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Miscellaneous

The global burden of peptic ulcer disease in 204 countries and territories from 1990 to 2019: a systematic analysis for the Global Burden of Disease Study 2019

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Abstract

Background: Peptic ulcer disease is one of the most common diseases in gastroenterology clinics. However, reported data about the global burden of peptic ulcer disease are still scarce.

Methods: This was a secondary data analysis on the prevalence, mortality and disability-adjusted life years (DALYs) due to peptic ulcer disease by sex, age group and socio-demographic index (SDI) at the global level in 21 regions and 204 countries and territories between 1990 and 2019 using the Global Burden of Diseases, Injuries, and Risk Factors Study 2019.

Results: Globally, the prevalence cases of peptic ulcer disease increased from 6 434 103 (95% uncertainty interval 5 405 963 to 7 627 971) in 1990 to 8 090 476 (6 794 576 to 9 584 000) in 2019. However, the age-standardized prevalence rate decreased from 143.4 (120.5 to 170.2) per 100 000 population in 1990 to 99.4 (83.9 to 117.5) per 100 000 population in 2019. Moreover, the age-standardized mortality rate decreased by 59.4% (55.3 to 63.1) and the DALYs rate fell by 60.6% (56.8 to 63.9) from 1990 to 2019. Across SDI quintiles, low-middle and low SDI quintiles had the highest age-standardized prevalence, mortality and DALYs rates from 1990 to 2019.

Conclusion: The age-standardized prevalence, mortality and DALYs estimates of peptic ulcer disease decreased from 1990 to 2019 globally, but more efforts are needed for the prevention, early diagnosis and treatment of peptic ulcer disease in low SDI and low-middle SDI groups of countries.

Key words: Peptic ulcer disease, Global Burden of Disease, prevalence, mortality, disability-adjusted life years

Key Messages

- The age-standardized prevalence, mortality and disability-adjusted life years (DALYs) estimates of peptic ulcer disease decreased from 1990 to 2019 at the global level.
- Low-middle and low socio-demographic index (SDI) quintiles had the highest age-standardized prevalence, mortality and DALYs rates of peptic ulcer disease from 1990 to 2019.
- Males had a higher age-standardized prevalence rate of peptic ulcer disease than females, except in the age group <25 years in 2019 and in the low SDI quintile from 1990 to 2019.
- The decrease in the age-standardized prevalence rate from peptic ulcer disease is likely in large part due to a decrease in *Helicobacter pylori* infection, more rational use of non-steroidal anti-inflammatory drugs and wider usage of proton-pump inhibitors and histamine$_2$ receptor antagonists.

Introduction

Peptic ulcers, which usually occur in the stomach and proximal duodenum, can lead to severe acute upper abdominal pain or have a more insidious onset and then develop into a chronic disease with asymptomatic and symptomatic periods.[1] The symptomatic period can present as abdominal pain, bloating, nausea and early satiety.[2] Regardless of the duration of the disease, acute and severe complications, including bleeding, perforation or gastric outlet obstruction, can develop.[3] Moreover, chronic gastric ulcer disease predisposes patients to gastric cancer.[3] Those severe outcomes can result in a substantial medical and social burden.[4,5]

The majority of gastric and duodenal ulcers are thought to be associated with infection by *Helicobacter pylori* and the widespread usage of non-steroidal anti-inflammatory drugs (NSAIDs).[6] Meanwhile, at least one-fifth of idiopathic peptic ulcer cases are *H. pylori*-negative and NSAID-negative.[7] Life-threatening trauma,[8] psychological stress,[9] being male,[10] smoking,[11] being of older age[11] and having chronic medical conditions[11] are associated with a higher prevalence of peptic ulcer disease. Early diagnosis and treatment of peptic ulcer disease and its sequelae have been thoroughly discussed.[12] Peptic ulcer disease is one of the most common diseases in gastroenterology clinics, causing substantial morbidity and mortality until the last decade of the twentieth century.[13] Subsequently, the use of effective acid suppressants and antibiotics has resulted in a significant decrease in peptic ulcer disease as well as its complications around the world.[2]

