Current Science
CS 5 (3), 2317-2334 (2025)
Received 18 Feb 2025 | **Revised 14 March** 2025 | **Accepted 10 April**. 2025 | **Online Available 13 May** 2025
https://doi.org/ 10.52845/CS/2025-5-3-22

Current Science

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OPEN ACCESS

ISSN (O) 2795-8639

Original Article

Global Trends and Regional Disparities in Inflammatory Bowel Disease Burden: Insights from the GBD 2021 Study

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Abstract: Background: Inflammatory bowel disease (IBD) is a complex and challenging health problem that exerts a significant impact on the quality of life of millions of individuals worldwide.
Methods: Data on prevalence, incidence, mortality, and disability-adjusted life years (DALYs) were extracted from the Global Burden of Disease (GBD) 2021 study. Joinpoint regression was employed to analyze trends, and Bayesian age-period-cohort (BAPC) models were used to forecast future burden. The socio-demographic index (SDI) was used to assess socioeconomic impact. In addition, the driving factors for IBD burden variation were further analyzed using decomposition analysis. Frontier analysis was used to visually demonstrate the potential for burden reduction in each country or region based on their development levels.
Results: In 2021, the global prevalence of IBD was 3.83 million cases (95% UI: 3.31 to 4.51 million) with an age-standardized prevalence rate (ASPR) of 44.88 per 100,000. The incidence was 375,140 cases (95% UI: 327,686 to 436,925), showing a modest global increase since 1990. The mortality rate decreased to 42,423 deaths in 2021, with an age-standardized mortality rate (ASMR) of 0.52 per 100,000. Significant regional disparities were found, with the highest burden in high-income regions and the lowest in lower SDI regions. Projections suggest a continued decline in incidence and mortality by 2036.
Conclusions: This study provides an important basis for future disease management and public health policies.
Keywords: Inflammatory bowel disease, Disability-adjusted life years, Epidemiology, Joinpoint regression analysis, Prediction

Introduction

Inflammatory bowel disease (IBD) is a group of chronic non-specific inflammatory diseases of the gastrointestinal tract, including Crohn's disease (CD) and Ulcerative colitis (UC)[1-4]. The etiology and pathogenesis of IBD are still unclear, and the current research is believed to be related to genetic susceptibility, immune imbalance, living environment, infections, diet, lifestyle, ethnicity, geography, and changes in intestinal microecology, etc[5-9]. IBD has a complex clinical presentation, and the electron microscopic and pathological manifestations of IBD are not specific, therefore, the diagnosis is more difficult, and even missed or misdiagnosed.

Data show that at present, about 70%~80% of CD patients may have complications such as intestinal obstruction, abdominal abscess, intestinal perforation, intestinal impotence, haemorrhage, etc., and thus need to undergo one or even multiple surgical treatments, about 30% of UC patients may need total colorectal resection, which has a high disability rate, therefore, IBD is also

referred to as a ‘green cancer’[10]. IBD has a long course and is prone to recurrent episodes, causing serious damage to the patient's physical and mental health, often leading to a decline in quality of life and work efficiency, and even depression and other symptoms[11-13]. At the same time, IBD patients need to be hospitalised repeatedly and many times, and the use of surgery and medicines, especially biologics, also requires high medical expenses. To date, there is still no cure for IBD, and lifelong care and medication are often required, which causes serious economic pressure and medical burden to families and societies around the world[14, 15].

Multiple previous epidemiological studies[16-18], the global prevalence of lBD has shown an increasing trend from year to year, with one Global Burden of Disease (GBD) study showing a significant increase of 175,904 people diagnosed with IBD from 1990 to 2019. In addition, the burden of IBD shows significant differences across regions and age populations[17]. In particular, the prevalence of IBD is higher in western countries, such as North America and Europe[19, 20]. Data show that since the second half of the 20th century, the incidence rate in North America has risen from about 5 cases per 100,000 people to about 20 cases per 100,000 people[21]. In recent years, there has also been a gradual increase in the incidence rate in developing countries, which is related to changes in lifestyles, westernisation of dietary structure and the influence of environmental factors. In terms of age and gender distribution[22], studies show that IBD is commonly found in young adults, especially those between the ages of 15 and 30[17, 23]. There is a difference in the proportion of females versus males, with a gradual increase in prevalence in females. These studies highlight the crucial role of early diagnosis of IBD in prevention and disease control efforts.

The latest GBD Study 2021 offers an in-depth assessment of health detriments associated with 369 diseases, injuries,and impairments, as well as 88 risk factors, encompassing 204 nations and territories, utilizing the most recent epidemiological data and enhanced standardized methodologies[23-25].Compared with previous studies on IBD using GBD data, we gained information from IBD-specific data from the latest 2021 GBD study.In this study, we systematically and comprehensively analysed the variations in disease burden of IBD from 1990 to 2021 and projected epidemiological trends up to 2036. The present analysis is poised to assist clinicians, epidemiologists, and health policymakers in enhancing the distribution of medical resources and in formulating more robust public health strategies.

Methods

Data Acquisition and Sources

The GBD study, accessible through the Global Health Data Exchange (GHDx) online platform (https://vizhub. healt hdata. org/ gbd- resul ts/), served as the primary data source for this research on IBD burden. The methodological framework for data acquisition, processing, and analysis in the GBD 2021 study has been extensively documented in previous publications[26, 27].Utilizing the GBD 2021 dataset, we extracted annual statistics on IBD incidence, prevalence, mortality, disability-adjusted life years (DALYs), and their corresponding age-standardized rates (ASRs) for the period 1990–2021.For GBD studies, the Institutional Review Board of the University of Washington reviewed and approved a waiver of informed consent. This work has been reported in line with the STROCSS criteria[28].

Joinpoint Regression Analysis

Joinpoint regression analysis is particularly adept at discerning the impact of interventions or events on disease incidence or mortality rates. Joinpoint Regression Program (Statistical Methodology and Applications Branch, National Cancer Institute, Bethesda, Maryland, USA) was used to identify trend changes and calculate annualised percentage change (APC) in leukaemia burden indicators. The average annual percentage change (AAPC), derived from APC, provided a comprehensive overview of IBD trends, aiding in understanding its temporal dynamics[29, 30].We also analysed turning points in the year, marking the most pronounced trend deviations. We analysed multiple line segments on a logarithmic scale; the intersections are termed ‘joinpoints’. The maximum number of joinpoints is based on the number of data points in the series.

In addition, pearson correlation coefficient was calculated for the AAPCs and the socio-demographic index (SDI), supplemented by Spearman’s rank-order correlation to assess the

relationships between the ASRs and the SDI to elucidate associations between socioeconomic indicators and changing ASR trends[31].

Measurement Health Inequalities

We analyzed the total DALYs and age-standardized DALY rates to assess income-related health disparities. Following The World Health Organization (WHO) recommendations, we employed two standardized measures: the slope index of inequality (SII) and the concentration index (CI)[32, 33]. SII represents the regression slope between country-level DALYs and healthcare facility availability. At the same time, the relative inequality index (RII) was derived by dividing the SII by the global ASMR. The CI was calculated using the Lorenz curve of cumulative DALYs relative to population size, with CI values ranging from -1 to 1, where negative values indicate a higher burden in lower-SDI countries.

Bayesian Age-Period-Cohort (BAPC) Model Prediction

To project future trends in IBD burden, we employed the Bayesian Age-Period-Cohort (BAPC) model, which incorporates demographic data and considers age, period, and cohort effects. This model allows us to estimate how disease incidence and mortality will evolve, taking into account shifts in population structure, changes in healthcare practices, and broader societal influences[34-36].

The BAPC model uses a Bayesian framework that integrates prior knowledge and observed data. For this study, demographic projections were downloaded from the GBD 2021 database, and the model was implemented using R software (version 4.3.3) with the 'BAPC' and 'INLA' packages. The priors of the model were specified based on historical trends observed from 1990 to 2021, and the projections were validated against known disease dynamics[37]. This approach provides robust estimates of future trends in age-standardized incidence rates (ASIR) and ASMR, which are beneficial for long-term health planning and resource allocation.

