The national burden of inflammatory bowel disease in the United States from 1990-2019: results from the Global Burden of Disease study database

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Abstract

Background Inflammatory bowel disease (IBD) epidemiology has changed rapidly in recent years. We aimed to provide a systematic report of the burden of IBD at a state level in the United States (US), and to study the age- and sex-specific trends of incidence, prevalence and mortality rates for the past 3 decades.

Methods Using the Global Burden of Disease (GBD) 2019 Study Database, we examined the incidence, prevalence and mortality rate, and the disability-adjusted life-years from GBD 2019 at national and state level from 1990-2019.

Results There was an overall decrease in incidence and prevalence rates of IBD in the US from 1990-2019, while a simultaneous increase in the overall mortality rates was identified. However, a distinct trend of increasing incidence and prevalence rates emerged starting in 2000, with incidence rates rising from 21 cases per 100,000 persons in 2000 to 23 cases per 100,000 persons in 2019. From 1990-2019, incidence and prevalence decreased in males at a higher rate than in females. However, mortality rates increased more in females than males. Incidence rates were highest in Midwestern and Eastern states, and were lowest across the northern Great Plains and Western states, with the highest incidence noted in Michigan (31 cases per 100,000 persons). California had the greatest decrease in incidence rates from 1990-2019 (-63.3%).

Conclusion Our results concerning recent trends and geographic variations in IBD offer policymakers crucial insights for informed decision-making in policy, research, and investment, facilitating more effective strategies and allocation of resources.

Keywords Inflammatory bowel disease, epidemiology, burden, trends, mortality

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Conflict of Interest: None

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Introduction

Inflammatory bowel disease (IBD) is characterized by idiopathic chronic inflammation of the gastrointestinal tract, comprising Crohn's disease and ulcerative colitis [1]. Although the etiology is yet to be completely understood, it has been hypothesized to be the result of an inappropriate immune response in genetically-prone individuals [2]. IBD is now being found in every population around the globe, shattering ethnic and geographic boundaries. In the absence of a cure, the economic burden of this lifelong disease on healthcare systems and governments worldwide has been rapidly increasing. In the United States (US) alone, annual costs have been estimated to exceed $25 billion dollars in 2016, making IBD one of the top 5 most expensive gastrointestinal conditions [3]. Thus, understanding the epidemiological trends within the US is imperative to effectively address the impact of IBD on both healthcare and economic fronts.

The resultant burden due to IBD can vary considerably by geographic location, sex and age group [4,5]. Accurately assessing the incidence, prevalence and mortality rates of IBD in these demographics remains an ongoing challenge. There remains a paucity of comprehensive data regarding the disease burden specific to geographic location, sex and age at a more granular state level within the US [6]. This information is valuable in order to appropriately and effectively allocate both medical and financial resources throughout the country.

The Global Burden of Disease (GBD) 2019 framework provides comprehensive epidemiological data on incident cases, deaths and disability-adjusted life years (DALYs) of 369 diseases and injuries across a range of 204 countries and territories. While the global IBD burden has been thoroughly described based on the GBD 2019 study [7,8], the available information about its effect on individual states and the recent disease burden trends is notably deficient. Therefore, we aimed to provide a systematic report of the IBD burden, including incidence, prevalence, mortality and DALYs at a state level in the US. Additionally, we aimed to study the age- and sex-specific incidence, prevalence and mortality rates trends of IBD in the US from 1990-2019, using the GBD 2019 database.

Materials and methods

Background

A population-based time-trend analysis of IBD incidence, prevalence and mortality rates in the US from 1990-2019 was conducted from the GBD 2019 study database. This is a publicly accessible database containing anonymized, de-identified data. The institutional review board's policy deemed this study exempt from review based on the recommendations of the National Human Research Protections Advisory Committee.

Data source

IBD incidence, prevalence, and death rates in the US between 1990 and 2019 were gathered from the GBD 2019 study. The GBD 2019 methodically and comprehensively evaluated 286 causes of death, 369 illnesses and injuries, and 87 risk factors for 204 nations and territories. The GBD 2019 study was conducted by the Institute for Health Metrics and Evaluation at the University of Washington. The GBD study provides a comprehensive and comparable analysis of various health metrics, such as incidence, prevalence, death and DALYs, for various diseases and injuries, as well as demographic and geographical variations.

Data sources and methods for GBD 2019 study estimate have been previously outlined in detail [9-11]. Briefly, the population counts for each state were acquired from the US Census Bureau. Structured literature reviews were conducted to find published and unpublished incidence, prevalence, case fatality, and mortality data associated with IBD. The National Center for Health Statistics provided state-specific information on death certificates. The International Classification of Diseases (ICD)-9 and ICD-10 codes (ICD-10: K50-K51.319, K51.5-K52, K52.8-K52.9) (ICD-9: 555-556.9, 558-558.9, 564.1, 569.5) were obtained for each IBD case definition and used to determine the yearly incidence, prevalence and mortality rates for IBD, stratified by age, sex, year and state. Cause of Death Ensemble model (CODEm), spatiotemporal Gaussian process regression (ST-GPR), and the Bayesian meta-regression tool DisMod-MR were the main methods used to estimate the prevalence, incidence, deaths and DALYs by cause, age, sex, year and location for the GBD 2019 study [10]. The GBD 2019 Data Input Sources Tool webpage contains detailed information on the original data sources utilized in the present study [https://ghdx.healthdata.org/gbd-2019/data-input-sources].

Definitions

Age-standardized rate was defined as a weighted average of the age-specific rates, where the weights are the proportions of a standard population in the corresponding age groups. The number of patients diagnosed with IBD per 100,000 in a particular calendar year was described as the incidence. The mortality rate was defined as the number of deaths per 100,000 population attributable to IBD in a particular calendar year. The annual percentage change (APC) was defined as the percentage change in IBD incidence, prevalence or mortality rates between consecutive years, whereas the average APC (AAPC) was defined as the mean percentage change per year for the whole study period. Increasing and decreasing trends were defined as statistically significant positive and negative values of APC or AAPC, whilst statistically non-significant values were taken as indicating stability. The population was divided into 2 age categories based on a 50-year cutoff: older adults (50-79 years) and younger adults (15-49 years).

Statistical analysis

The Joinpoint Regression Program, v5.0.2 (NCI), which builds best-fit models for a sequence of logarithmic data, was used to quantify temporal trends [12]. The joinpoint regression model, a collection of linear statistical models, was employed to assess the temporal trends in disease burdens associated with IBD. This model uses the least squares method to estimate the

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changing patterns of illness rates, thus mitigating the subjectivity inherent in conventional trend analyses based on linear trends. By calculating the sum of squared residuals between the estimated and actual values, the joinpoint regression model identifies the turning point where the trend shifts [13]. The analysis was performed with a minimal number of joinpoints (zero, indicating a straight line), followed by model-fitting tests with a maximum of 5 joinpoints. The program employs Monte Carlo permutation analysis to determine the minimum number of joinpoints required to construct a segmented line that depicts time-dependent change [13]. The APC and AAPC were computed using parametric estimates and a 2-sided *t*-test to determine statistical significance [14]. A pairwise comparison was made to determine parallelism and homogeneity. The parallelism test determines if the 2 segmented linear regression mean functions are parallel. The statistical significance of the absolute difference between the AAPCs was estimated using a Taylor series expansion. A P-value <0.05 was considered statistically significant in all analyses.

Results

IBD burden in the US

In 2019, there were 762,890 cases (95% confidence interval [CI] 712,357-813,654) of IBD in the US (56.4% were women). Despite an increase in absolute numbers of IBD cases from 1990-2019, age-standardized incidence and prevalence rates decreased between 1990 and 2019. The overall age-standardized incidence rates (ASIRs) of IBD in the US decreased from 35 (95%CI 30-40) per 100,000 population in 1990 to 23 (95%CI 21-25) per 100,000 population in 2019. The decrease in ASIRs was greater in men (-33%) compared to women (-31%). Females had a higher ASIR in 2019 than males, 23.5 (95%CI 21.5-25.5) per 100,000, vs. 22.8 (95%CI 20.8-24.8) per 100,000. The age-standardized mortality rate (ASMR) increased for both sexes by 53% from 1990-2019. Age-standardized DALYs decreased for both sexes, with a larger decrease for men (26% vs. -20%) (Table 1).

ASIRs

ASIR by state

Overall, the ASIRs declined in all states from 1990-2019. Initially, rates dropped from 35 (95%CI 30-40) in 1990 to 21 (95%CI 19-23) per 100,000 in 2000. There has been an uptrend since 2000, reaching 23 (95%CI 21-25) per 100,000 in 2019. ASIRs were highest in many Midwestern and Eastern states and lowest across the northern Great Plains and Western states. The highest ASIR was noted in Michigan, 31 (95%CI 28-34) per 100,000, followed by West Virginia and Kentucky (Fig. 1A). There was a wide geographical variation in the percentage of this decline between 1990 and 2019, with the largest percentage change occurring in California (-63.3%) (Fig. 1B). In 2019, incidence rates were nearly similar in men and women (22.89 and 23.53 per 100,000 persons, respectively) (Supplementary Table 1).

