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Original Research Article

A retrospective study to assess temporal trends in mortality for colon cancer and non-infective enteritis and colitis among U.S. adults, 1999-2020

Harshita Bedi[1], Nilay Pawanarkar[2], Chirag Golani[3], Deepak Singh[4], Neeraj Namasivayam[5]*

[1]Department of Surgery, KS Hedge Medical Academy, Mangaluru, Karnataka, India
[2]Department of Surgery, JJM Medical College Davanagere, Karnataka, India
[3]Department of Surgery, GMERS Medical College, Vadnagar, Gujarat, India
[4]Department of Surgery, Tbilisi, Georgia73 Chargali St, Tbilisi, Georgia
[5]Department of Surgery, Sri Lakshmi Narayana Institute of Medical Sciences, Puducherry, India

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***Correspondence:**
Dr. Neeraj Namasivayam,
E-mail: neerajnneeru@gmail.com

ABSTRACT

Background: Colon cancer and non-infective enteritis and colitis continue to be major causes of gastrointestinal deaths in the United States, despite improvements in screening, diagnosis, and treatment. This study to evaluate long-term mortality trends and demographic differences in colon cancer and non-infective enteritis and colitis among U.S. adults aged 25 years and older, between 1999 and 2020.
Methods: In this retrospective, STROBE-compliant study, data was obtained from the CDC Multiple Cause of Death database (1999-2020). Deaths were categorised by colon cancer (C18) as the underlying cause and non-infective enteritis and colitis (K50-K52) as a contributing cause. Age-adjusted mortality rates (per 1,000,000 population) and temporal trends were assessed using Joinpoint regression. Associations with sex, race, urbanization, and place of death were also evaluated.
Results: A total of 2,885 deaths were analyzed. Of these, 53.2% were males and 46.8% females; 92.1% were White and 6.4% Black; 80.9% lived in metropolitan areas, including 27.5% in large central areas. 47.6% of deaths occurred in medical facilities, 28.4% at home, and 13.1% in nursing homes. Mortality rates were higher among males and residents of metropolitan areas. Joinpoint regression revealed significant temporal changes in mortality over the study period.
Conclusions: Mortality from colon cancer and non-infective enteritis/colitis showed changes over time from 1999 to 2020, with overall declines but with higher mortality rates among males and those in metropolitan areas. These findings highlight the importance of improving screening, early detection, and targeted interventions to reduce disparities and improve outcomes in high-risk populations.

Keywords: Colon cancer, Non-infective enteritis/colitis, Mortality trends, United States

INTRODUCTION

Colorectal malignancies and chronic inflammatory conditions of the large intestine remain significant contributors to morbidity and mortality worldwide. In the United States, colon cancer (ICD-10 C18) continues to be a leading cause of cancer-related deaths, despite notable advances in screening and treatment. National surveillance data indicate a steady decline in age-adjusted colorectal cancer mortality over the past two decades, largely due to widespread colonoscopy screening and improvements in oncologic care.[1] However, this decline has not been uniform across all demographic groups;

disparities related to race, sex, and geographic location persist, highlighting the need for on-going trend analyses.[2]

In parallel, non-infective enteritis and colitis (ICD-10 K50-K52) including Crohn's disease and ulcerative colitis have shown variable mortality patterns in the U.S. population. Overall survival has improved with earlier diagnosis and the advent of biologic therapies, yet recent data suggest a modest rise in age-adjusted mortality among older adults and individuals in non-metropolitan regions.[3] These contrasting trends underscore the importance of examining temporal changes in disease-specific mortality across different population strata.

Joinpoint regression analysis provides a robust statistical framework to evaluate such trends. By fitting segmented linear models to long-term data, this method identifies significant "joinpoints," where the direction or rate of change in mortality trends shifts.[4] It also allows calculation of annual percent change (APC) and average annual percent change (AAPC), providing insights into whether mortality rates are increasing, decreasing, or remaining stable within specific subgroups. Applying joinpoint regression to U.S. death-certificate data helps pinpoint periods of epidemiologic transition and relate them to public health initiatives or evolving clinical practices.

