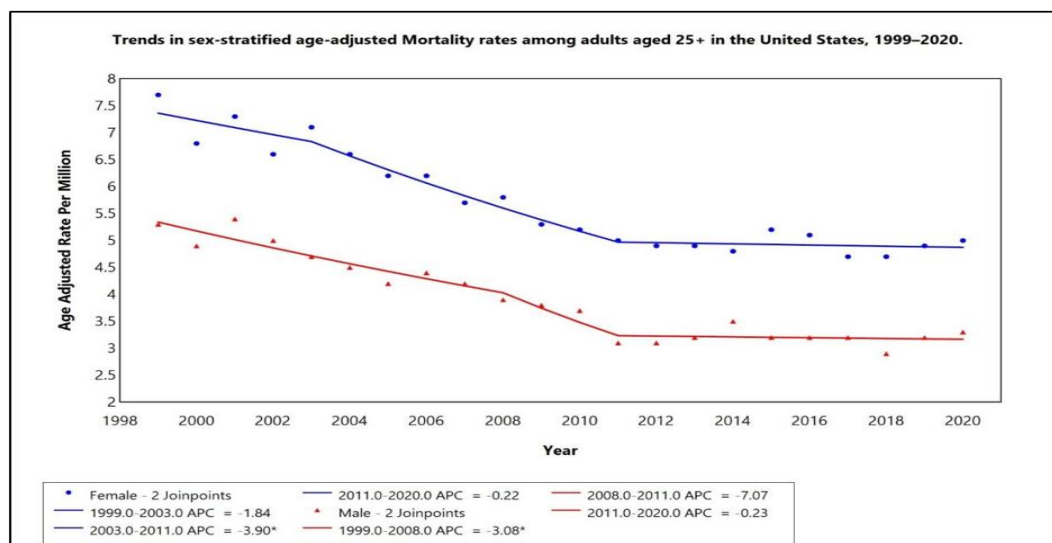


Figure 2: Trends in sex-stratified age-adjusted Mortality rates among adults aged 25+ in the United States, 1999–2020.

*Indicates that the Annual Percentage Change (APC) is significantly different from zero at $\alpha=0.05$ level.

Race specific trends: Racial disparities were observed in mortality trends. Mortality declined significantly in both racial groups until approximately 2011, after which rates plateaued among White adults but modestly increased among Black or African American adults. In white adults the APC was -2.76 from 1999 to 2006 a significant decline;

-4.45 from 2006 to 2011 a steeper significant decline and -0.28 from 2011 to 2020 a non-significant change, while in Black or African American adults the APC was -4.07 from 1999 to 2008 a significant decline; -7.30 from 2008 to 2022 sharpest significant decline; +0.77 from 2011 to 2020 with modest increase in mortality as shown in figure 3.

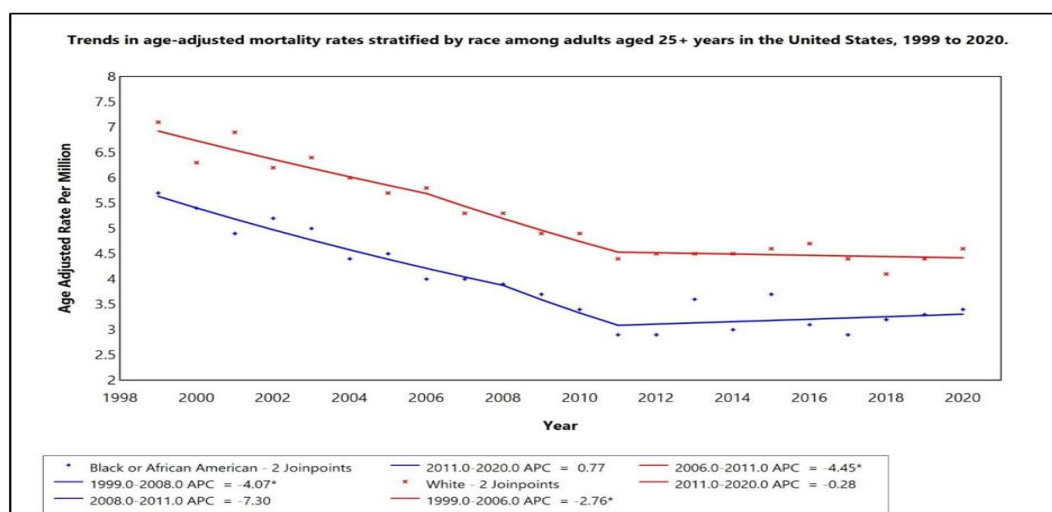


Figure 3: Trends in age-adjusted mortality rates stratified by race among adults aged 25+ years in the United States, 1999 to 2020.