Frontier Analysis

To produce a non-linear frontier, this frontier implies the lowest achievable burden determined according to development status. We used non-parametric data envelope analysis and referenced detailed descriptions in previous studies[38]. The distance between the observed DALYs rate in a country and its frontier, defined as the effective difference, represents an unrealized health gain that exists based on the current level of development in the country or region.

Decomposition Analysis

Decomposition analysis was used to visually demonstrate the role of the three factors driving changes in incidence and mortality between 1990 and 2019 (i.e., aging, population, and epidemiology changes). Epidemiological changes refer to the underlying age and population-adjusted mortality and incidence rates. Integrating the basic methodology with advanced refinements facilitated a nuanced dissection of the respective influences of these determinants on overarching changes in incidence and mortality[37, 39].

Statistical Analysis and Data Visualisation

Prevalence, incidence, mortality, and DALYs for IBD were reported per 100,000 individuals with corresponding 95% uncertainty intervals (UIs).Statistical analyses and visualization were conducted using the WHO Health Equity Assessment Toolkit and R software (version 4.3.3), with a P-value threshold of <0.05 to establish statistical significance.

Results

Global Trends

In 2021, there were an estimated 3,830,119 global cases of IBD (95% UI: 3,312,834 to 4,511,555), with an ASPR of 44.88 per 100,000 people (95% UI: 38.8 to 52.86) (**Table 1**). The global incidence was 375,140 cases (95% UI: 327,686 to 436,925), with an ASIR of 4.45 per 100,000 people (95% UI: 3.87 to 5.19) (**Table 1**). Between 1990 and 2021, ASIR increased by 0.16 per 100,000 (95% UI: 0.07 to 0.24). In 2021, the number of IBD-related deaths was 42,423 (95% UI: 37,537 to 46,502), and the ASMR was 0.52 per 100,000 (95% UI: 0.46 to 0.57), reflecting a reduction of 0.49 per 100,000 from 1990 (95% UI: -0.68 to -0.29). The global DALYs burden in 2021 was 1,510,784 (95% UI: 1,308,508 to 1,750,363), with an age-standardized DALY rate of 18.07 per 100,000 (95% UI: 15.67 to 20.91), representing a decline of 0.57 per 100,000 from 1990 (95% UI: -0.68 to -0.46).

Table 1. Prevalence, incidence, deaths, and DALYs for males and females with IBD in 2021, and Average Annual Percentage Change (AAPC) from 1990 to 2021

Location	Prevalence (95% uncertainty interval)			Incidence (95% uncertainty interval)			Deaths (95% uncertainty interval)			DALYs (95% uncertainty interval)		
	Counts (2021)	Age-standardised rates per 100,000 (2021)	AAPC (Aaverage annual percentage changes, 95% CI), 1990-2021	Counts (2021)	Age-standardised rates per 100,000 (2021)	AAPC (Average annual percentage changes, 95% CI), 1990-2021	Counts (2021)	Age-standardised rates per 100,000 (2021)	AAPC (Aaverage annual percentage changes, 95% CI), 1990-2021	Counts (2021)	Age-standardised rates per 100,000 (2021)	AAPC (Average annual percentage changes, 95% CI), 1990-2021
Global	3830119 (3312834, 4511555)	44.88 (38.8, 52.86)	-0.22 (-0.27 – -0.17)	375140 (327686, 436925)	4.45 (3.87, 5.19)	0.16 (0.07 – 0.24)	42423 (37537, 46502)	0.52 (0.46, 0.57)	-0.49 (-0.68 – -0.29)	1510784 (1308508, 1750363)	18.07 (15.67, 20.91)	-0.57 (-0.68 – -0.46)
High SDI	2012478 (1755438, 2316531)	132.76 (115.02, 154.34)	0.06 (0.01 – 0.11)	158046 (139737, 180170)	11.59 (10.14, 13.38)	0.27 (0.22 – 0.32)	19080 (16203, 20658)	0.8 (0.7, 0.86)	0.39 (0.07 – 0.70)	599038 (501803, 711056)	35 (28.33, 42.95)	0.12 (-0.06 – 0.29)
High-middle SDI	541766 (462605, 647488)	31.63 (27.06, 37.88)	-0.37 (-0.46 – -0.28)	53486 (46612, 63298)	3.29 (2.84, 3.9)	0.28 (0.20 – 0.37)	7445 (6481, 8795)	0.4 (0.35, 0.47)	-0.82 (-1.17 – -0.47)	229281 (197044, 267170)	13.07 (11.2, 15.2)	-1.21 (-1.44 – -0.98)
Middle SDI	544518 (460464, 659902)	19.59 (16.62, 23.77)	1.12 (0.82 – 1.43)	64887 (56016, 78446)	2.36 (2.04, 2.85)	1.37 (1.11 – 1.62)	7911 (6468, 9100)	0.33 (0.27, 0.39)	-1.48 (-1.71 – -1.26)	285305 (240198, 329976)	10.92 (9.23, 12.63)	-1.17 (-1.33 – -1.02)
Low-middle SDI	561436 (475598, 680836)	32.46 (27.47, 39.12)	0.47 (0.36 – 0.58)	75380 (64725, 91310)	4.27 (3.7, 5.13)	0.54 (0.45 – 0.62)	5211 (4305, 6489)	0.38 (0.31, 0.47)	-0.74 (-0.94 – -0.53)	257852 (210807, 312042)	15.37 (12.63, 18.66)	-0.43 (-0.51 – -0.35)
Low SDI	166793 (140414, 203986)	22.84 (19.41, 27.61)	0.32 (0.24 – 0.39)	23065 (19690, 27960)	2.99 (2.59, 3.57)	0.52 (0.46 – 0.58)	2741 (1910, 3422)	0.47 (0.34, 0.58)	-0.41 (-0.56 – -0.25)	138076 (98060, 170355)	17.98 (13.29, 21.83)	-0.21 (-0.30 – -0.13)
Central Europe, eastern												