In European and non-European countries, surveys in 2007 revealed a decline in mortality from gastric and duodenal ulcers.[14,15] Across Sweden, the UK, the USA, Israel and Denmark, a 2009 study conducted by Sung *et al.* indicated that the prevalence of peptic ulcer disease varied from 0.1% to 4.7% between 1977 and 2002.[16] For India, the burden of peptic ulcer disease showed a 25.4% decrease in the prevalence rate and a 70.0% decrease in the mortality rate from 1990 to 2016.[17] However, the aforementioned studies only covered a limited number of countries. Reported data about the global burden of peptic ulcer disease are still scarce. In addition, the association between the burden of peptic ulcer disease and the socio-demographic index (SDI) of countries have not been analysed. Therefore, we studied the prevalence, mortality and disability-adjusted life years (DALYs) due to peptic ulcer disease by time, location, sex, age and SDI level dimensions using data from the Global Burden of Disease, Injuries, and Risk Factors Study (GBD) 2019.[3] These results will provide researchers and policymakers with valuable epidemiological information to promote effective strategies, such as specific countries investing in health systems and raising public awareness, to improve the management of peptic ulcer disease.

Materials and methods

Overview

The GBD 2019 is the first systematic database to analyse 369 diseases and injuries, 286 causes of death and 87 risk factors for the global level, 21 regions and 204 countries and territories from 1990 to 2019.[3] The overall objectives, methods and organization of GBD 2019 have been extensively reported.[3,18]

In brief, for estimates of the non-fatal burden due to peptic ulcer disease, the GBD 2019 gathered data from hospital discharges and claims with any peptic ulcer disease International Classification of Disease (ICD) code, from peer-reviewed publications and from household surveys to estimate prevalence by location, year, age and sex using the disease model-Bayesian meta-regression (DisMod-MR) 2.1 model. Furthermore, the severity of peptic ulcer disease was assigned using different disability weights. Each sequela prevalence rate was multiplied by a

sequela-specific disability weight to calculate the years lived with disability.

For estimates of the fatal burden, vital registration data and vital registration sample data from the cause of death database were collected by the GBD 2019 to model the mortality by location, year, age and sex attributed to peptic ulcer disease with a standard Cause of Death Ensemble modelling approach.[19] The years of life lost due to peptic ulcer disease were calculated using standard global life expectancy and the number of deaths according to age. Peptic ulcer disease DALYs, which represented the total number of years lost to illness, disability or premature death, were calculated as the sum of years lived with disability and years of life lost. Uncertainty intervals were defined as the 2.5% and 97.5% values of the posterior distribution.

Case definition

In the GBD 2019, peptic ulcer disease, a digestive disorder, was defined as defects in the stomach (gastric ulcers) or the duodenum (duodenal ulcers) extending through to the muscularis mucosa into the submucosa. Detailed information about the ICD codes (ICD-10) is provided in Supplementary Table S1 (available as Supplementary data at *IJE* online).

SDI and geographic regions

The SDI is a composite indicator of the background social and economic conditions that influence health outcomes in each location. It ranges from 0 (worst) to 100 (best), calculated from national-level income per capita, mean years of education among persons >15 years old and total fertility rate among women aged <25 years. It is used to categorize the countries and territories into five SDI quintiles (high, high-middle, middle, low-middle and low levels). Meanwhile, the GBD 2019 categorized 204 countries and territories into 21 geographic regions. The included countries and territories for each geographical region are listed in Supplemental Table S2 (available as Supplementary data at *IJE* online).