In this observational, review-based study, we analysed national mortality data from the Centers for Disease Control and Prevention (CDC WONDER) covering 1999-2020. Our aim was to characterize trends in deaths attributed to colon cancer (C18) and non-infective enteritis/colitis (K50-K52) among adults aged >25 years. By examining demographic and urbanization subgroups, we sought to identify differential trend patterns and highlight areas where healthcare policy and preventive interventions may be optimized. The main aim of this study is to assess temporal trends in mortality for colon cancer (ICD-10 C18) and non-infective enteritis/colitis (ICD-10 K50-K52) among U.S. adults aged > 25 years from 1999 to 2020 using joinpoint regression analysis, and to evaluate demographic and regional differences in these trends.

METHODS

Study design and setting

This retrospective observational study (STROBE-compliant)5 analyzed United States mortality trends from 1999 to 2020. Using publicly available, de-identified CDC-MCD database data, the research was exempt from formal Ethics Committee approval.[6-8]

Study population and data source

We analyzed available mortality records from the U.S. population aged more than or equal to 25 years across the 1999-2020 periods that met the specified criteria. The data was sourced from the Centers for Disease Control and Prevention (CDC) WONDER Multiple Cause of Death (MCD) database.[9] Case identification utilized the International Classification of Diseases, Tenth Revision (ICD-10) codes.[10] Inclusion criteria required deaths with malignant neoplasm of colon (ICD-10 C18) as the underlying cause of death and non-infective enteritis and colitis (ICD-10 K50-K52) listed as a multiple cause of death. Records with suppressed data or those outside the age range were excluded.

Variables and data extraction

Mortality data was extracted using a sequential, step-by-step approach from the CDC WONDER 9 database. The database was initially filtered for all deaths in the United States between 1999 and 2020, and the inclusion criteria were then applied. Finally, the deaths were stratified by the following key variables: Gender (Male, Female), Race (American Indian/Alaska Native, Asian/Pacific Islander, Black/African American, White), Urbanization (Metropolitan/Non-Metropolitan areas), and Place of Death (e.g., Medical Facility, Decedents' home). For each stratum, age-adjusted mortality rates were calculated per 1,000,000 populations, standardized to the 2000 U.S. standard population.[11]

Statistical analysis

Comparison of group differences

The statistical significance of differences in age-adjusted mortality rates between various demographic strata (e.g., sex, race) was determined using a two-sided statistical test for the comparison of two age-adjusted rates, utilizing the standard errors of the rates.

Temporal trend analysis

Temporal trends were analyzed using the Joinpoint Regression Program 4, Version 5.3.0.0 (November 2024). Joinpoint analysis was performed on overall mortality rates, and rates stratified by sex and race. The analysis utilized the Monte Carlo permutation test to select the optimal number of trends change points (joinpoints), allowing for a maximum of three segments. This method estimated the Annual Percentage Change (APC) for each identified trend segment. The statistical significance of the APC, tested against the null hypothesis that the trend was zero, was determined using a two-tailed t-test. Trends were considered statistically significant if the 95% Confidence Interval for the APC did not include zero (i.e., different from zero at the alpha = 0.05 level)

RESULTS

According to the data gathered between 1999 and 2020 a total of 2,885 deaths were recorded amongst adults aged 25 and above with Malignant Neoplasm of the Colon

(C18) as the underlying cause of death. These primarily represented cases among American Indian or Alaska Native populations in the United States. Out if the 2,935 initially screened cases from the CDC Multiple Cause of Death (MCD) database, 50 were excluded because of suppressed data (counts <10, as per CDC data confidentiality policy). The final analysis was made based on disease, demographic and variable correlation evaluation.

Disease characteristics

Malignant Neoplasm of the Colon (C18) is considered as the primary condition for underlying cause of death, while noninfective enteritis and colitis (K50–K52) as the secondary cause.