ASIR by sex

Over 30 years, there was an overall decrease in ASIRs among men (AAPC -1.5%, 95%CI -1.6% to -1.4%; P<0.001) and women (AAPC -1.2%, 95%CI -1.3% to -1.1%; P<0.001), with an absolute AAPC difference of 0.2% (95%CI 0.1%-0.4%; P=0.003) (Fig. 2A). Sex-specific trends were non-identical (P<0.001) and not parallel (P<0.001), suggesting that ASIRs were different and decreasing at a greater rate in women compared to men. Interestingly, since 2000 ASIRs have increased in both sexes (Supplementary Table 2).

ASIR by age

Similarly, age-specific trends were decreasing among younger adults (AAPC -1.5%, 95%CI -1.6% to -1.4%; P<0.001) and older adults (AAPC -1.5%, 95%CI -1.7% to -1.4%; P<0.001), without a significant difference (P=0.46) (Fig. 2B). The major decrease in ASIR among both age groups and sexes was from 1990-1999, followed by an overall increase from 2000-2019 (Supplementary Table 2).

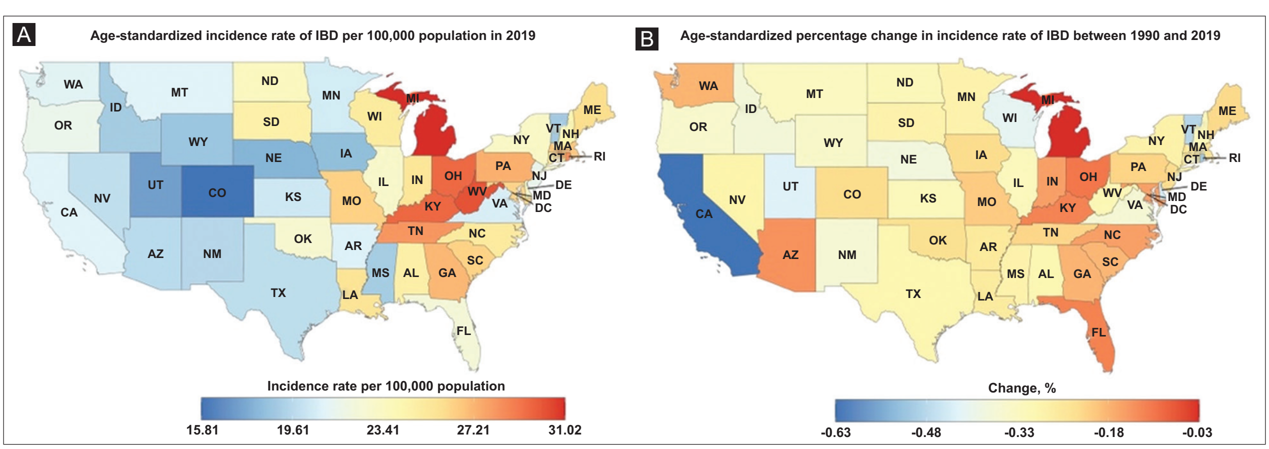

Figure 1 (A) Age-standardized incidence rate (ASIR) of inflammatory bowel disease (IBD) per 100,000 population in 2019. (B) Percentage change (%) in ASIRs of IBD between 1990 and 2019

Table 1 Total and age-standardized rate of all-age, all-inflammatory bowel disease incidence, prevalence, mortality, DALYs, YLLs, and YLDs and their percentage change by United States State in 1990 and 2019

Sex	DALYs all ages number 1990	DALYs all ages number 2019	Change 2019/1990	DALYs age-standardized rate 1990	DALYs age-standardized rate 2019	Change 2019/1990
Male	81412 (59751-107549)	92367 (73240-110534)	13.5%	60.6 (44.7-80.2)	44.8 (35.6-54.4)	-26%
Female	104945 (77694-136704)	122922 (99666-146519)	17.1%	68.5 (49.9-68.5)	54.6 (43.7-66.6)	-20%
Both	186357 (137531-243644)	215289 (175991-256059)	15.5%	64.7 (47.5-84.9)	49.8 (50.4-60.2)	-23%
	Deaths all ages number 1990	Deaths all ages number 2019	Change 2019/1990	Death age-standardized rate 1990	Death age-standardized rate 2019	Change 2019/1990
Male	825 (731-1174)	2315 (1607-2582)	180.6%	0.7 (0.6-0.9)	0.9 (0.6-1.0)	45%
Female	1346 (1176-1647)	3596 (2773-3966)	167.2%	0.67 (0.6-0.83)	1.08 (0.8-1.2)	60%
Both	2171 (1940-2662)	5910 (4622-6464)	172.2%	0.67 (0.6-0.8)	1.02 (0.8-1.1)	53%
	Incidence all ages number 1990	Incidence all ages number 2019	Change 2019/1990	Incidence age-standardized rate 1990	Incidence age-standardized rate 2019	Change 2019/1990
Male	47640 (40887-55039)	41506 (37932-45834)	-12.9%	35 (30-40)	23 (21-25)	-33%
Female	48873 (41984-57526)	43882 (39953-48871)	-10.2%	34 (29-39)	24 (21-26)	-31%
Both	96513 (83182-112507)	85388 (77956-94653)	-11.5%	35 (30-40)	23 (21-25)	-35%
	Prevalence all ages number 1990	Prevalence all ages number 2019	Change 2019/1990	Prevalence age-standardized rate 1990	Prevalence age-standardized rate 2019	Change 2019/1990
Male	435028 (373792-501730)	332233 (310460-354531)	-23.6%	321 (277-372)	170 (159-170)	-47%
Female	547954 (472643-629408)	430656 (402201-459131)	-21.4%	364 (314-420)	215 (200-231)	-41%
Both	982982 (846833-1129783)	762890 (712357-813654)	-22.4%	343 (295-395)	193 (179-207)	-44%
	YLDs all ages number 1990	YLDs all ages number 2019	Change 2019/1990	YLDs age-standardized rate 1990	YLDs age-standardized rate 2019	Change 2019/1990
Male	62292 (41039-87157)	47517 (32921-64112)	-23.7%	46 (30-64)	25 (17-34)	-40%
Female	80353 (53053-112250)	63186 (44158-84948)	-21.4%	54 (35-76)	32 (22-44)	-45%
Both	142645 (93978-199761)	110702 (76973-148846)	-22.4%	50 (33-70)	29 (20-39)	-48%
	YLLs all ages number 1990	YLLs all ages number 2019	Change 2019/1990	YLLs age-standardized rate 1990	YLLs age-standardized rate 2019	Change 2019/1990
Male	19120 (17258-26774)	44850 (31470-49131)	134.6%	15 (14-18)	20 (14-22)	36%
Female	24592 (22460-30495)	59737 (46718-64640)	142.9%	15 (14-18)	22 (17-24)	52%
Both	43712 (40217-54587)	104587 (82095-112252)	139.3%	15 (14-18)	21 (217-23)	44%

DALYs, disability-adjusted life years; YLDs, years lived with disability; YLLs, years of life lost

ASMRs

ASMR with geographic variation

A total of 5910 patients died due to IBD (60.1% women) in 2019 compared to 2171 in 1990. There was a wide geographic variation in the ASMR of IBD in 2019 across the states. The lowest ASMRs were noted in Hawaii and California (0.7 and 0.8 deaths per 100,000), while nearly double that rate was observed in Vermont (1.4 cases per 100,000) (Fig. 3A, Supplementary Table 3). The ASMR increased in all the states from 1990-2019, with the largest relative growth in West Virginia, Kentucky and Iowa (+86.9%, +83.2%, and +82.7%) (Fig. 3B).