Europe, and central Asia												
Central Asia	44278 (37279, 53732)	45.59 (38.65, 54.99)	-0.04 (-0.06 – -0.02)	5018 (4317, 6101)	5.16 (4.47, 6.22)	0.51 (0.48 – 0.55)	259 (222, 301)	0.3 (0.26, 0.35)	-0.63 (-1.07 – -0.18)	17039 (14249, 20607)	17.89 (15.04, 21.59)	-0.60 (-0.85 – -0.34)
Central Europe	102432 (88116, 120328)	67.08 (57.41, 78.79)	0.06 (-0.06 – 0.18)	9297 (8128, 10754)	6.48 (5.61, 7.73)	0.61 (0.54 – 0.68)	864 (788, 948)	0.4 (0.36, 0.44)	-0.43 (-0.82 – -0.04)	33737 (28347, 40508)	19.99 (16.36, 24.17)	-0.37 (-0.67 – -0.07)
Eastern Europe	101044 (85760, 121703)	35.36 (29.96, 42.61)	-0.15 (-0.19 – -0.11)	11229 (9681, 13550)	4.1 (3.56, 4.95)	0.58 (0.55 – 0.60)	1827 (1674, 1972)	0.54 (0.5, 0.58)	-0.58 (-1.84 – 0.70)	60784 (54388, 68505)	20.1 (17.78, 22.73)	-0.63 (-1.44 – 0.18)
High-income												
Australasia	80697 (69821, 95000)	203.27 (174.69, 240.93)	0.18 (0.10 – 0.26)	7307 (6372, 8465)	19.66 (17.07, 23.2)	0.27 (0.17 – 0.37)	449 (370, 504)	0.73 (0.61, 0.81)	2.68 (1.45 – 3.94)	18181 (14279, 22717)	41.73 (31.88, 53.8)	0.63 (0.17 – 1.09)
High-income Asia Pacific	103656 (88507, 124314)	37.3 (31.63, 44.99)	0.62 (0.28 – 0.97)	6531 (5695, 7659)	2.78 (2.41, 3.33)	0.83 (0.66 – 0.99)	670 (520, 893)	0.12 (0.1, 0.16)	-3.31 (-3.77 – -2.85)	26078 (20507, 32420)	8.4 (6.37, 10.68)	-1.20 (-1.38 – -1.02)
High-income North America	997968 (872986, 1147776)	198.43 (172.53, 231.7)	-0.07 (-0.11 – -0.03)	84757 (75246, 95386)	18.51 (16.34, 21.17)	0.33 (0.28 – 0.38)	6601 (5760, 7049)	0.97 (0.86, 1.03)	1.15 (0.88 – 1.41)	266271 (220857, 319149)	49.59 (40.23, 60.57)	0.38 (0.28 – 0.47)
Southern Latin America	41020 (34731, 50197)	52.39 (44.32, 64.38)	0.23 (0.21 – 0.24)	3615 (3128, 4385)	4.75 (4.1, 5.81)	0.18 (0.16 – 0.19)	194 (176, 208)	0.22 (0.2, 0.24)	-1.61 (-2.39 – -0.83)	10421 (8332, 13030)	13.05 (10.32, 16.43)	-0.79 (-1.24 – -0.35)
Western Europe	929733 (806000, 1081441)	156.52 (134.53, 181.9)	0.28 (0.21 – 0.34)	66438 (58285, 76430)	12.74 (11.08, 15.02)	0.29 (0.25 – 0.33)	12791 (10650, 13952)	1.11 (0.95, 1.2)	1.08 (0.67 – 1.49)	318237 (270223, 372594)	42.86 (34.92, 52.29)	0.42 (0.06 – 0.78)
Latin America and Caribbean												
Andean Latin America	8917 (7559, 10768)	13.64 (11.6, 16.44)	0.11 (0.09 – 0.13)	1050 (896, 1298)	1.59 (1.37, 1.96)	0.51 (0.48 – 0.53)	88 (67, 112)	0.15 (0.11, 0.19)	-1.36 (-1.59 – -1.12)	4056 (3243, 5112)	6.33 (5.07, 7.98)	-1.72 (-1.91 – -1.53)
Caribbean	14187 (11971, 16921)	27.5 (23.24, 32.78)	-0.05 (-0.07 – -0.03)	1379 (1182, 1660)	2.71 (2.32, 3.27)	0.58 (0.55 – 0.62)	187 (151, 234)	0.35 (0.28, 0.44)	-1.81 (-2.16 – -1.46)	7921 (6413, 9847)	15.47 (12.47, 19.3)	-1.07 (-1.30 – -0.84)
Central Latin America	14704 (12236,	5.56 (4.62, 6.66)	-0.00 (-0.03 –	1502 (1263, 1849)	0.57 (0.48, 0.69)	-0.03 (-0.22	887 (797, 976)	0.36 (0.32, 0.4)	0.06 (-0.78 –	26766 (24122, 29560)	10.4 (9.38, 11.48)	0.16 (-0.67

	17650)		0.03)			– 0.16)			0.91)			– 0.98)
Tropical Latin America	52828 (44696, 63509)	20.38 (17.31, 24.44)	1.47 (1.15 – 1.79)	7616 (6550, 9287)	2.95 (2.54, 3.59)	1.43 (1.10 – 1.76)	1298 (1199, 1375)	0.52 (0.48, 0.55)	0.06 (-0.40 – 0.53)	43913 (40418, 47689)	17.22 (15.86, 18.63)	0.07 (-0.66 – 0.82)
North Africa and Middle East												
North Africa and Middle East	215400 (179465, 259039)	35.66 (29.95, 42.92)	0.67 (0.56 – 0.77)	19656 (16586, 24187)	3.18 (2.73, 3.87)	0.49 (0.46 – 0.51)	1055 (857, 1389)	0.26 (0.21, 0.34)	-0.41 (-0.73 – -0.09)	65235 (52158, 81440)	11.76 (9.47, 14.59)	-0.19 (-0.35 – -0.03)
South Asia												
South Asia	802536 (676700, 975731)	46.19 (39.17, 55.73)	0.55 (0.44 – 0.67)	106215 (91605, 128247)	6 (5.21, 7.23)	0.60 (0.49 – 0.71)	4718 (3511, 6288)	0.34 (0.26, 0.45)	-1.18 (-1.56 – -0.79)	269363 (211770, 341921)	16.09 (12.71, 20.42)	-0.64 (-0.79 – -0.48)
Southeast Asia, east Asia, and Oceania												
East Asia	172201 (145043, 206864)	9.07 (7.72, 10.9)	1.57 (1.19 – 1.95)	25532 (22107, 30530)	1.39 (1.2, 1.66)	2.05 (1.49 – 2.61)	5967 (4700, 7910)	0.33 (0.26, 0.44)	-2.65 (-2.87 – -2.43)	143569 (116156, 180091)	7.77 (6.32, 9.64)	-2.84 (-3.04 – -2.63)
Oceania	642 (534, 789)	5.57 (4.64, 6.76)	-0.13 (-0.15 – -0.11)	90 (76, 112)	0.76 (0.65, 0.93)	0.50 (0.47 – 0.53)	21 (14, 29)	0.25 (0.17, 0.35)	-1.58 (-1.70 – -1.46)	884 (631, 1235)	8.46 (6.06, 11.62)	-1.45 (-1.58 – -1.32)
Southeast Asia	42506 (35567, 51597)	5.68 (4.78, 6.87)	0.08 (0.04 – 0.13)	5035 (4271, 6181)	0.68 (0.58, 0.83)	0.56 (0.52 – 0.60)	1236 (888, 1470)	0.22 (0.16, 0.26)	-1.34 (-1.44 – -1.25)	40665 (30950, 47973)	6.14 (4.63, 7.23)	-1.19 (-1.27 – -1.10)
Sub-Saharan Africa												
Central Sub-Saharan Africa	11350 (9614, 13814)	12.52 (10.6, 15.03)	-0.17 (-0.21 – -0.12)	1751 (1488, 2156)	1.83 (1.59, 2.22)	0.94 (0.91 – 0.98)	222 (146, 321)	0.39 (0.26, 0.55)	-0.11 (-0.20 – -0.02)	10677 (7389, 14923)	12.61 (8.99, 17.32)	-0.11 (-0.19 – -0.04)
Eastern Sub-Saharan Africa	34879 (29436, 42004)	12.88 (10.94, 15.42)	0.42 (0.40 – 0.44)	4903 (4178, 5999)	1.67 (1.45, 1.99)	0.68 (0.66 – 0.71)	738 (487, 996)	0.41 (0.27, 0.57)	-0.11 (-0.17 – -0.06)	33535 (23245, 43657)	13.12 (9.12, 17.26)	-0.01 (-0.08 – 0.06)
Southern Sub-Saharan Africa	12192 (10352, 14773)	17.26 (14.78, 20.71)	0.58 (0.55 – 0.60)	1285 (1101, 1551)	1.72 (1.49,2.04)	0.17 (0.11 – 0.23)	210 (163, 254)	0.38 (0.29, 0.45)	0.01 (-0.23 – 0.25)	8962 (7397, 10630)	13.13 (10.92, 15.55)	-0.03 (-0.19 – 0.12)

Western Sub-Saharan Africa	46950 (39669, 56938)	15.84 (13.47, 19.19)	0.68 (0.65 – 0.72)	4933 (4236, 5971)	1.49 (1.3, 1.77)	0.25 (0.22 – 0.29)	2140 (1338, 2907)	0.77 (0.52, 1.02)	-0.01 (-0.11 – 0.08)	104491 (64783, 142649)	30.2 (19.84, 40.71)	0.15 (0.06 – 0.24)

Regional Trends

In 2021, regions with High SDI had the highest ASPR for IBD at 132.76 per 100,000 (95% UI: 115.02 to 154.34) (**Table 1**). The highest ASPRs were found in the High-income Australasia (203.27 per 100,000; 95% UI: 174.69 to 240.93) and High-income North America (198.43 per 100,000; 95% UI: 172.53 to 231.7) regions (**Table 1 and Figure 1A**). In contrast, High-income Asia Pacific (37.3 per 100,000; 95% UI: 31.63 to 44.99) and the Southern Latin America (52.39 per 100,000; 95% UI: 44.32 to 64.38) reported the lowest ASPRs (**Table 1 and Figure 1A**).