Demographic characteristics

The total number of cases was divided based on geographic distribution, metropolitan areas accounted for 80.9% of all deaths, with the highest proportion from large central metro (27.5%), followed by large fringe metro (23.5%), medium metro (20.4%), and small metro (9.5%). The remaining 19.1% occurred in non-metropolitan regions (micropolitan 10.8%, non-core 8.3%). The majority of them were White (92.1%), followed by Black or African American (6.4%) and Asian or Pacific Islander (1.5%). Finally based on their gender out of the 2,885 deaths 1,536 (53.2%) were male and 1,349 (46.8%) were female.

Place of death and urbanization

Almost half of all deaths (47.6%) occurred in medical facilities, followed by decedent's home (28.4%), nursing homes/long-term care facilities (13.1%), and hospice facilities (6.9%). A majority of deaths occurred in metropolitan areas 2,332 (80.9) while non-metropolitan areas accounted for 553 (19.1) deaths.

The overall results represent that disparities in mortality due to Colon Cancer were quite evident based on this analysis conducted in the United States. Mortality was more evident amongst the residents of metropolitan areas particularly the Male gender. Most deaths occurred within hospital settings, emphasizing the need for early diagnosis, community-based screening, and improved palliative care access.

Overall temporal trends

The overall mortality trend for the study population shows a gradual decline from 1999 to 2006 (APC = –1.94), followed by a sharp decrease between 2006 and 2009 (APC = –14.31). After 2009, however, the trend shifted to a slow but steady rise in mortality extending through 2020 (APC = 1.06), as represented in Figure 1. This figure highlights two major inflection points, one in the mid-2000s where rates fell significantly, and another around 2009 where the trend reversed direction. The upward trajectory after 2009 suggests a gradual resurgence in mortality.

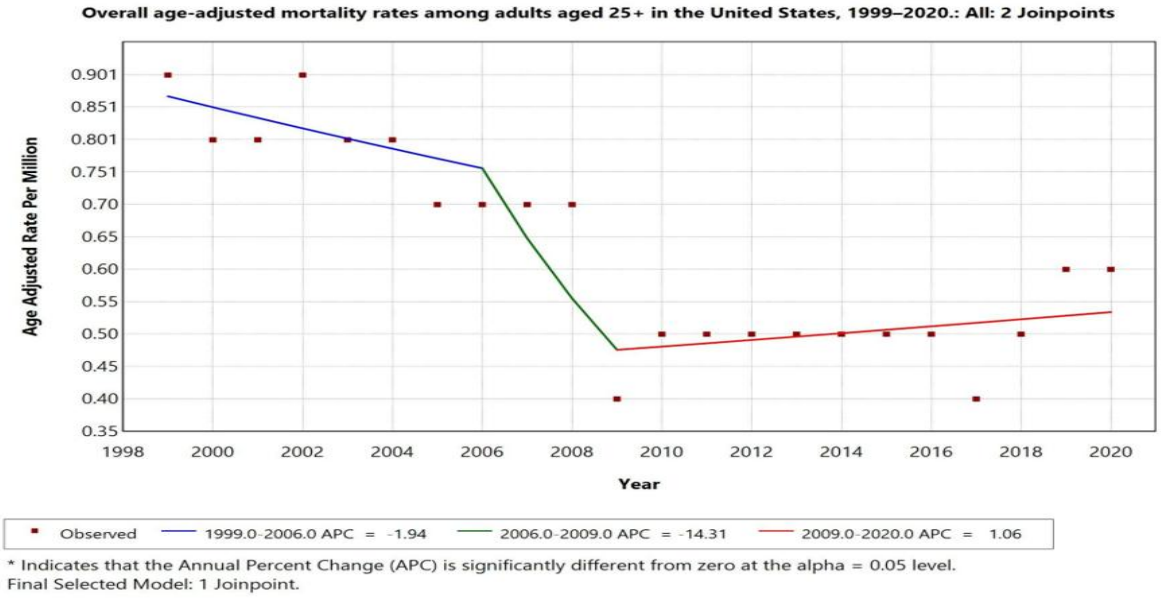

Figure 1: Overall age-adjusted mortality rates among adults aged 25 + in the United States, 1999–2020.