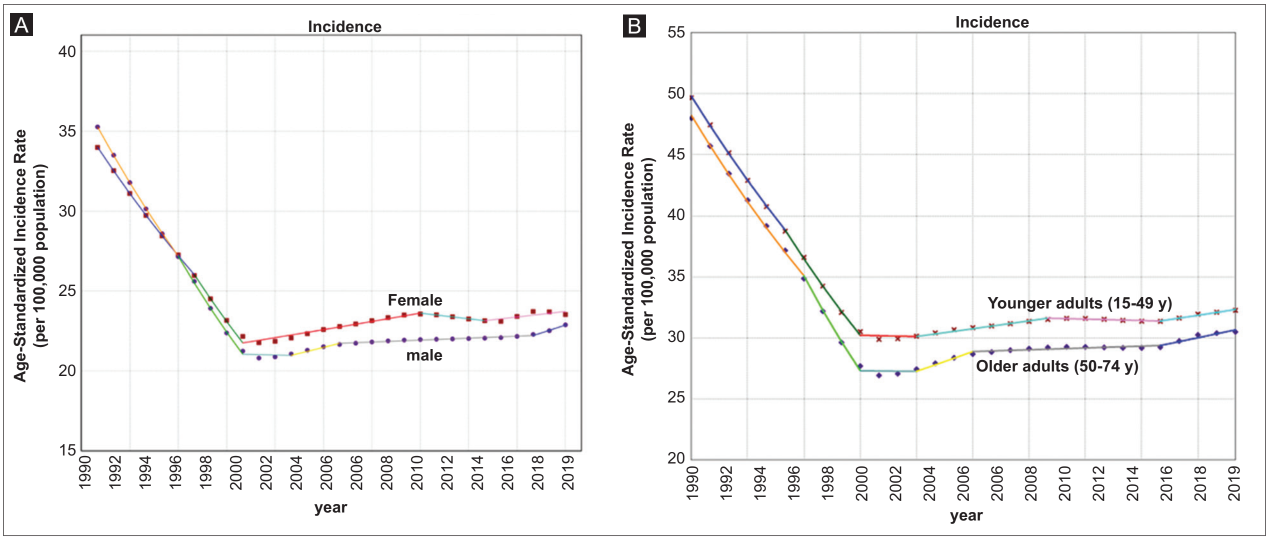

Figure 2 (A) Sex-specific trends in age-standardized incidence rates (ASIRs) of inflammatory bowel disease (IBD). (B) Age-specific trends in ASIRs of IBD

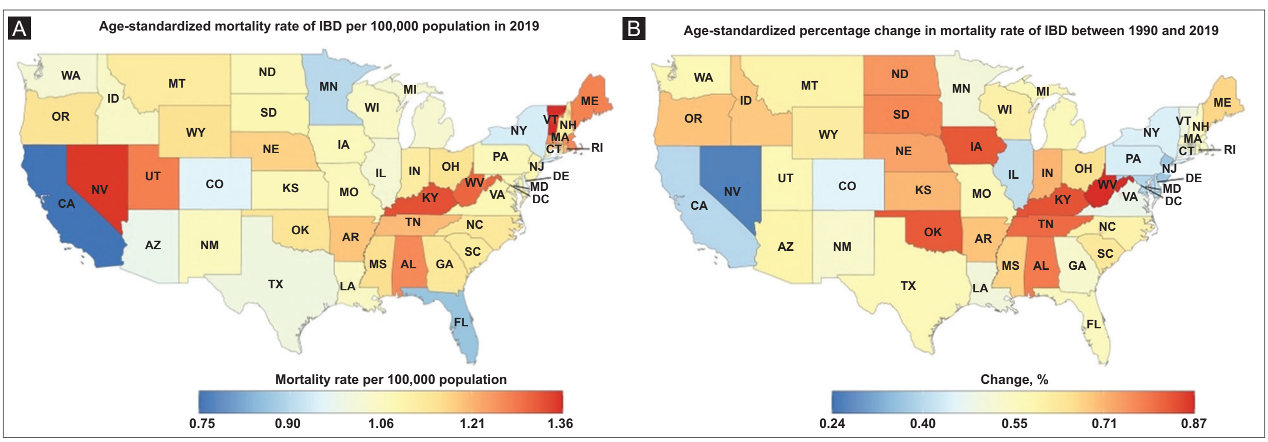

Figure 3 (A) Age-standardized mortality rate (ASMR) of inflammatory bowel disease (IBD) per 100,000 population in 2019. (B) Percentage change (%) in ASMRs of IBD between 1990 and 2019

ASMR by sex

Overall, between 1990 and 2019, sex-specific ASMRs were increasing in men (AAPC 1.3%, 95%CI 1.2-1.4%; P<0.001) and women (AAPC 1.7%, 95%CI 1.4-1.9%; P<0.001) with an absolute AAPC difference of 0.4% (95%CI 0.1-0.6%; P=0.008) (Fig. 4A). While females' ASMRs decreased during 2009-2019 (APC -0.5%, 95%CI -0.8% to -0.2%; P<0.001), there was an increase in males' rates (APC 0.1, 95%CI 0.0-0.2%; P=0.01). Sex-specific trends were neither parallel (P<0.001) nor identical (P<0.001), suggesting that ASMRs among women are different and relatively increasing at a greater rate than men (Supplementary Table 4).

ASMR with age variation

Similar to the younger adults (AAPC 1.4, 95%CI 1.2-1.6%; P<0.001), older adults had an overall increase in ASMR (AAPC 1.5, 95%CI 1.3-1.7%; P<0.001), with a steady increase from 2001-2019 (APC 1.3, 95%CI 1.3-1.4%; P<0.001) (Fig. 4B). However, no significant absolute AAPC difference was observed (P=0.41) (Supplementary Table 4).

Age-standardized prevalence rates (ASPRs)

ASPRs with geographic variation

There were an estimated 762,889 prevalent cases of IBD during 2019 in the US, less than in 1990, when there were 982,981 cases. There was wide geographic variation in the ASPR among US states in 2019. The highest ASPR was in Rhode Island, 287 (95%CI 264-310) per 100,000, followed by Massachusetts and Connecticut (Fig. 5A). Interestingly, all states saw a significant decrease in prevalent cases from 1990-2019. The most notable decrease was in California, which

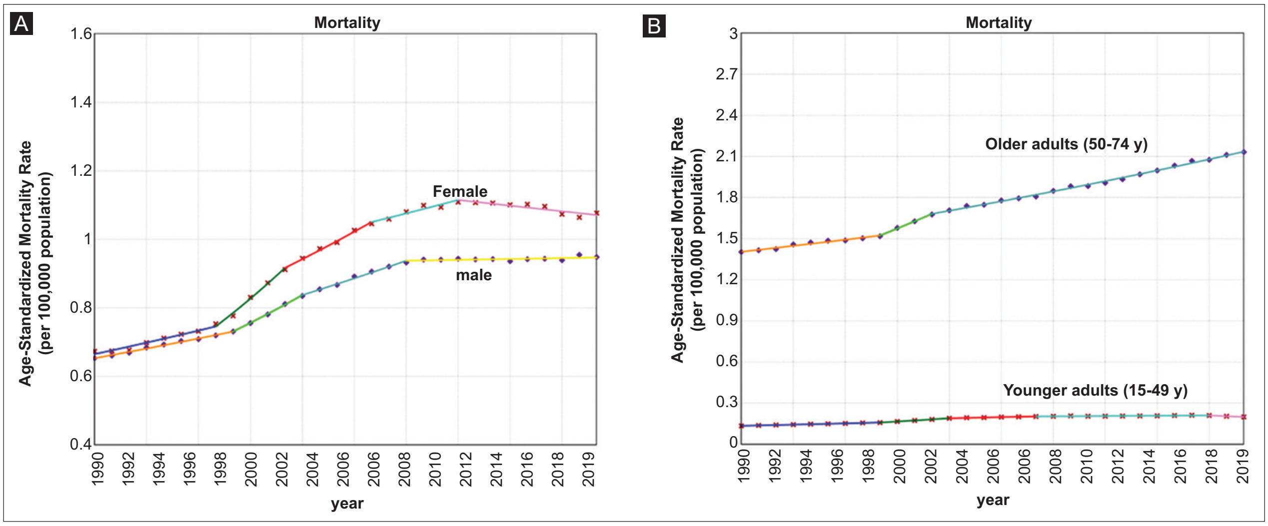

Figure 4 (A) Sex-specific trends in age-standardized mortality rates (ASMRs) of inflammatory bowel disease (IBD). (B) Age-specific trends in ASMRs of IBD