Between 1990 and 2021, ASIR trends varied by region. In Middle SDI regions, the ASPR increased modestly by 1.37 per 100,000 (95% UI: 1.11 to 1.62)(**Table 1**). Central Latin America showing a decrease of 0.03 per 100,000 (95% UI: -0.22 to -0.16)(**Table 1**). East Asia recorded the most significant increase in ASIR, rising by 2.05 per 100,000 (95% UI: 1.49 to 2.61), followed by the Tropical Latin America (1.43 per 100,000; 95% UI:1.10 to 1.76) (**Table 1 and Figure 1B**).

Regarding mortality, the hHigh SDI regions had the highest ASMR at 0.8 per 100,000 (95% UI: 0.7 to 0.86), while the Middle SDI regions reported the lowest at 0.33 per 100,000 (95% UI: 0.27 to 0.39) (**Table 1**). The Middle SDI regions experienced the most significant reduction in ASMR, with a decrease of 1.48 per 100,000 (95% UI: -1.17 to -1.26) (**Table 1**). Western Europe had the highest ASMR at 1.11 per 100,000 (95% UI: 0.95 to 1.2), while High-income Australasia had an ASMR of 0.73 per 100,000 (95% UI: 0.61 to 0.81) (**Table 1 and Figure C**). In contrast,the High SDI and High-income Australasia saw increases, with ASMRs rising to 0.39 per 100,000 (95% UI: 0.07 to 0.70) and 2.68 per 100,000 (95% UI: 1.45 to 3.94), respectively (**Table 1 and Figure 1C**).

Globally, the age-standardized DALYs rate for IBD has also shown an overall downward trend.The most notable reductions were observed in East Asia (-2.84 per 100,000 persons; 95% UI: -3.04 to -2.63), the Andean Latin America(−1.72 per 100,000 persons; 95% UI: -1.91 to -1.53), and Oceania (-1.45 per 100,000 persons; 95% UI: -1.58 to -1.32) (**Table 1 and Figure 1D**).

National Trends

Nationally, the ASPR for IBD in 2021 ranged from 1.86 to 326.63 per 100,000 people. The Canada reported the highest ASPR of 326.63 per 100,000 (95% UI: 278.93 to 385.55), followed by Netherlands (278.47 per 100,000; 95% UI: 241.04 to 327.43), San Marino (269.34 per 100,000; 95% UI: 230.40 to 321.10), and Germany (244.23 per 100,000; 95% UI: 206.67 to 291.64) (**Figure 1A and Supplementary Table S1**). In contrast, Mexico (1.86 per 100,000; 95% UI: 1.54 to 2.28) and Philippines (4.29 per 100,000; 95% UI: 3.58 to 5.23) had the lowest ASPRs (**Figure 1A and Supplementary Table S1**).

In terms of ASMR, Netherlands (2.21 per 100,000; 95% UI: 1.84 to 2.42) and Germany (1.91 per 100,000; 95% UI: 1.63 to 2.10) had the highest rates, while Afghanistan (0.29 per 100,000; 95% UI: 0.13 to 0.68) and Albania (0.57 per 100,000; 95% UI: 0.34 to 0.82) reported the lowest (**Figure 1C and Supplementary Table S3**). For more information about ARIS and DALYs, see **Figure 1D**; **Supplementary Tables S2 and S4**.

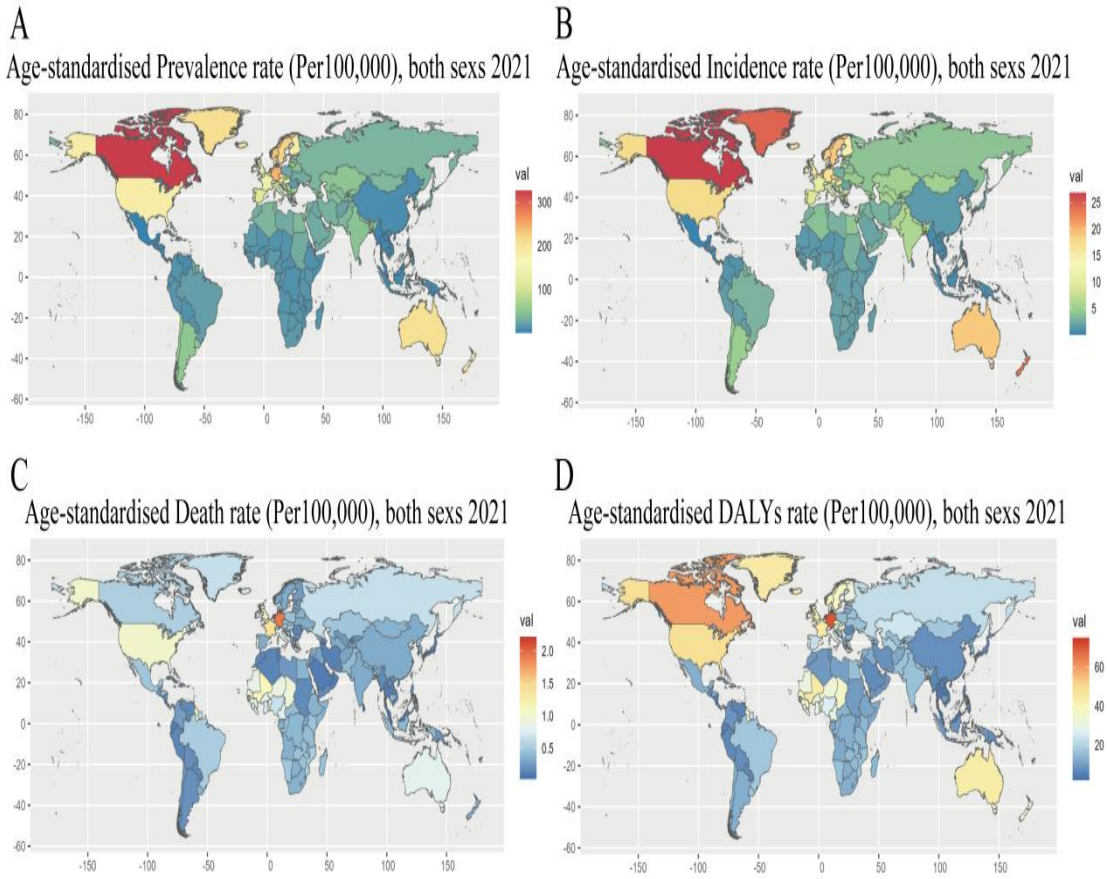

Figure 1. Global distribution of IBD disease burden in 2021. (A) Age-standardized prevalence rates. (B) Age-standardized incidence rates. (C) Age-standardized mortality rates. (D) Age-standardized DALYs rates.

Age and Sex Patterns

In 2021, for the numbers of prevalence, the global burden of IBD was the highest in the 50-54 age group. However, sex-specific prevalence patterns differed, with males showing the highest prevalence in the 90-94 age group and females in the 95+ age group (**Figure 2A-B and Supplementary Tables S5**). In 2021, the incidence rates of IBD was higher in males (9.48) compared to females (9.1) in the 50-54 age group (**Figure 2C-D and Supplementary Tables S6**).The mortality rates was highest in the 95+ age group, followed by the 90-94 and 85–89 age groups, with no significant gender differences across age groups. Notably, in the 95+ age group, the female mortality rates contribution per 100,000 was greater than that of males (46.49 vs. 32.4) (**Figure 2E-F and Supplementary Tables S7**).

The DALYs rates analysis revealed a trend similar to that of the prevalence, with DALYs decreasing with age. However, there was an increased DALYs rates in the 95+ age group compared to the 90-94 age group (**Figure 2G and Supplementary Tables S8**). The largest disparities in DALYs rates between sexes were observed in the 95+ age group (females 393.33 vs. males 279.54), the 75-79 age group (females 68.6 vs. males 83.2), and the 60-64 age group (females 36.54 vs. males 45.42) (**Figure 2H and Supplementary Tables S8**).The age distribution of the population is critical to understanding the IBD burden. In particular, those aged ≥90 years are a high-risk group.