Data extraction and analyses

This is a secondary analysis based on data of the prevalence, mortality and DALYs in terms of numbers, age-standardized rates and percentage change in the age-standardized rates due to peptic ulcer disease by sex, age group and SDI in the global level, 21 regions and 204 countries and territories between 1990 and 2019 extracted from the GBD 2019 (publicly available online). Prevalence, mortality and DALYs rates refer to total cases, deaths and DALYs per 100 000 population. Furthermore, the associations between SDI and age-standardized prevalence, mortality and DALYs rates in 2019 or the percentage change in the age-standardized prevalence, mortality and DALYs rates from 1990 to 2019 were measured using Spearman's rank sum correlation tests[20] and were visualized by Locally Weighted Scatterplot Smoothing curves.[21,22] All statistical analyses were performed using R software (Version 4.0.3, R core team).

Results

Prevalence burden of peptic ulcer disease

Globally, the prevalence cases of peptic ulcer disease increased from 6 434 103 (95% uncertainty interval: 5 405 963 to 7 627 971) in 1990 to 8 090 476 (6 794 576 to 9 584 000) in 2019. However, the age-standardized prevalence rate per 100 000 population was 143.4 (120.5 to 170.2) in 1990 and 99.4 (83.9 to 117.5) in 2019—a decrease of 30.7% (28.7 to 32.6) from 1990 to 2019 (Table 1). In detail, the global age-standardized prevalence rate decreased from 1990 to 2015 and then showed a mild increase from 2015 to 2019 (Figure 1A). Among the 21 GBD regions, the highest age-standardized prevalence rate of peptic ulcer disease was reported in Eastern Europe [157 (129.2 to 188.8)] and South Asia [156.6 (130.6 to 187)] per 100 000 population. In addition, Central Latin America [33 (28.5 to 38.5)] and Southern Latin America [35.4 (29.5 to 42)] presented the lowest age-standardized prevalence rate per 100 000 population in 2019 (Table 1 and Supplementary Figure S1A, available as Supplementary data at *IJE* online). The highest decrease in the age-standardized prevalence rate occurred in Tropical Latin America [−70% (−71.4 to −68.6)] from 1990 to 2019 (Table 1 and Supplementary Figure S1B, available as Supplementary data at *IJE* online). Among the 204 countries and territories, the age-standardized prevalence rate of peptic ulcer disease in 2019 ranged from 15.19 to 330.32 per 100 000 population. The highest age-standardized prevalence rate was found in Kiribati and Vanuatu (Figure 2A and Supplementary Table S3, available as Supplementary data at *IJE* online). The change in the age-standardized prevalence rate was different between 1990 and 2019 among the 204 countries and territories, with the largest decreases reported in Bangladesh and Brazil (Supplementary Figure S2A and Supplementary Table S3, available as Supplementary data at *IJE* online).

Mortality burden of peptic ulcer disease

The number of deaths due to peptic ulcer disease decreased from 278 979 (259 455 to 301 112) in 1990 to 236 139

Table 1 Prevalence, mortality and DALYs for peptic ulcer disease in 2019 and percentage change in the age-standardized rate from 1990 to 2019