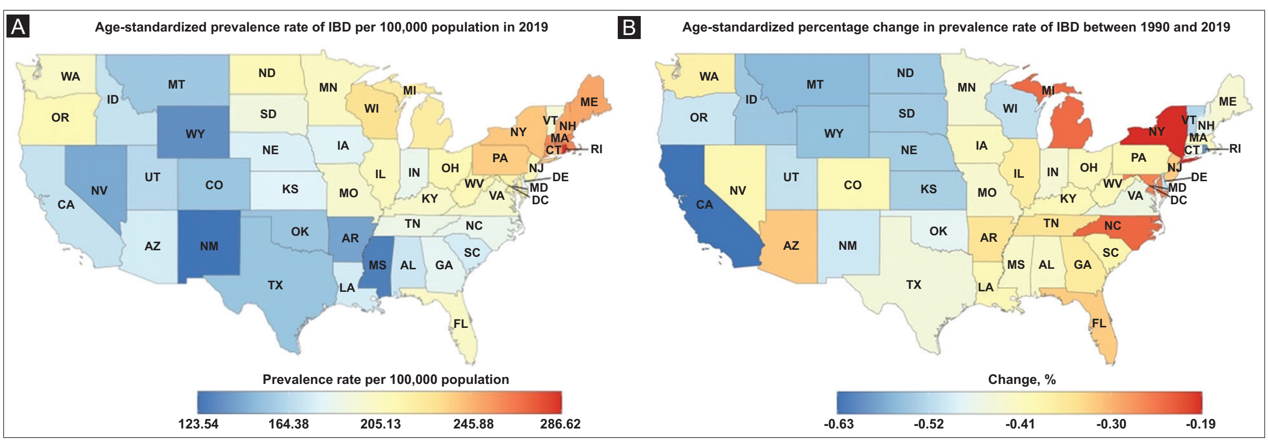

Figure 5 (A) Age-standardized prevalence rate (ASPR) of inflammatory bowel disease (IBD) per 100,000 population in 2019. (B) Percentage change (%) in ASPRs of IBD between 1990 and 2019

decreased from 462 (95%CI 404-528) in 1990 to 169 (95%CI 157-181) per 100,000 in 2019 (Fig. 5B). Although all age groups saw a decrease in prevalence rates, people aged 50-74 had the most notable decrease, from 718 per 100,000 in 1990 to 332 per 100,000 in 2019, with a relative decrease of 53.7% (Supplementary Table 5).

ASPR by sex

Overall, sex-specific ASPR was decreasing in men (AAPC -1.8%, 95%CI -1.9% to -1.7%; P<0.001) and women (AAPC -2.2%, 95%CI -2.3% to -2.1%; P<0.001), showing an absolute difference of 0.4 (95%CI 0.3-0.5; P<0.001) with non-parallel trends, suggesting that ASPRs among women are different and decreasing at a greater rate than in men (Fig. 6A). The largest drop in ASPRs among both sexes was observed during 1996-1999, in males (APC -7.15, 95%CI -6.5 to -7.6; P<0.001) and females (APC -6.61, 95%CI -5.9 to -7.3; P<0.001) (Supplementary Table 6).

ASPR with age variation

Compared to the younger adults (AAPC -1.6%, 95%CI 1.8% to -1.4%; P<0.001), older adults had a greater decrease in ASPR (AAPC -2.6%, 95%CI 2.8% to -2.4%; P<0.001), with an absolute AAPC difference of 1% (95%CI 0.9-1.1%; P<0.001) (Fig. 6B). Age-specific trends were non-identical (P<0.001) and not parallel (P<0.001), suggesting that ASPRs among older adults are different and decreasing at a greater rate than in younger adults (Supplementary Table 6).

Discussion

In this study, we demonstrated that, according to our analysis of GBD 2019, there was an overall decrease in ASIRs and ASPRs in the US from 1990-2019, whereas there was a simultaneous increase in the overall ASMRs. The ASPR

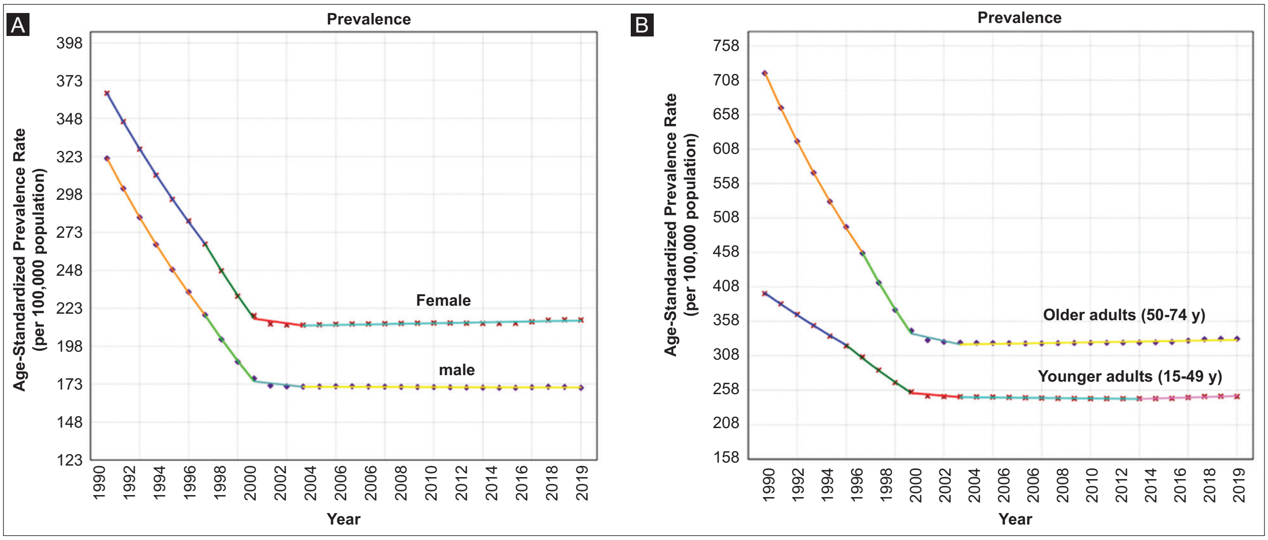

Figure 6 (A) Sex-specific trends in age-standardized prevalence rates (ASPRs) of inflammatory bowel disease (IBD). (B) Age-specific trends in ASPRs of IBD

dropped from 343 (95%CI 295-395) per 100,000 in 1990 to 193 (95%CI 179-207) per 100,000 in 2019. However, a distinct trend emerged of increasing incidence and prevalence rates starting in 2000, with ASIRs rising from 21 (95%CI 19-23) per 100,000 in 2000 to 23 (95%CI 21-25) per 100,000 in 2019. A study by Park *et al* showed that the decrease in US ASPRs during the past 3 decades was the biggest worldwide [7]. Notably, our data showed that the period 1990-2000 had the most pronounced decrease in incidence and prevalence rates. Although the exact reason for this decrease in incidence and prevalence has not been identified, it was probably due to an array of factors. Among these, exercise, nutritional awareness, migration trends, and saturation of genetic and environmental factors contributing to the development of IBD are likely to have played major roles [15-17]. These may provide some insight into the potential reasons that the state of California experienced the largest decline in the incidence and prevalence of IBD throughout the US.

California is distinguished by its substantial Latino population, which exhibits a higher growth rate than any other state [18]. This trend is largely due to the influx of Latinos and other ethnic minorities migrating into California, thereby contributing to the state's largest immigrant population nationwide [19]. Studies have consistently shown lower levels of IBD within these populations, further reinforcing the potential influence of migration trends and demographic factors on disease prevalence [5,20,21]. In addition, recent population-level changes in diet may be more pronounced in some states, contributing to the different rates of IBD. The California state government, for example, regularly funds large healthy eating initiatives. One example is the Healthy Eating, Active Communities (HEAC) Program, a 4-year, $26 million investment to help prevent childhood obesity and diabetes that has consistently shown positive results [22]. In a study by Ye *et al*, diets that were richer in soluble fibers were found to be protective against IBD [23].

On the other hand, our results indicate a lower incidence of IBD in the Northern Great Plains and Western states, while Midwestern and Northeastern states struggle with higher incidence and prevalence rates. These results are supported by studies by Sonnenberg *et al* and Kappelman *et al*, which both demonstrated higher incidence and prevalence rates of IBD in the Midwestern and Northeastern states [24,25]. Considering the predominantly white demographics in these regions [26], studies demonstrating the association between being white and the development of IBD [25,27] provide insight into the elevated rates of incidence and prevalence observed in these states [21].

When investigating the propensity of the disease to affect different sexes, we report that both males and females had a major decline in both incidence and prevalence between the years 1990 and 1999, followed by a steady rise in incidence and prevalence rates until 2019. This trend was followed by both the younger and older age groups. The reason for this more recent increase in incidence is unclear, but it could be due to increased awareness of patients and healthcare providers about IBD and better access to diagnostic tools such as endoscopy, imaging, and stool testing for intestinal inflammation. Another factor that could explain changes in IBD epidemiology is trends in early-life exposure to various microbes. As industrialization and modernization continue in the US and in nations around the world, children are exposed to a more sterilized environment and may not develop immune tolerance, thus leading to an inappropriate immune response to harmless intestinal microbes later in life [28]. Moreover, increased early-life exposure to antibiotics may result in decreased intestinal microbial diversity and species richness, a factor known to be strongly associated with IBD [29].