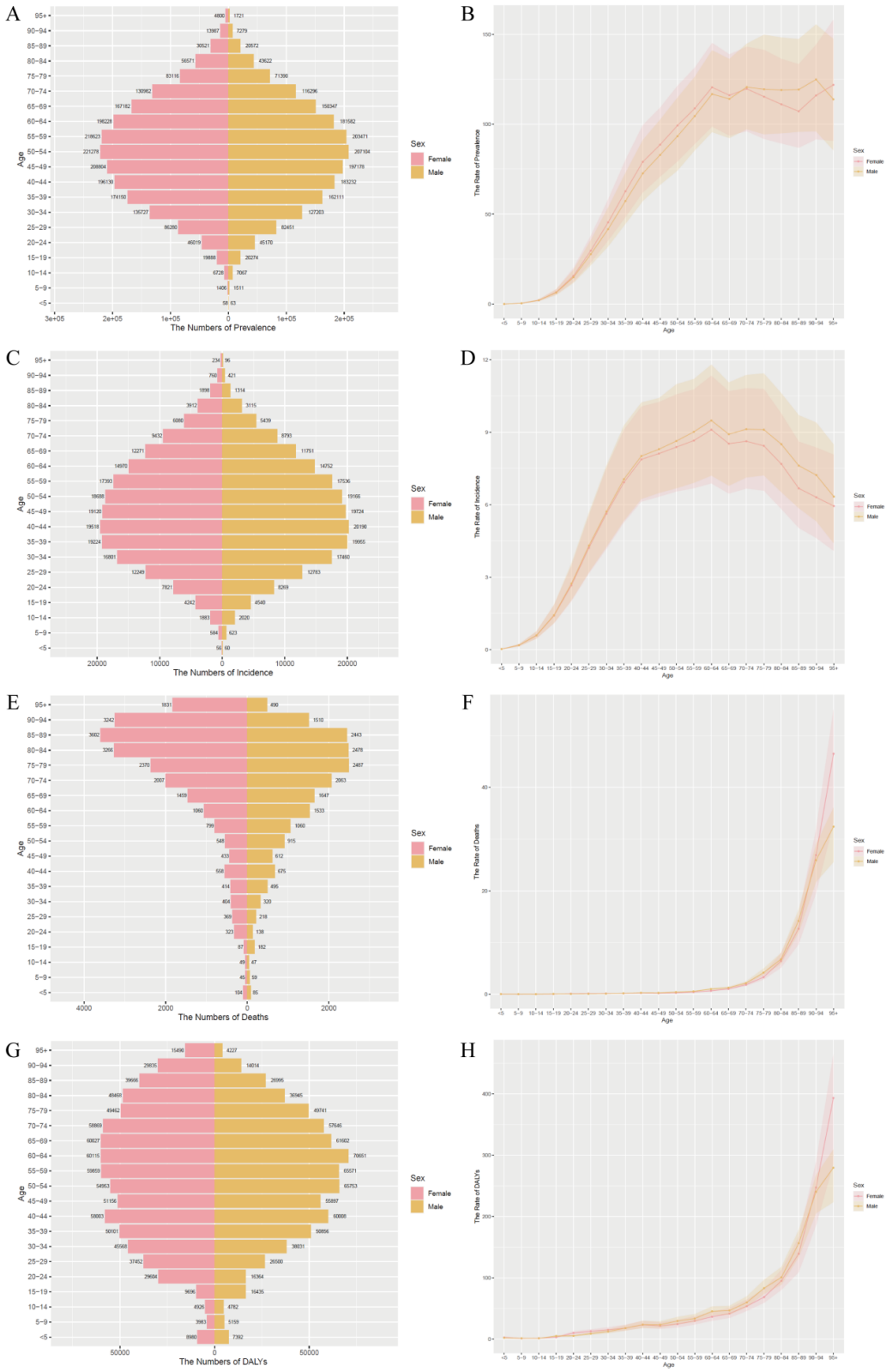

Figure 2. Sex- and age-structured analysis of IBD disease burden in 2021. (A) The numbers of prevalence. (B) Age-standardised prevalence rates. (C) The numbers of incidence. (D) Age-standardised morbidity rates. (E) The numbers of deaths. (F) age-standardised mortality rates. (G) The numbers of DALYs. (H) Age-standardised DALY rates.

Overall Temporal Trends in Gender and Age Structures

From 1990 to 2021, the IBD prevalence, incidence, mortality, and DALY rates showed a modest but consistent increase, followed by a slight decline across all age groups. Prevalence, mortality, and DALY rates were consistently

higher in females than males throughout the study period (**Figure 3A-D and Supplementary Tables S9-S1**2). It is worth noting that there was a significant upward trend in the number of female deaths between 2011 and 2013. For more detailed age- and sex-specific global prevalence incidence, mortality, and DALY rates data from 1990 to 2021, refer to Supplementary Material (**Supplementary Tables S9-S12**).

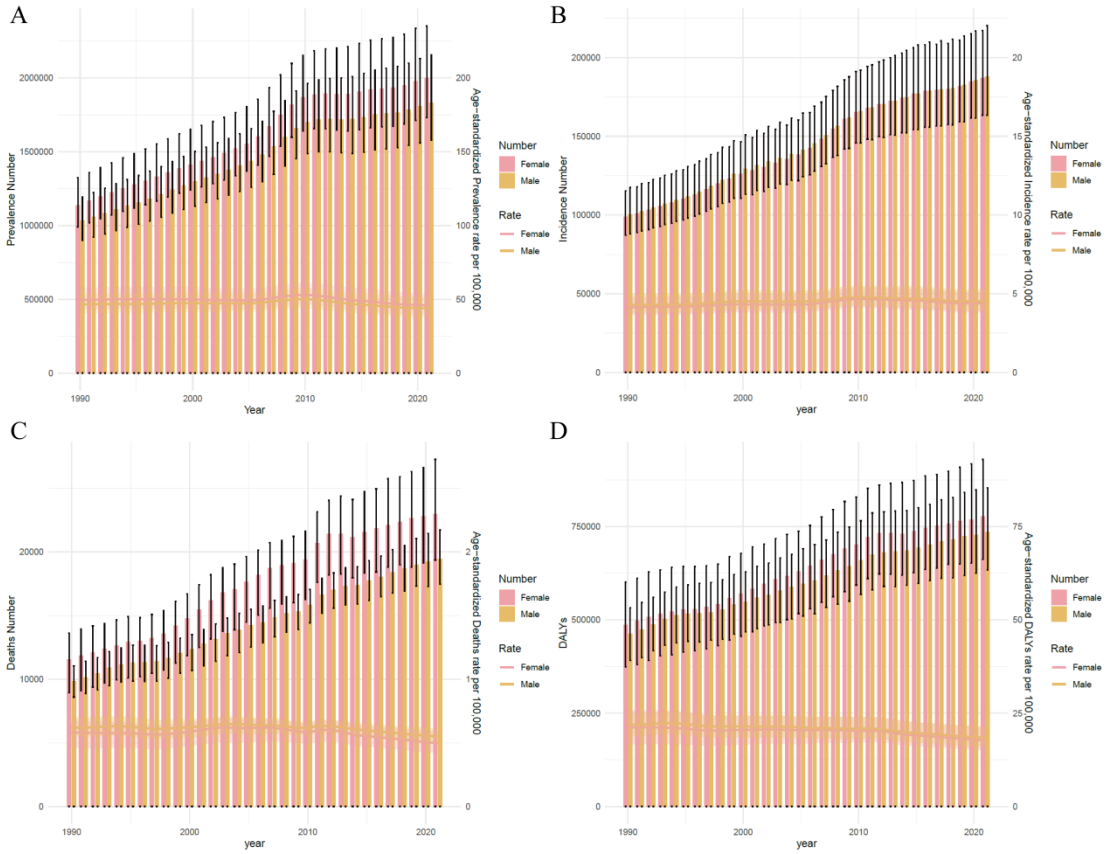

Figure 3. Global temporal trends in IBD disease burden, 1990-2021. (A) Prevalence in all age groups. (B) Incidence in all age groups. (C) Mortality in all age groups. (D) DALY rate in all age groups.