Sex-specific trends

When stratified by sex, males, mortality declined steadily between 1999 and 2005 (APC = –2.67), followed by a steeper decline from 2005 to 2017 (APC = –4.32). After 2017, an increase in the number of cases was seen, with rates increasing sharply through 2020 (APC = 13.30). Female mortality followed a similar pattern, though with

slightly lower mortality rates throughout the study period. Female mortality declined modestly from 1999 to 2002 (APC = –0.34), followed by a substantial decline between 2002 and 2017 (APC = –5.01). After 2017, female mortality increased markedly (APC = 14.49), as shown in Figure 2. Overall, both sexes demonstrated a long-term declining trend followed by an abrupt increase in the late 2010s, with males consistently exhibiting higher mortality rates across all years.

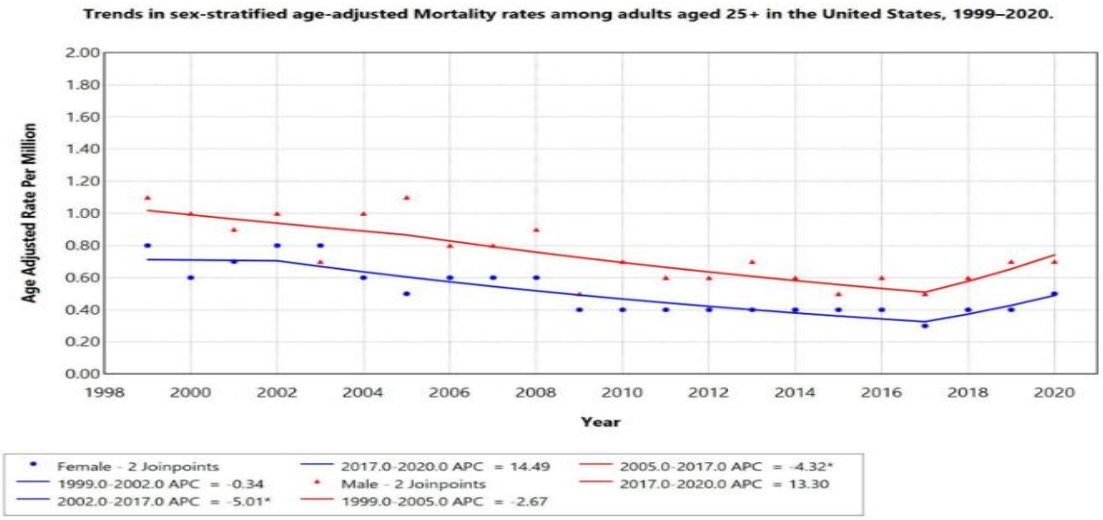

Figure 2: Sex-stratified trends in age-adjusted mortality rates among adults aged 25 + in the United States, 1999–2020.

Race-specific trends

Figure 3 displays white adults, the only racial subgroup with sufficient data for trend analysis. Mortality rates decreased significantly from 1999 to 2015 (APC = –3.92), representing the longest sustained decline observed across any demographic subgroup. This was followed by a period of relative stability from 2015 to 2018 (APC = –0.64). Beginning in 2018, the trend reversed sharply, with mortality rising substantially through 2020 (APC = 18.75). The steep increase seen in the later decade suggests a concerning increase in mortality in recent years after nearly 2 decades of improvement.