A closer look at the results also reveals a significant upswing in the incidence of IBD among females over the years 2017 and 2019, in contrast to males, who continued to maintain only a steady increase in incidence. Notably, the existing literature has reported an increase in the incidence of autoimmune diseases over the past decades [30]. These conditions have been hypothesized to stem from various factors, including genetic predisposition and environmental exposures, such as diet and stress, ultimately resulting in an impaired immune response [31]. Evidence from a recent study suggests that adopting a "Western diet," which is typically high in saturated fats and sucrose, coupled with a low intake of dietary fibers, may precipitate the development and exacerbation of autoimmune conditions such as IBD [32]. Furthermore, multiple studies have consistently provided evidence supporting a clear sex-related bias in autoimmune diseases, specifically towards women, with some reporting a risk up to 4 times greater in women than men [33].

In regard to mortality related to IBD, our results illustrated an overall increase over the last 30 years. Although the mortality rates in all age groups and sexes were similar in 2019, our data illustrated a downtrend of the rate in females between 2009 and 2019, while it increased in males during this time period. The differences in environmental factors between males and females resulting from biological, social, and economic exposures may be implicated in this trend discrepancy between the 2 sexes. Of these factors, the increasing, and ultimately higher, prevalence of smoking in males is likely to have contributed to this uptick in mortality, given that it has been one of the most examined environmental factors in patients with IBD [4]. Simultaneously, smoking prevalence was both lower and down-trending in females during this period [34,35]. Moreover, smoking significantly increases the risk of cancer and mortality in these individuals, further underscoring the adverse consequences associated with smoking in this patient population [36].

Moreover, while we witnessed an increase in the mortality rate in all states throughout the US, the largest relative increase was seen in Mideastern states. In recent years, these states have experienced an aging population, with a greater proportion of their residents falling into the older age group [37], which, according to the data from our study, had significantly higher mortality rates than the younger age group. A long-term outcome study by Jess *et al* has highlighted the association between older age and a higher IBD-related mortality rate. The results from this study indicated that there may be an increased likelihood of dying with IBD from secondary comorbidities such as cardiovascular disease or chronic lung disease [38]. Furthermore, emerging evidence suggests that the significant increase in the risk of both intestinal and extraintestinal malignancies observed in IBD patients may be attributed to several factors, including the presence of extraintestinal manifestations of IBD, comorbidities, and the use of immunosuppressive drugs [39].

This study possesses various noteworthy strengths. To the best of our knowledge, our study represents the most recent estimates of IBD prevalence, incidence and mortality rates throughout the US population, specifically looking at these trends at the state level. Moreover, the major strength of this study is its comprehensive coverage over the last 3 decades, surpassing the scope of most previous studies. In addition, this study provides valuable information and insight into the mortality rates attributed to IBD, an aspect of IBD that has been addressed by relatively few studies in the existing literature. Several limitations should also be noted. First, the study estimated rates of IBD as a whole, overlooking the potential differences in rates between ulcerative colitis and Crohn's disease. If Crohn's disease and ulcerative colitis were reported separately, variations in the incidence and prevalence rates between males and females might be revealed. Second, the study could not determine the cause of increased mortality in IBD patients, thus making it difficult to suggest a course of corrective action.

Overall, IBD has a protracted disease course, and associated mortality is low relative to other chronic diseases. However, as the absolute number of patients with IBD cases increases, a compound prevalence phenomenon will continue to weigh heavily on the US healthcare system. Moreover, despite their effectiveness, the cost of biological drugs poses a significant financial burden on both the patients and the healthcare system. Emerging reports have suggested that up to 25% of adults experience financial difficulties due to IBD-related medical expenses, and around 16% of adults are burdened by cost-related nonadherence to their prescribed medication [40]. As a result, it is imperative to conduct more comprehensive epidemiological studies on IBD, aiming to learn more about its etiology and geographic distribution so that we can continue to intelligently allocate medical, educational, and financial resources to areas predicted to have the most need.

Acknowledgments

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Summary Box

What is already known:

- Inflammatory bowel disease (IBD) has a significant impact on healthcare systems
- IBD burden varies by geographic location, sex, and age group
- IBD is more prevalent in Northeastern states

What the new findings are:

- There was a wide geographic variation in IBD burden within the United States, with higher incidence rates in Midwestern and Eastern states and lower rates in the Northern Great Plains and Western states
- Overall incidence and prevalence rates of IBD decreased from 1990-2019, with increasing trends since 2000
- Mortality rates of IBD have increased in both sexes since 1990, with a larger increase in women

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Supplementary material

Supplementary Table 1 Total and age-standardized incidence rate (ASIR) of all-age, all-inflammatory bowel disease incidence, and percentage change of incidence by Unites States state in 1990 and 2019

State	ASIR 1990			ASIR 2019			Change 2019/1990	Incidence all ages Number 1990			Incidence all ages Number 2019			Change 2019/1990
	Both	Upper	Lower	Both	Upper	Lower		Both	Upper	Lower	Both	Upper	Lower	
Alabama	35.6	30.1	42.6	24.7	22.3	27.7	-30.6%	1605	1360	1916	1378	1247	1540	-14.1%
Alaska	39.4	33.8	46.0	25.0	22.6	28.0	-36.5%	241	202	286	216	195	242	-10.3%
Arizona	22.8	19.8	26.3	19.7	17.8	21.8	-13.8%	922	799	1067	1585	1437	1751	72.0%
Arkansas	28.2	24.2	32.8	20.8	18.9	23.0	-26.1%	732	635	851	708	642	785	-3.4%
California	57.1	49.6	65.9	20.9	19.0	23.1	-63.3%	18936	16346	21956	9607	8728	10622	-49.3%
Colorado	20.6	17.7	24.1	15.8	14.3	17.6	-23.1%	767	659	910	955	865	1062	24.4%
Connecticut	35.1	30.0	41.0	25.3	22.8	28.3	-28.0%	1335	1145	1567	1046	946	1162	-21.6%
Delaware	41.6	35.3	49.2	22.9	20.9	25.4	-44.8%	314	267	373	256	232	284	-18.7%
District of Columbia	39.1	33.3	46.8	26.8	23.9	30.1	-31.4%	285	243	341	215	191	241	-24.6%
Florida	25.5	21.9	30.0	22.4	20.4	24.9	-12.2%	3731	3221	4408	5335	4873	5973	43.0%
Georgia	33.1	28.2	39.2	27.1	24.7	30.1	-18.1%	2397	2037	2848	3236	2951	3573	35.0%
Hawaii	23.6	19.9	28.0	14.8	12.7	17.5	-37.4%	297	250	352	257	223	303	-13.3%
Idaho	30.5	25.9	36.0	19.0	17.2	21.3	-37.7%	325	275	383	356	324	398	9.7%
Illinois	34.1	28.9	39.9	22.9	20.7	25.5	-32.8%	4369	3695	5101	3310	3001	3672	-24.2%
Indiana	30.2	25.6	35.3	25.5	23.1	28.2	-15.7%	1863	1585	2179	1900	1729	2107	2.0%
Iowa	23.8	20.3	28.1	18.4	16.6	20.4	-22.9%	727	623	859	623	565	693	-14.3%
Kansas	29.9	25.6	35.0	20.3	18.4	22.6	-32.2%	814	695	952	662	599	736	-18.7%
Kentucky	33.8	28.9	40.2	29.6	26.7	32.7	-12.4%	1394	1193	1661	1493	1350	1644	7.1%
Louisiana	34.9	30.0	40.7	25.6	23.0	28.2	-26.8%	1589	1361	1865	1300	1173	1438	-18.2%
Maine	33.6	28.6	39.6	26.0	23.2	29.1	-22.7%	464	395	550	394	354	445	-15.1%
Maryland	31.1	27.0	36.3	26.2	23.7	29.1	-15.7%	1712	1481	2006	1796	1631	2005	4.9%
Massachusetts	35.4	29.8	41.6	26.7	24.1	30.0	-24.5%	2449	2060	2899	2045	1852	2294	-16.5%
Michigan	32.1	27.9	36.9	31.0	28.0	34.1	-3.3%	3315	2876	3831	3358	3058	3690	1.3%
Minnesota	28.9	25.2	33.5	20.5	18.5	22.9	-29.2%	1400	1211	1625	1246	1129	1393	-10.9%
Mississippi	26.9	22.7	31.6	19.0	17.2	21.0	-29.1%	739	626	872	639	580	706	-13.5%
Missouri	33.2	28.3	39.1	26.4	23.7	29.2	-20.7%	1896	1614	2225	1830	1657	2019	-3.5%
Montana	31.5	26.9	36.8	21.0	19.0	23.3	-33.5%	278	238	326	248	225	276	-10.9%
Nebraska	29.1	24.6	34.0	18.0	16.3	19.9	-38.1%	502	426	587	380	343	421	-24.3%
Nevada	28.1	24.4	32.7	19.8	18.1	21.8	-29.4%	389	336	455	728	665	801	87.1%
New Hampshire	35.7	30.4	41.9	24.1	21.8	26.9	-32.3%	451	381	530	368	332	412	-18.5%
New Jersey	27.7	24.1	32.5	21.4	19.4	23.7	-22.9%	2470	2149	2893	2155	1953	2404	-12.7%
New Mexico	30.7	26.2	36.6	19.5	17.7	21.4	-36.5%	503	428	599	489	446	538	-2.9%
New York	32.4	28.1	37.2	23.1	20.9	25.7	-28.7%	6667	5776	7696	5080	4587	5640	-23.8%
North Carolina	29.8	26.0	34.9	25.2	22.9	27.7	-15.7%	2255	1966	2642	2976	2713	3292	32.0%
North Dakota	34.4	29.2	40.3	23.5	21.0	26.4	-31.8%	236	201	276	189	168	214	-20.1%