Temporal Joinpoint Analysis

Joinpoint regression analysis identified ASR trends for IBD prevalence, incidence, mortality, and DALYs from 1990 to 2021 in global and 5 SDI regions(**Figure 4A-D**).

Globally, the overall trend in IBD prevalence decreased, with an AAPC of -0.22% (95% CI: -0.27% to -0.17%; P < 0.001) (**Figure 4A and Supplementary Table S13**). The most significant decrease occurred between 2010 and 2014 (APC = -1.80%; 95% CI: -2.00 % to -1.61%; P < 0.001), while the sharpest increase were observed between 2005 and 2010 (APC = 1.53%; 95% CI: 1.41% to 1.66%; P < 0.001).The overall trend in IBD incidence increased, with an AAPC of 0.16% (95% CI: 0.07% to 0.24%; P < 0.001) . Notably, the most significant increase occurred between 2005 and 2010 (APC = 1.58%; 95% CI: 1.29 % to 1.88%; P < 0.001).The overall trend in IBD mortality decreased, with an AAPC of -0.49% (95% CI: -0.68% to -0.29%; P < 0.001) .The most significant decrease occurred between 2012 and 2021 (APC = -1.75%; 95% CI: -2.00 % to -1.50%; P < 0.001).The overall trend in IBD DALYs decreased, with an AAPC of -0.57% (95% CI: -0.68% to -0.46%; P < 0.001) (**Figure 4A-D and Supplementary Tables S13-S16**).The details of the ASR trends for IBD prevalence, incidence, mortality, and DALYs from 1990 to 2021 in the 5 SDI regions were provided in the **Supplementary Tables S13-S16**.

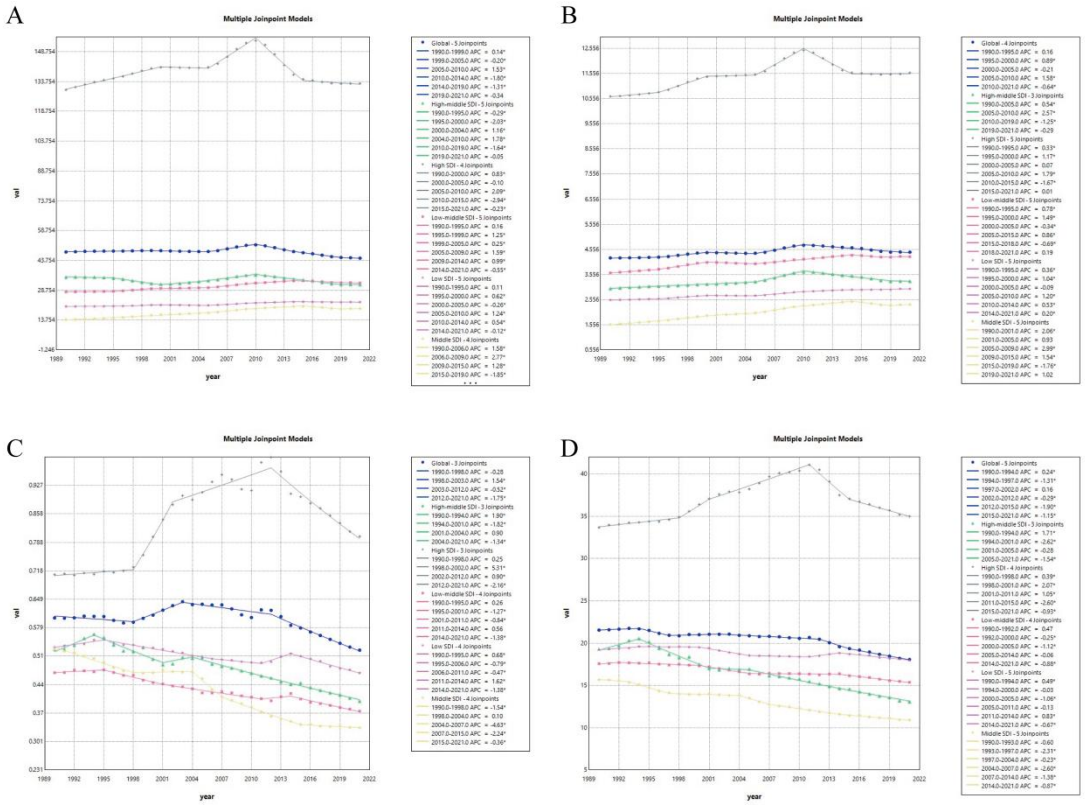

Figure 4. Joinpoint regression analysis of the IBD disease burden temporal trends, 1990-2021. (A) Age-standardized prevalence rates. (B) Age-standardized incidence rates. (C) Age-standardized mortality rates. (D) Age-standardized DALYs rates.

Changing Patterns at Different SDI Levels and Baseline Burden

SDI, a measure derived from the GBD database, assesses the level of socioeconomic development in a country or region. At the regional level, there was an overall positive correlation between ASIR and SDI, suggesting that the IBD burden decreases with higher socioeconomic development (**Figure 5A and Supplementary Table S17**).The burden in Australasia and High-income North America was much higher than expected levels in 2021.Interestingly, a 'W-shaped' relationship between ASMR and SDI was observed(**Figure 5B and Supplementary Table S18**).

At the national level, positive correlations were estimated between SDI and ASIR. It is obvious that the positive correlation trend between SDI and ASIR is more significant when SDI is greater than 0.75. The burden in Canada, Greenland, New Zealand and Netherlands was much higher than expected levels in 2021(**Figure 5C and Supplementary Table S19**).The correlation between SDI and ASMR showed a fluctuating trend. The positive correlation trend between SDI and ASMR is more significant when SDI is greater than 0.83.The burden in Netherlands, Germany, France and Cyprus was much higher than expected levels in 2021(**Figure 5D and Supplementary Table S20**).