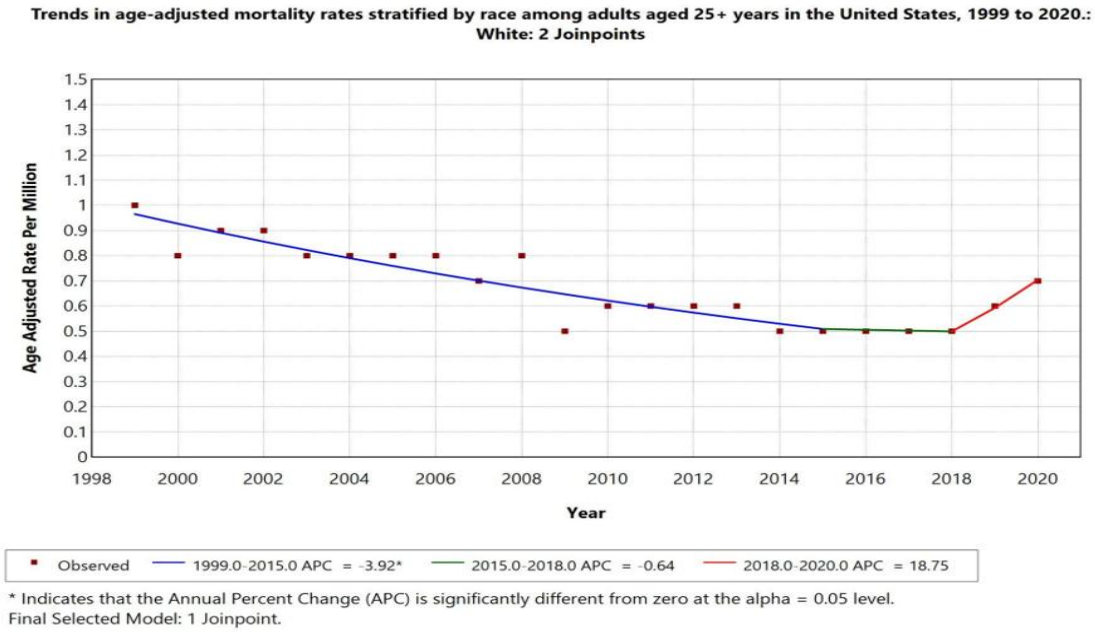

Figure 3: Race-stratified trends in age-adjusted mortality rates among White adults aged 25+ in the United States, 1999–2020.

DISCUSSION

Our analysis of 1999–2020 U.S. mortality data collected using CDC WONDER brings to light noteworthy mortality trends among colon cancer and non-infective enteritis/colitis (IBD). Across the study period, 2,885 deaths were discovered, aligning with a crude mortality rate of 0.6 per million. Colon cancer mortality has declined remarkably over the past two decades reflecting adequate screening methods and better treatments.[1-12] However there are existing differences based on gender, race, and age in CRC-associated mortality.[12]

Our study showed that males accounted for 53.2% of deaths, exceeding females by 7%. This male predominance in our study is a reflection of several national reports. Colorectal cancer (CRC) mortality declined from 20.7 to 12.5 per 100,000 between 1999 and 2020, yet men consistently exhibited higher mortality than women (18.8 vs 13.4 per 100,000).[1] Also, males showed a consistently higher Age associated mortality rate than females in a study conducted in 2024.[12]

Our analysis found that CRC mortality among White individuals comprised 92.08%, preceding all other racial groups due to the high population of white individuals in the United States. However, based on US national rates, incidence and mortality rates of colorectal cancer among Black persons were initially higher than White persons. Variance in screening methods and quality as well as the differences in compliance with follow-up and treatment could be reasons for the higher rates of mortality among black individuals.[13] It can also be due to differences in insurance coverage and increased comorbidity burden.[14] It was established that the difference between mortality rates among black and white individuals dropped from 21.6 cases to 1.6 cases per 100,000 in a study conducted over the time period of 2007 to 2017.[13] Hence, the racial gaps were narrowed but disparities remain. New strategic plans that address structural racism are critical for closing the racial gaps completely by ensuring multilevel interventions.[14,15] In this study, Black or African Americans accounted for 6.4%, and Asian or Pacific Islanders 1.53%.

Joinpoint regression analysis identified significant annual percentage changes (APC) in age-adjusted mortality rate (AAMR) overall and within sex-stratified groups. Early-onset colorectal cancer mortality is curiously rising, despite overall declines. Younger adults (<50) experienced upticks in deaths with the U.S. crude mortality rate increasing significantly during 2011-2020.[16-18] Hypotheses include lifestyle changes and microbiome shift.[17-19] This has prompted lowering the screening age to 45 and focusing on the need to expand screening access for younger individuals since most of them get diagnosed at later stages of the disease.[19]