(*Contd...*)

Supplementary Table 1 (*Continued*)

State	ASIR 1990			ASIR 2019			Change 2019/1990	Incidence all ages Number 1990			Incidence all ages Number 2019			Change 2019/1990
	Both	Upper	Lower	Both	Upper	Lower		Both	Upper	Lower	Both	Upper	Lower	
Ohio	33.1	27.9	38.8	29.5	26.7	32.9	-10.7%	4010	3391	4699	3838	3470	4251	-4.3%
Oklahoma	30.0	25.4	35.0	22.8	20.8	25.2	-23.9%	1044	890	1219	1007	918	1113	-3.6%
Oregon	33.3	28.4	38.9	21.5	19.6	24.0	-35.3%	1069	909	1252	973	878	1087	-9.1%
Pennsylvania	35.1	29.9	40.8	27.4	24.7	30.3	-22.0%	4744	4046	5530	3983	3612	4410	-16.0%
Rhode Island	58.2	49.9	68.7	28.4	25.7	31.6	-51.2%	665	570	782	345	312	384	-48.2%
South Carolina	32.3	27.5	38.2	26.3	23.9	29.0	-18.5%	1252	1067	1482	1503	1364	1657	20.0%
South Dakota	34.7	29.5	41.1	24.6	22.1	27.5	-29.1%	257	218	303	235	212	262	-8.5%
Tennessee	36.3	30.9	42.9	28.2	25.5	31.1	-22.3%	2012	1717	2375	2119	1924	2352	5.3%
Texas	28.4	23.4	33.9	19.8	17.8	22.2	-30.2%	5240	4290	6299	6215	5595	6968	18.6%
Utah	30.7	26.3	36.4	17.3	15.7	19.3	-43.5%	514	437	613	575	521	639	11.9%
Vermont	36.9	31.4	43.4	18.9	16.8	21.4	-48.7%	234	198	276	138	123	157	-41.0%
Virginia	32.7	27.8	38.9	20.7	18.6	23.1	-36.9%	2321	1972	2782	2002	1806	2241	-13.7%
Washington	25.7	21.9	30.3	21.0	19.1	23.5	-18.2%	1409	1196	1666	1699	1539	1897	20.6%
West Virginia	43.6	37.2	50.9	30.1	27.3	33.5	-30.9%	889	761	1033	644	587	714	-27.5%
Wisconsin	43.2	36.5	51.2	25.1	22.7	28.2	-42.0%	2344	1973	2779	1622	1470	1823	-30.8%
Wyoming	28.7	24.3	33.8	18.7	16.8	21.0	-34.9%	142	120	167	131	117	148	-7.9%

Supplementary Table 2 Trend analysis of inflammatory bowel disease age-standardized incidence rate with sex and age variations from 1990-2019

Incidence	Trends[a]			Gender/ Age-specific AAPC difference (95%CI)	Pairwise comparison P-values		
	Time period	APC (95%CI)	AAPC (95%CI)		Sex/ Age-specific AAPC difference	Coincidence[b]	Parallelism[c]
				Sex			
Male	1990-1995	-5.1 (-5.2 to -5.0)	-1.5 (-1.6 to -1.4)	0.2 (0.1-0.4)	<0.001sssssssse	<0.001	<0.001
	1995-1999	-6.2 (-6.4 to -6.0)					
	1999-2002	-0.1 (-0.5 to 0.2)					
	2002-2005	1.2 (0.8 to 1.5)					
	2005-2017	0.2 (0.2 to 0.2)					
	2017-2019	1.5 (1.1 to 1.8)					
Female	1990-1996	-4.4 (-4.6 to -4.2)	-1.2 (-1.4 to -1.1)				
	1996-1999	-5.8 (-6.9 to -4.6)					
	1999-2010	0.8 (0.7 to 0.8)					
	2010-2014	-0.5 (-1.1 to 0.1)					
	2014-2019	0.5 (0.2 to 0.8)					
				Age			
50-74 years	1990-1996	- 5.2 (-5.3 to -5.0)	-1.6 (-1.7 to -1.4)	0.1 (-0.1-0.3)	0.46	0.44	0.23
	1996-1999	-8.0 (-9.0 to -7.0)					
	1999-2002	-0.1 (-1.1 to 1.0)					
	2002-2005	1.9 (0.9 to 3.0)					
	2005-2015	0.2 (0.1 to 0.3)					
	2015-2019	1.1 (0.7 to 1.4)					
15-49 years	1990-1995	- 4.9 (-5.0 to -4.8)	-1.5 (-1.5 to -1.4)				
	1995-1999	-6.1 (-6.3 to -5.9)					
	1999-2002	-0.1 (-0.6 to 0.4)					
	2002-2009	0.7 (0.6 to 0.8)					
	2009-2015	-0.1 (-0.2 to -0.0)					
	2015-2019	0.7 (0.6 to 0.9)					

[a]Time-trends were computed using the Joinpoint Regression Program (v5.0.2, NCI) with 5 maximum joinpoints allowed (6-line segments)
[b]Tests whether sex- and age-specific trends were identical. A significant p-value indicates that the trends were not identical (i.e., they had different incidence rates and coincidence was rejected)
[c]Tests whether sex- and age-specific trends were parallel. A significant p-value indicates that the trends were not parallel (i.e., parallelism was rejected)
AAPC, average annual percentage change

Supplementary Table 3 Total and age-standardized mortality rate (ASMR) of all-age, all-inflammatory bowel disease mortality, and percentage change of mortality by Unites States state in 1990 and 2019