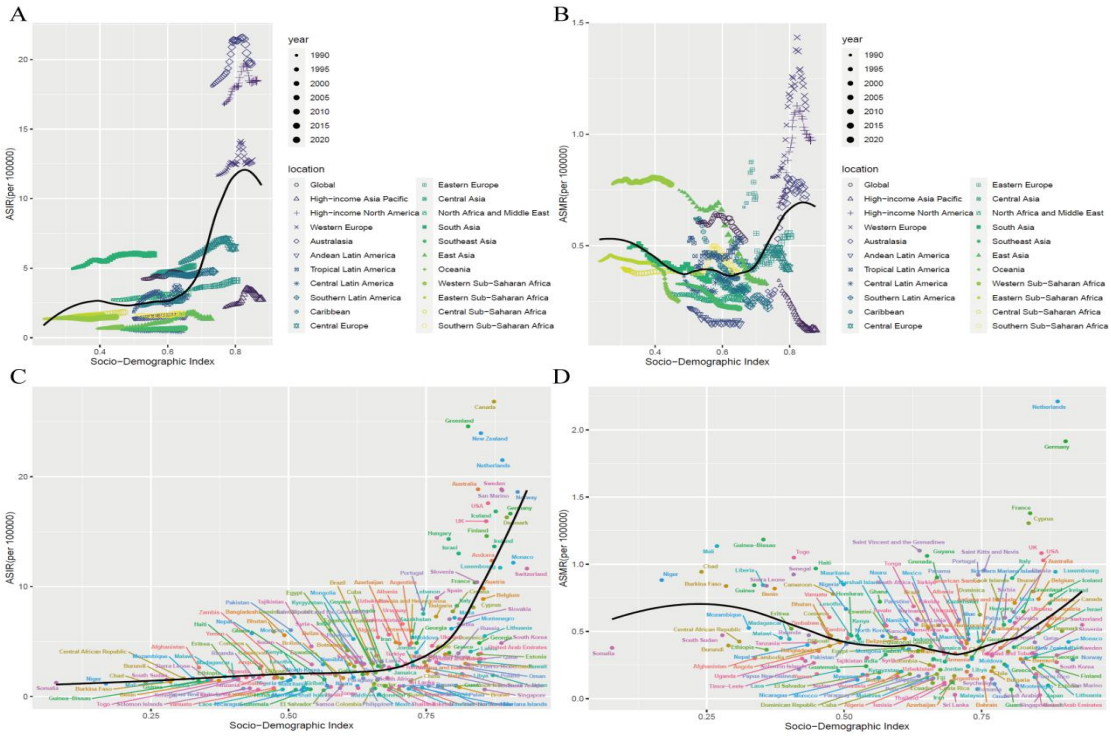

Figure 5. The burden of IBD globally and in 204 countries and 21 regions, as shown by SDI. (A) ASIR globally and in 21 GBD regions, 1990-2021. (B) ASMR globally and in 21 GBD regions, 1990-2021. (C) IBD ASIR and SDI in 204 countries and regions, 2021. (D) IBD ASMR and SDI in 204 countries and regions, 2021.

Cross-National Health Inequality in IBD Burden

We calculated the SII for the DALYs to assess the income-related disparities in the burden of IBD. In 1990 and 2021, the SII (per 100,000 population) for DALYs were 20.23 (95% CI 14.71 to 25.74) and -3.68 (95% CI -9.47 to 2.11) respectively, indicating a negative correlation between age-standardized DALY rates and SDI index (**Figure 6A**).This significant decline suggests a reduction in the inequality of age-standardized burden of IBD between high-income and low-income countries during this period. Between 1990 and 2021, the concentration index for DALYs and Deaths has shown an increasing trend (**Figure 6B**). Although inequalities in the burden of IBD between poor and rich countries have decreased across regions, inequalities persist. This indicates that while the gap between rich and poor has narrowed in some regions, global inequality in IBD remains a persistent issue.

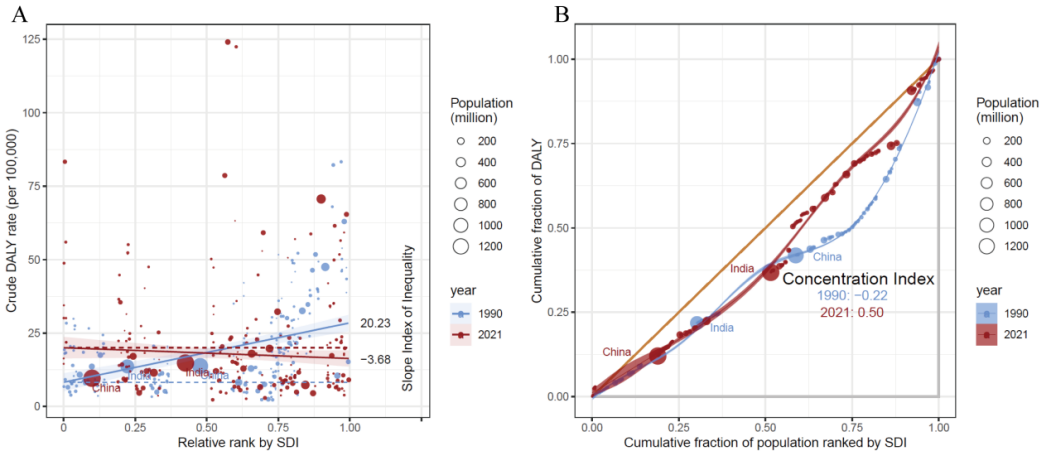

Figure 6. SII analysis and Concentration index analysis. (A) Absolute income-related healthy inequality in IBD burden, presented using regression lines, 1990 vs. 2021. (B) Relative income-related healthy inequality in IBD burden, presented using concentration curves, 1990 vs. 2021.

Global Disease Burden Projections for IBD (2022-2036)

Using the BAPC model, we projected the global burden of IBD from 2022 to 2036. The model accounts for age, period, and cohort effects and incorporates data from 1990 to 2021. By 2036, the ASIR for IBD is projected to decrease to 43.9 per 100,000 for males and 41.6 per 100,000 for females, representing reductions of 3.09% and 4.56%, respectively, compared with 2021 (**Figure 7A-B and Supplementary Table S21 and S23**).

Similarly, global ASMR is expected to continue declining. By 2036, the ASMR is forecasted to be 4.66 per 100,000 for males and 4.00 per 100,000 for females, reflecting a decrease of 16.93% and 20.79%, respectively, compared to 2021 (**Figure 7C-D; Supplementary Table S22 and S24**). Notably, the decline in IBD incidence and mortality is expected to be more pronounced among females, contributing significantly to the overall reduction in global IBD burden.

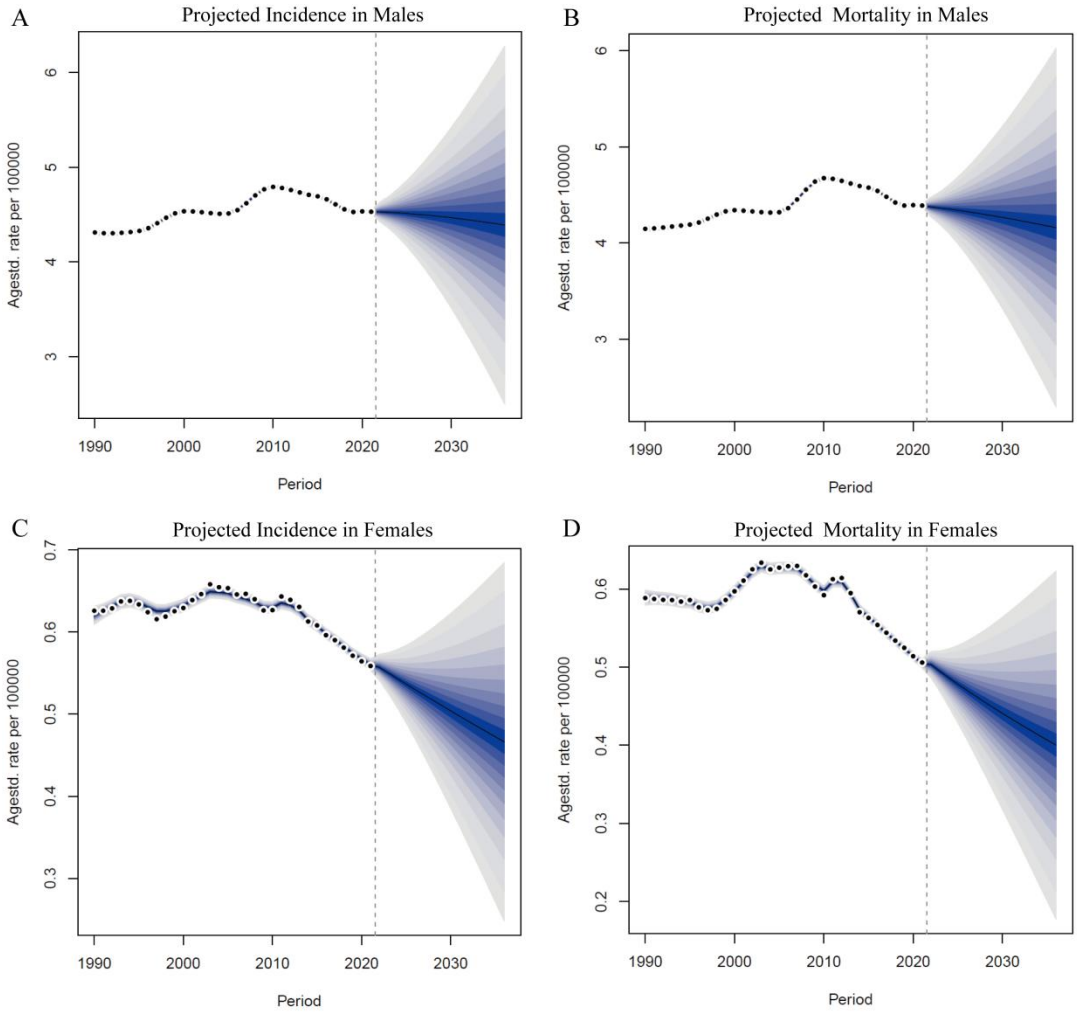

Figure 7 Projects the global age-standardized incidence and age-standardized mortality rate of IBD for both sexes from 2022 to 2036. (A) Projected Incidence in Males. (B) Projected Mortality in Males. (C) Projected Incidence in Females. (D) Projected Mortality in Females.