In contrast, mortality directly from IBD is very low. Decreased age-adjusted mortality rates among adults with IBD from 1999-2018, reflecting biological therapies and multidisciplinary care.[13] Yet, after 2018, mortality increased sharply. Crohn's disease mortality rose from 0.79 to 0.97 per 100,000, with a significant APC of +11%; ulcerative colitis showed similar rises (+12%).[20,21] This coincided with COVID-19 disruptions and several studies suggested exacerbation of IBD during the pandemic due to certain risk factors like male sex, use of corticosteroids, and a decrease in screening and treatment facilities due to high demand whether this is a transient irregularity or a persistent shift requires monitoring.[22-24] Stratifying results reveals deeper insights that are hidden in the overall findings. Males account for higher mortality rates due to IBD which is in line with our study (53% male deaths).[25] But sex patterns differ by subtype: the female gender appears to be a promoting factor in CD onset, whereas it may exert a protective role in UC.[26] Males older than 45 years of age appear to have a 20% higher incidence rate of UC compared to women.[27]

Whites accounted for >90% of deaths, consistent with epidemiology, though prevalence is rising in non-White groups.[20] Urban areas recorded >80% of deaths, but some studies report higher IBD mortality in rural regions, likely due to limited specialist access.[28] Nearly half of IBD deaths occurred in hospitals, suggesting acute complications (perforation, sepsis) often precede fatal outcomes, unlike colon cancer where end-of-life care often occurs at home or hospice.[29] In summary, colorectal cancer mortality has fallen steadily over the past two decades, reflecting the benefits of early detection and improved therapies, yet disparities by sex, race, and age remain. The continued higher mortality among men, the narrowing but persistent racial gap, and the rising burden of early-onset disease shows areas of concern. Overall mortality for IBD is low, but the recent increase following 2018 and the high proportion of hospital-based deaths point to acute complications and gaps in on-going care. These findings highlight the need for suitable attention to equity in prevention and treatment, as well as system-level strategies that can address both chronic disease screening and management.

Limitations

This study has several limitations. Firstly, the use of CDC WONDER mortality data depends on accurate death certificate reporting. Errors in classification may have influenced the results. Second, the analyses of racial and ethnic subgroups were limited by data suppression for smaller populations, thus restricting interpretation of trends in suppressed groups. Third, while joinpoint regression identified shifts in mortality trends, individual-level confounders such as socioeconomic status, comorbidities, or healthcare access could not be incorporated. These factors are likely contributed to the observed disparities across sex, race, and geography. Similarly, broad classifications were used for urban-rural mortality analysis that may not capture variations in healthcare infrastructure or specialist availability. Our

analysis lacked detailed clinical information, such as stage at diagnosis, treatment regimens (e.g., use of biologics, immunosuppressants, or chemotherapy), adherence, disease duration. Similarly, place-of-death variables are derived from death certificates and may be influenced by reporting practices rather than true clinical patterns.

Finally, the increase in IBD mortality following 2018 was temporally associated with the COVID-19 pandemic, but causality cannot be inferred from population-level data. Patient-level studies are needed to clarify whether treatment delays, corticosteroid use, or infection-related complications were responsible. Despite these limitations, the study's large sample size and long follow-up period provides a broad overview of mortality patterns and highlights important areas for future research.

CONCLUSION

In summary, colorectal cancer mortality in the United States has declined steadily from 1999 to 2020, showing advances in screening and treatment. However, disparities persist. Men continue to face higher mortality than women, racial gaps remain despite narrowing, and early-onset colorectal cancer is increasing, emphasising the need for targeted prevention and earlier screening in younger adults.

For inflammatory bowel disease, mortality remains comparatively low but has risen since 2018. The timing suggests a link to COVID-19-related healthcare disruptions, although further research is needed to establish causation. The finding that nearly half of IBD deaths occur in hospitals emphasizes the role of acute complications and highlights the importance of timely intervention and specialist access.

Overall, the results demonstrate both progress and on-going challenges in gastrointestinal disease outcomes. While increased knowledge about preventive strategies and therapeutic innovation has reduced colorectal cancer mortality, inequities in certain areas continue to shape outcomes. Sustained investment in adequate screening, management, and structural reforms will be critical to ensuring that future gains in survival are distributed more evenly across all populations.

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