State	ASMR 1990			ASMR 2019			Change 2019/1990	Mortality all ages Number 1990			Mortality all ages Number 2019			Change 2019/1990
	Both	Upper	Lower	Both	Upper	Lower		Both	Upper	Lower	Both	Upper	Lower	
Alabama	0.7	0.9	0.6	1.3	1.5	1.0	78.5%	38	33	48	108	84	129	183.1%
Alaska	0.9	1.1	0.7	1.1	1.3	0.9	29.1%	2	2	3	11	8	12	406.9%
Arizona	0.6	0.7	0.5	1.0	1.2	0.7	59.3%	28	25	34	126	91	155	349.3%
Arkansas	0.7	0.8	0.6	1.2	1.4	0.9	69.5%	25	22	30	64	48	78	153.1%
California	0.5	0.8	0.5	0.8	0.9	0.6	39.4%	178	155	254	493	389	602	176.1%
Colorado	0.7	0.9	0.6	1.0	1.2	0.8	44.9%	24	20	30	81	65	98	243.5%
Connecticut	0.7	0.8	0.6	1.1	1.3	0.8	48.0%	34	29	39	81	57	101	138.6%
Delaware	0.7	0.9	0.6	1.0	1.2	0.8	40.4%	6	5	8	18	14	21	220.1%
District of Columbia	0.8	1.2	0.7	1.0	1.3	0.8	23.9%	8	6	11	10	8	12	34.4%
Florida	0.6	0.7	0.5	0.9	1.1	0.7	55.4%	125	107	161	396	294	484	217.0%
Georgia	0.7	0.9	0.7	1.1	1.4	0.9	53.1%	51	45	65	172	131	206	235.9%
Hawaii	0.5	0.7	0.4	0.7	0.9	0.6	49.4%	6	5	8	23	17	28	280.7%
Idaho	0.6	0.8	0.5	1.0	1.2	0.8	68.7%	8	7	10	29	23	35	283.5%
Illinois	0.7	0.9	0.6	1.0	1.2	0.7	40.8%	110	97	134	235	173	283	114.0%
Indiana	0.7	0.8	0.6	1.1	1.3	0.9	71.3%	48	42	60	128	98	154	168.1%
Iowa	0.6	0.7	0.5	1.1	1.3	0.8	82.7%	27	24	35	67	53	81	146.5%
Kansas	0.6	0.8	0.5	1.1	1.3	0.8	70.9%	24	20	29	56	43	68	137.3%
Kentucky	0.7	0.9	0.6	1.3	1.6	1.0	83.2%	36	31	44	102	74	124	185.0%
Louisiana	0.7	0.9	0.6	1.0	1.3	0.9	50.5%	34	30	44	77	62	93	124.8%
Maine	0.8	0.9	0.7	1.3	1.5	0.9	67.0%	13	12	16	37	27	45	177.7%
Maryland	0.8	1.0	0.7	1.1	1.3	0.8	39.2%	42	37	52	111	84	134	165.9%
Massachusetts	0.8	0.9	0.7	1.3	1.6	0.9	54.6%	73	64	82	167	111	207	130.7%
Michigan	0.7	0.8	0.6	1.0	1.2	0.8	56.2%	76	67	96	192	145	230	151.9%
Minnesota	0.6	0.8	0.5	0.9	1.1	0.7	50.8%	37	31	47	93	73	112	150.9%
Mississippi	0.7	0.8	0.6	1.2	1.4	0.9	67.4%	23	20	29	56	44	69	144.6%
Missouri	0.7	0.8	0.6	1.1	1.3	0.8	57.1%	52	46	64	121	90	145	132.1%
Montana	0.7	0.8	0.6	1.1	1.4	0.9	60.0%	8	7	9	23	17	28	200.3%
Nebraska	0.7	0.8	0.6	1.2	1.4	0.9	73.5%	17	14	20	41	30	49	145.4%
Nevada	1.1	1.2	0.9	1.4	1.6	0.9	25.8%	11	10	12	63	42	77	485.6%
New Hampshire	0.7	0.9	0.6	1.1	1.3	0.9	54.4%	10	9	12	29	23	35	195.6%
New Jersey	0.8	0.9	0.7	1.1	1.3	0.8	36.2%	85	75	98	185	129	229	119.5%
New Mexico	0.7	0.9	0.6	1.1	1.3	0.8	53.3%	11	10	14	41	31	50	261.2%
New York	0.7	0.8	0.6	0.9	1.2	0.7	44.3%	163	142	201	358	252	443	119.4%
North Carolina	0.7	0.9	0.6	1.1	1.4	0.9	59.8%	57	51	71	201	152	244	249.4%
North Dakota	0.6	0.8	0.5	1.1	1.3	0.8	75.1%	6	5	7	15	11	18	150.3%
Ohio	0.7	0.8	0.6	1.1	1.4	0.9	65.2%	101	89	123	250	186	305	146.2%
Oklahoma	0.6	0.8	0.5	1.1	1.4	0.9	82.6%	28	24	37	75	60	91	166.6%
Oregon	0.7	0.8	0.6	1.1	1.4	0.8	69.7%	27	23	32	89	65	109	233.4%

(*Contd...*)

Supplementary Table 3 (*Continued*)

State	ASMR 1990			ASMR 2019			Change 2019/1990	Mortality all ages Number 1990			Mortality all ages Number 2019			Change 2019/1990
	Both	Upper	Lower	Both	Upper	Lower		Both	Upper	Lower	Both	Upper	Lower	
Pennsylvania	0.7	0.9	0.7	1.1	1.3	0.8	44.0%	138	121	159	283	212	341	104.8%
Rhode Island	0.8	0.9	0.7	1.2	1.5	0.9	55.7%	12	10	14	26	18	32	114.1%
South Carolina	0.7	0.9	0.6	1.1	1.4	0.9	63.5%	27	24	35	97	75	118	259.2%
South Dakota	0.6	0.7	0.5	1.1	1.3	0.8	76.6%	7	6	8	18	14	22	168.7%
Tennessee	0.7	0.8	0.6	1.2	1.5	0.9	80.4%	43	38	55	139	107	169	221.5%
Texas	0.6	0.8	0.6	1.0	1.2	0.8	57.4%	117	103	151	395	297	477	237.5%
Utah	0.8	0.9	0.7	1.3	1.5	0.9	57.7%	13	11	15	49	33	58	278.8%
Vermont	0.9	1.0	0.8	1.4	1.6	0.9	49.5%	7	6	7	18	12	21	176.8%
Virginia	0.7	0.9	0.6	1.1	1.3	0.8	48.0%	50	44	61	153	115	185	206.8%
Washington	0.6	0.8	0.6	1.0	1.2	0.8	58.0%	39	34	48	129	99	156	234.8%
West Virginia	0.7	0.8	0.6	1.3	1.6	1.0	86.9%	19	16	23	49	36	59	156.8%
Wisconsin	0.6	0.8	0.6	1.0	1.3	0.8	60.8%	46	40	55	116	89	140	155.0%
Wyoming	0.7	0.9	0.6	1.1	1.4	0.9	61.6%	4	3	4	12	9	14	234.0%

Supplementary Table 4 Trend analysis of inflammatory bowel disease age-standardized mortality rate with sex and age variations from 1990-2019

Mortality	Trends[a]			Sex/Age-specific AAPC difference (95%CI)	Pairwise comparison P-values		
	Time period	APC (95%CI)	AAPC (95%CI)		Sex/Age-specific AAPC difference	Coincidence[b]	Parallelism[c]
				Sex			
Male	1990-1998	1.4 (1.3 to 1.6)	1.3 (1.2 to 1.4)	0.4 (0.1-0.6)	<0.001	<0.001	<0.001
	1998-2002	3.5 (2.8 to 4.1)					
	2002-2008	1.9 (1.6 to 2.2)					
	2008-2019	0.1 (0.0 to 0.2)					
Female	1990-1997	1.7 (1.3 to 2.0)	1.7 (1.4 to 1.9)				
	1997-2001	5.3 (4.1 to 6.6)					
	2001-2006	2.8 (2.0 to 3.5)					
	2006-2011	1.2 (0.4 to 2.0)					
	2011-2019	-0.5 (-0.8 to -0.2)					
				Age			
50-74 years	1990-1998	1.0 (0.9 to 1.2)	1.5 (1.3 to 1.6)	0.1 (0.1-0.3)	0.414	0.45	0.33
	1998-2001	3.4 (1.8 to 4.9)					
	2001-2019	1.3 (1.3 to 1.4)					
15-49 years	1990-1998	2.1 (1.9 to 2.2)	1.4 (1.2 to 1.5)				
	1998-2002	4.6 (3.8 to 5.4)					
	2002-2007	1.4 (0.9 to 1.8)					
	2007-2017	0.3 (0.2 to 0.5)					
	2017-2019	-2.7 (-4.2 to -1.2)					

[a]Time-trends were computed using the Joinpoint Regression Program (v5.0.2, NCI) with 5 maximum joinpoints allowed (6-line segments)
[b]Tests whether sex- and age-specific trends were identical. A significant P-value indicates that the trends were not identical (i.e., they had different mortality rates and coincidence was rejected)
[c]Tests whether sex- and age-specific trends were parallel. A significant P-value indicates that the trends were not parallel (i.e., parallelism was rejected)
AAPC, average annual percentage change

Supplementary Table 5 Total and age-standardized prevalence rates (ASPRs) of all-age, all-inflammatory bowel disease prevalence, and percentage change of prevalence by Unites States state in 1990 and 2019