Frontier analysis of age-standardized DALYs Rates

The unrealized health gains of countries or regions at different levels of development during the period 1990–2021 are shown in **Supplementary Figure S1A**. **Supplementary Figure S1B** shows the DALYs burden and the effective difference in countries or regions with different sociodemographic development levels in 2019. With sociodemographic development, effective difference generally increased to some extent, indicating that countries or regions with a higher SDI have greater burden improvement potential.

The frontier is delineated in solid black color; countries and territories are represented as dots. The top 15 countries with the largest effective difference (IBD DALYs gap from the frontier) are labeled in black; examples of frontier countries with low SDI (< 0.5) and low effective difference are labeled in blue (e.g., Papua New Guinea, Yemen, and Timor-Leste), and examples of countries and territories with high SDI (> 0.85) and relatively high effective difference for their level of development are labeled in red (e.g., Canada, Germany and Netherlands). Red dots indicate an increase in age-standardized IBD DALYs rate from 1990 to 2021; blue dots indicate a decrease in age-standardized IBD DALYs rate between 1990 and 2021(**Supplementary Figure S1A-B**).

Decomposition Analysis

For incidence decomposition analysis,the past 30 years have seen a significant global increase in both sexes. Of these, the increase in population growth (72,060.81 vs. 64,460.54) and epidemiological changes trends were greater for males than for females.For mortality decomposition analysis, the past 30 years also have seen a significant global increase in both sexes.It is noteworthy that the number of deaths increased more among females than males (11,411.10 vs. 9,593.93). Decomposition analyses can therefore help us understand the extent to which these three factors individually influence the burden of disease in IBD. We can thus infer that the number of IBD cases may increase with age. As the population grows, it may result in more people having IBD. The epidemiological changes trends (incidence), such as the emergence of new diseases or new treatments, may alter the incidence of IBD (**Supplementary Figure S2A-B and Supplementary Table S25 and S26**).

Discussion

IBD is a complex and challenging health problem that exerts a significant impact on the quality of life of millions of individuals worldwide[40, 41].The results of this study highlight the evolving global burden of IBD from 1990 to 2021, with notable trends in incidence, mortality, and DALY rates across various sociodemographic regions. The global IBD burden continues to be influenced by regional disparities, age distribution, and sex-specific patterns, further complicated by differences in SDI.

Globally, there has been a modest increase in IBD incidence, particularly in high-income regions such as Australasia and North America, which consistently report the highest ASPRs. This trend is in line with earlier research that associates urbanization, industrialization, and dietary shifts toward a Westernized diet with an increased incidence of IBD in these regions. Meanwhile, lower SDI regions, including parts of Asia and Latin America, have experienced a more gradual rise in prevalence, likely due to delayed industrialization and lifestyle changes[42].

Age and sex patterns underscore a significant global health challenge. The higher burden of IBD in older age groups, particularly among females, may reflect not only population aging but also sex-specific biological differences in immune response and hormonal influences. The observed increases in DALY rates among the 95+ age group emphasize the growing need for tailored healthcare approaches for elderly populations.

Interestingly, although the overall trend for IBD-related mortality has declined, mortality rates in some High SDI regions, such as Western Europe, continue to be elevated. This could be attributed to the long-term complications of IBD, including colorectal cancer and other comorbidities that remain prominent despite advances in therapeutic interventions. The projected decline in global mortality rates by 2036, particularly among females, reflects potential gains in healthcare access and the effectiveness of newer biological therapies targeting IBD.

The SDI appears to play a crucial role in shaping these trends, as evidenced by the significant positive correlation between SDI and ASIR across several regions. The ‘W-shaped’ relationship between ASMR and SDI suggests that higher income countries may face a paradox where better healthcare access leads to earlier detection but also results in long-term management challenges for chronic conditions like IBD.

Despite the overall decline in health disparities between high- and low-income countries, inequalities persist in the global burden of IBD. The SII analysis indicates that while income-related disparities have decreased over the last three decades, certain regions, particularly low SDI areas, continue to face a disproportionate

burden due to limited healthcare resources. These findings underscore the need for targeted public health interventions to address both the rising incidence of IBD in low- and middle-income countries and the ongoing management of chronic disease in high-income settings.

In conclusion, the global trends in IBD burden reveal important regional, age, and sex disparities that must be addressed through tailored healthcare strategies. Future research should focus on further exploring the underlying mechanisms driving these disparities, especially in the context of changing lifestyle patterns and environmental risk factors. Moreover, continued monitoring of sociodemographic shifts and the long-term impacts of new therapies will be critical to reducing the global burden of IBD.

Strengths and Limitations

This is one of the most comprehensive analyses of the global burden of IBD to date, covering key indicators such as incidence, mortality and DALYs. It also predicts future changes in the global burden of IBD, particularly in terms of declining trends in incidence and mortality. In addition, the role of gender and age in disease progression was considered, revealing a high burden in older and female populations and providing a basis for precision medicine.

Despite the aforementioned strengths of this study, there are several limitations, which are reflected in the quality of the data, risk factor analysis and predictive modelling. Firstly, there are significant differences in data quality and availability across countries and regions, particularly in the absence of robust disease surveillance systems in parts of low- and middle-income countries. This may lead to an underestimation or inaccurate reflection of the global burden of IBD, especially in rural areas with inadequate healthcare infrastructure. Secondly, this study did not analyse all potential risk factors for IBD, for example, other important factors such as genetic susceptibility, environmental exposures and diet were not adequately included, potentially limiting the full understanding of IBD risk factors. Thirdly, the study's projections of the future burden of IBD were based on current trends and patterns, but could not adequately account for possible future changes in risk factors, advances in screening and treatment technologies, and adjustments in health policy. Therefore, these projections should be interpreted with caution and updated regularly as new data become available. Finally, although the GBD methodological framework has been widely adopted in global burden of disease studies, it has its own limitations. For example, possible biases in data collection and model estimation, as well as the disability weights used in DALYs calculations may not fully reflect the actual experiences of patients in different cultural contexts. Future studies need to refining the data collection methods further and incorporating the assessment of risk factors in the analyses in order to provide a more comprehensive assessment of the burden of disease.

Conclusions

This study reveals the complexity of the global burden of IBD, especially the significant differences in regions with different levels of socioeconomic development. Despite a gradual decline in incidence and mortality globally, some high-income regions still face challenges in managing long-term complications of IBD. Future medical interventions and public health policies should be tailored to region-specific trends and disparities, focusing on improving the long-term management of high-burden populations and reducing global inequalities. Further reductions in the global health burden of IBD are expected through continuous monitoring and optimisation of treatment strategies.

Statement of Ethics

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Conflict of Interest Statement

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Funding

This study was supported by Scientific and technological innovation project of China Academy of Chinese Medical Sciences (No.CI2021A00801 and No.CI2021A00806) and

Sanming Proiect of Medicine in Shenzhen (No.SZZYSM202311014).

Authors Contributions

Conceptualization, XFY

Investigation, XFY,GZW

Methodology, XFY,GZW

Writing–original draft XFY

Reviewing–editing LYP, LWL

All authors have read and agreed to the published version of the

manuscript.

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Data availability statement

Availability of data and materials: Relevant data can be retrieved through the available website (**https://vizhub.healthdata.org/gbd-results/**).

Acknowledgements

We thank the Institute of Health Metrology and Evaluation for sharing valuable GBD data.

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