*Indicates that the Annual Percentage Change (APC) is significantly different from zero at $\alpha=0.05$ level. Temporal trends for American Indian/Alaska Native and Asian or Pacific Islander are not displayed due to data suppression for counts <10 , limiting reliable trend analysis.

DISCUSSION

The total number of deaths due to diverticular disease of the intestine and Septicemia from 1999 to 2020 in the United States is at a crude rate of 5.2 per million. Our data demonstrate that, overall, AAMR (Age-adjusted Mortality Rates) for Diverticular disease and Septicemia from 1999-2020 showed a general decrease in mortality rates for patients aged 25 years and older.

The trend decreased gradually from 1999 to 2006, then steepened until 2011, after which it remained stable, with minimal decline from 2011 to 2020. Females had consistently higher AAMRs than men. The sex-stratified AAMR trends were consistent with overall trends. Among the races, the white population was observed to have higher AAMRs than the black or African-American population. The AAMR trends stratified by race were also consistent with the overall trends.

The incidence of diverticulitis increased by 50% from 1990-1999 to 2000-2007, and it was more common among younger people.¹⁵ Although the incidence of diverticulitis was increased, Diverticular disease and septicemia-related mortality were decreased in our study findings. This may be due to early use of empirical antibiotics and improvements in sepsis management over the years.

The presence of mucosal inflammation, which was seen on colorectal biopsies, was a predictor of increased mortality in colonic diverticular disease.¹⁶ This inflammation and associated infection and sepsis are most likely causes for increased complications and mortality rates. In a study from a general practitioner sample population in the UK, compared with patients with uncomplicated Colonic diverticular disease, patients with complicated diverticulitis have shown two times the risk of mortality.¹⁷

Although complicated diverticular disease and complications are associated with increased mortality, our study has shown decreased mortality trends over the years. In a previous study from the Center for Disease Control (CDC) mortality database, from 1999 to 2016, 68% of diverticulitis deaths involved women and were also more likely than men to experience severe diverticular disease and secondary causes of death due to infection, obstruction, perforation or fistulae.¹⁸ Our study findings are also consistent with trends showing increased mortality in women.

Broadly, isolated Colonic diverticular disease without severe complications is associated with a slight increase in mortality when compared to the general population and siblings. The risk of morbidity and mortality is increased due to progression to diverticulitis in colonic diverticular disease.¹⁶ Worldwide, there is marked variability in mortality rates associated with diverticular disease. In a study using the World Health Organization mortality database, developing nations had higher diverticular disease mortality than developed nations.¹⁹

There was one study derived from two multicenter observational studies, CIAO (Complicated Intra-Abdominal Infection Observational Study) and CIAOW (Complicated Intra-Abdominal Infection Observational World Study), which showed that factors associated with mortality included delays in initial intervention and critical care admission secondary to severe sepsis from diverticular disease and intra-abdominal infection.²⁰ The mortality trends shown in the current study showed a gradual decrease from 1999 to 2020, which is most likely secondary to early empiric antibiotic therapy for diverticulitis and intra-abdominal infection, and early recognition and resuscitation of associated septicemia patients.

Limitations

The current study has several intrinsic limitations, so the results should be interpreted with caution. There is a possibility of reporting errors in the cause of death on the certificate, which affects the accuracy of the data. Also, data on admission vital signs, comorbidities, lifestyle risk factors, including long-standing constipation and the severity of sepsis, are unavailable, which would help better understand the trends. Finally, the study also lacks information on social determinants of health, especially those related to healthcare access differences across races/ethnicities.

CONCLUSION

Current study from the CDC WONDER database on diverticular disease of the intestine and related mortality showed a steady decline from 1999 to 2011, followed by a flattening from 2011 to 2020. The white population and females had higher Age adjusted mortality rates. This study contributes to the literature on diverticular disease of the intestine and septicemia-related mortality by selectively highlighting demographic variations, including gender and race disparities. Further studies regarding finding risk factors and contributing comorbidities for increased mortality in the white population and the female gender need to be addressed. The decline in mortality from 1999 to 2020 is likely related to early recognition of diverticular disease from screening colonoscopies and, more importantly, early recognition and management of sepsis with administration of broad-spectrum antibiotics and adequate resuscitation per sepsis management guidelines.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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