State	ASPR 1990			ASPR 2019			Change 2019/1990	Prevalence all ages Number 1990			Prevalence all ages Number 2019			Change 2019/1990
	Both	Upper	Lower	Both	Upper	Lower		Both	Upper	Lower	Both	Upper	Lower	
Alabama	297.0	249.0	347.3	170.9	156.7	184.6	-42.5%	13830	11651	16098	10084	9303	10823	-27.1%
Alaska	327.8	282.5	376.5	203.0	185.8	221.1	-38.1%	1856	1578	2172	1874	1711	2042	1.0%
Arizona	256.2	224.2	292.0	174.6	163.6	186.5	-31.8%	10688	9359	12159	15225	14240	16206	42.4%
Arkansas	218.4	188.2	249.9	141.5	131.0	152.9	-35.2%	5910	5112	6745	5056	4710	5437	-14.5%
California	462.0	404.6	528.1	169.2	157.5	181.2	-63.4%	153010	133319	175568	81541	76201	86984	-46.7%
Colorado	255.4	220.3	297.0	154.5	143.9	165.5	-39.5%	9518	8168	11053	10111	9465	10784	6.2%
Connecticut	473.5	401.2	551.6	256.7	236.8	277.9	-45.8%	18912	16055	22007	11831	10968	12703	-37.4%
Delaware	379.4	317.1	444.1	183.4	169.5	198.5	-51.7%	2929	2453	3418	2210	2053	2378	-24.6%
District of Columbia	353.1	296.6	415.9	177.0	159.2	195.5	-49.9%	2627	2216	3092	1467	1320	1622	-44.2%
Florida	297.2	257.6	344.2	201.7	186.7	217.4	-32.1%	48131	41821	55493	53988	50348	57846	12.2%
Georgia	285.3	239.7	331.2	181.0	167.3	196.0	-36.5%	20541	17206	23994	22457	20811	24154	9.3%
Hawaii	307.6	259.8	361.0	147.8	127.5	170.9	-52.0%	3913	3301	4594	2836	2470	3220	-27.5%
Idaho	374.3	316.2	440.6	169.1	155.6	182.8	-54.8%	4111	3473	4826	3392	3127	3649	-17.5%
Illinois	327.0	277.6	381.5	205.1	189.3	222.5	-37.3%	42900	36479	50066	31922	29558	34430	-25.6%
Indiana	326.7	276.5	383.6	183.9	168.8	198.7	-43.7%	20762	17573	24327	14521	13401	15588	-30.1%
Iowa	306.4	263.0	358.2	179.3	166.2	193.1	-41.5%	10003	8599	11649	6585	6131	7037	-34.2%
Kansas	386.1	326.6	451.5	178.7	164.6	193.4	-53.7%	11028	9373	12830	6206	5745	6691	-43.7%
Kentucky	334.5	281.2	392.1	199.9	183.5	216.9	-40.2%	14248	12038	16688	10699	9923	11512	-24.9%
Louisiana	290.7	247.6	337.6	174.4	160.7	188.7	-40.0%	13362	11418	15487	9339	8623	10042	-30.1%
Maine	444.9	375.4	519.7	251.4	230.7	274.1	-43.5%	6448	5474	7531	4347	3997	4695	-32.6%
Maryland	290.9	251.6	336.6	215.7	199.8	232.2	-25.8%	16195	14004	18676	15883	14776	16993	-1.9%
Massachusetts	449.3	380.8	522.7	261.4	242.0	282.3	-41.8%	32146	27319	37207	21981	20429	23580	-31.6%
Michigan	291.2	255.7	329.3	221.8	205.8	238.6	-23.8%	30677	26950	34693	25724	23914	27534	-16.1%
Minnesota	363.4	315.0	418.1	203.9	189.1	220.4	-43.9%	17981	15596	20633	13511	12509	14543	-24.9%
Mississippi	223.0	187.4	261.0	127.9	118.0	137.7	-42.6%	6289	5312	7338	4511	4172	4835	-28.3%
Missouri	350.3	295.6	412.0	199.2	183.6	214.7	-43.1%	21003	17779	24486	14827	13701	15975	-29.4%
Montana	356.6	302.7	414.8	155.4	142.6	168.8	-56.4%	3313	2823	3854	2002	1845	2168	-39.6%
Nebraska	383.8	327.0	446.9	176.4	163.2	191.4	-54.0%	6989	5998	8097	4016	3708	4355	-42.5%
Nevada	235.7	204.3	270.3	143.2	133.7	153.5	-39.2%	3317	2872	3814	5538	5186	5923	66.9%
New Hampshire	472.0	402.7	556.6	249.9	230.6	269.7	-47.1%	6005	5121	7086	4308	3982	4634	-28.3%
New Jersey	312.8	272.3	362.8	212.1	197.1	227.9	-32.2%	29103	25431	33702	23526	21958	25156	-19.2%
New Mexico	248.8	209.8	290.1	123.6	114.3	133.1	-50.3%	4108	3463	4783	3291	3052	3546	-19.9%
New York	297.8	260.5	338.6	240.7	224.7	257.3	-19.2%	63142	55497	71859	58495	54701	62148	-7.4%
North Carolina	240.7	210.3	273.3	184.4	170.7	198.2	-23.4%	18517	16208	21025	23131	21474	24716	24.9%
North Dakota	460.6	388.3	541.5	209.2	190.2	230.9	-54.6%	3345	2829	3923	1828	1661	2017	-45.3%
Ohio	358.8	303.5	420.4	212.2	195.0	230.0	-40.9%	45247	38351	52959	29518	27246	31773	-34.8%
Oklahoma	295.4	250.1	347.0	154.0	142.5	165.9	-47.9%	10750	9117	12580	7148	6631	7665	-33.5%

(Contd...)

Supplementary Table 5 (*Continued*)

State	ASPR 1990			ASPR 2019			Change 2019/1990	Prevalence all ages Number 1990			Prevalence all ages Number 2019			Change 2019/1990
	Both	Upper	Lower	Both	Upper	Lower		Both	Upper	Lower	Both	Upper	Lower	
Oregon	427.0	359.7	495.8	211.2	195.6	228.4	-50.5%	14454	12194	16776	10534	9763	11343	-27.1%
Pennsylvania	394.6	332.0	462.2	238.7	220.5	257.9	-39.5%	57267	48507	66725	38100	35328	40899	-33.5%
Rhode Island	722.5	615.3	841.7	286.6	264.2	309.9	-60.3%	8733	7430	10133	3824	3542	4116	-56.2%
South Carolina	285.0	241.8	330.5	174.6	161.0	188.3	-38.7%	11206	9506	13076	10550	9775	11334	-5.9%
South Dakota	418.3	354.8	490.4	191.0	174.1	208.2	-54.3%	3296	2797	3833	1963	1787	2134	-40.4%
Tennessee	287.8	244.7	333.6	187.1	172.2	202.5	-35.0%	16409	14021	19019	14838	13722	15979	-9.6%
Texas	278.1	229.8	331.0	153.9	142.2	166.2	-44.7%	50853	42077	60463	50427	46701	54220	-0.8%
Utah	336.2	284.5	398.6	163.5	150.3	177.0	-51.4%	5412	4577	6415	5538	5100	5981	2.3%
Vermont	411.6	348.7	482.1	195.0	177.2	214.0	-52.6%	2647	2237	3103	1598	1457	1749	-39.6%
Virginia	366.6	309.3	429.1	199.4	183.9	216.9	-45.6%	26033	21847	30563	20913	19321	22558	-19.7%
Washington	323.8	277.6	375.4	201.8	187.5	217.1	-37.7%	18105	15517	21005	17710	16479	18935	-2.2%
West Virginia	352.6	295.4	410.3	210.0	193.4	227.5	-40.4%	7641	6449	8876	4876	4523	5249	-36.2%
Wisconsin	474.6	398.8	554.6	230.1	213.8	249.3	-51.5%	26573	22377	31043	16089	14991	17264	-39.5%
Wyoming	301.4	252.7	354.2	133.5	120.4	147.1	-55.7%	1499	1254	1763	1002	908	1102	-33.1%

Supplementary Table 6 Trend analysis of inflammatory bowel disease age-standardized prevalence rate with sex and age variations from 1990-2019

Prevalence	Trends[a]			Sex/Age-specific AAPC difference (95%CI)	Pairwise comparison P-values		
	Time period	APC (95%CI)	AAPC (95%CI)		Sex/Age-specific AAPC difference	Coincidence[b]	Parallelism[c]
			Sex				
Male	1990-1996	-6.2 (-6.3 to -6.2)	-2.2 (-2.2 to -2.1)	0.4 (0.2-0.5)	<0.001	<0.001	<0.001
	1996-1999	-7.2 (-7.6 to -6.7)					
	1999-2002	-0.7 (-1.1 to -0.3)					
	2002-2019	-0.0 (-0.0 to 0.0)					
Female	1990-1996	-5.2 (-5.3 to -5.0)	-1.8 (-1.9 to -1.7)				
	1996-1999	-6.6 (-7.3 to -5.9)					
	1999-2002	-0.7 (-1.4 to 0.0)					
	2002-2019	0.1 (0.1 to 0.1)					
			Age				
50-74 years	1990-1996	- 7.3 (-7.4 to -7.1)	-2.6 (-2.8 to -2.5)	1.0 (0.9-1.2)	<0.001	<0.001	<0.001
	1996-1999	-9.4 (-10.4 to -8.4)					
	1999-2002	-1.6 (-2.6 to -0.5)					
	2002-2019	0.1 (0.1 to o. 2)					
15-49 years	1990-1995	- 4.1 (-4.2 to -4.0)	-1.6 (-1.7 to -1.5)				
	1995-1999	-5.9 (-6.1 to -5.6)					
	1999-2002	-0.8 (-1.4 to -0.2)					
	2002-2013	-0.1 (-0.1 to -0.1)					
	2013-2019	0.3 (0.2 to 0.4)					

[a]Time-trends were computed using the Joinpoint Regression Program (v5.0.2, NCI) with 5 maximum joinpoints allowed (6-line segments)
[b]Tests whether sex- and age-specific trends were identical. A significant *P* value indicates that the trends were not identical (i.e., they had different prevalence rates and coincidence was rejected)
[c]Tests whether sex- and age-specific trends were parallel. A significant *P* value indicates that the trends were not parallel (i.e., parallelism was rejected)
AAPC, average annual percentage change