Measure	Prevalence (95% UI)			Mortality (95% UI)			Disability-adjusted life years (95% UI)		
	Cases	Age-standardized rate per 100 000 population	Percentage change in age-standardized rate per 100 000 population	Deaths	Age-standardized rate per 100 000 population	Percentage change in age-standardized rate per 100 000 population	Years	Age-standardized rate per 100 000 population	Percentage change in age-standardized rate per 100 000 population
Global	8 090 476 (6 794 576 to 9 584 000)	99.4 (83.9 to 117.5)	−30.7 (−32.6 to −28.7)	236 139 (216 762 to 261 413)	3 (2.7 to 3.3)	−59.4 (−63.1 to −55.3)	6 029 510 (5 586 598 to 6 641 773)	74.4 (69 to 81.9)	−60.6 (−63.9 to −56.8)
SDI									
High	1 210 512 (1 034 476 to 1 425 082)	81 (68.2 to 95.8)	−20.8 (−23.8 to −18.1)	25 352 (21 967 to 28 013)	1.2 (1 to 1.3)	−69 (−70.9 to −66.6)	431 321 (391 452 to 465 697)	24.2 (22.1 to 26.2)	−66.8 (−68.6 to −64.9)
High-middle	1 550 526 (1 285 171 to 1 857 861)	84 (69.9 to 100.3)	−29.7 (−31.7 to −27.7)	38 952 (35 625 to 41 836)	2 (1.8 to 2.1)	−57.2 (−61.1 to −53.5)	876 014 (810 892 to 942 390)	45.1 (41.8 to 48.6)	−59.4 (−63.4 to −55.5)
Middle	2 001 993 (1 652 545 to 2 392 497)	78.2 (65.3 to 92.9)	−34.4 (−37 to −31.7)	59 505 (54 130 to 66 054)	2.8 (2.5 to 3.1)	−61.9 (−66.3 to −56.5)	1 426 041 (1 313 180 to 1 583 778)	58.5 (53.8 to 65.1)	−65.1 (−69.1 to −60.3)
Low-middle	2 195 504 (1 832 150 to 2 613 422)	140.5 (117.9 to 166.2)	−41.7 (−43.5 to −39.8)	81 311 (72 346 to 93 692)	6.5 (5.8 to 7.5)	−61.4 (−67.1 to −54.3)	2 216 874 (1 988 317 to 2 550 606)	152.4 (136.7 to 175.2)	−65.5 (−70.2 to −59.3)
Low	1 128 658 (952 311 to 1 334 547)	145.3 (123.8 to 169.9)	−27.8 (−29.5 to −26.1)	30 884 (27 174 to 35 016)	6.2 (5.3 to 7)	−51.7 (−59.3 to −42.8)	1 075 653 (948 157 to 1 219 387)	155.1 (137.2 to 175.2)	−54.7 (−61.6 to −47.5)
21 regions									
East Asia	1 489 858 (1 219 467 to 1 820 690)	74.4 (61.6 to 89.6)	−46.3 (−48.3 to −44.4)	42 948 (36 862 to 50 139)	2.4 (2 to 2.8)	−68.7 (−74.6 to −61.8)	918 055 (788 014 to 1 073 456)	46.8 (40.4 to 54.4)	−73.4 (−78.7 to −66.9)
Southeast Asia	495 039 (407 014 to 594 480)	73.8 (61.8 to 87.6)	−21.8 (−24.6 to −19.2)	19 408 (17 285 to 22 253)	3.7 (3.3 to 4.2)	−57 (−63.4 to −47.7)	480 444 (424 499 to 562 739)	78.6 (69.7 to 91.4)	−61.4 (−67 to −53.4)
Oceania	13 860 (11 737 to 16 267)	129.9 (112.4 to 151.1)	−19.5 (−22.5 to −16.2)	477 (383 to 601)	7.2 (5.8 to 9)	−37 (−49.7 to −20.4)	17 041 (13 523 to 21 770)	185.5 (149.7 to 231.5)	−37.1 (−51.1 to −18)
Central Asia	82 145 (70 420 to 95 428)	92.7 (79.8 to 106.9)	−26.6 (−29.6 to −23.4)	2445 (2182 to 2768)	3.4 (3.1 to 3.9)	−15.1 (−24.2 to −2.9)	78 505 (69 726 to 88 632)	93.6 (83.6 to 105)	−24.9 (−33.2 to −15.5)
Central Europe	174 814 (151 160 to 200 646)	101.8 (87.9 to 118.3)	−10.7 (−13 to −8.5)	5923 (5181 to 6695)	2.8 (2.4 to 3.1)	−47 (−53.2 to −40)	120 052 (105 467 to 136 073)	62.1 (54.4 to 70.2)	−50.4 (−56.2 to −43.9)
Eastern Europe	439 985 (363 829 to 533 969)	157 (129.2 to 188.8)	−6.6 (−8.5 to −4.7)	11 874 (10 503 to 13 274)	3.6 (3.2 to 4)	−0.2 (−11.1 to 13.1)	312 622 (277 409 to 352 293)	102.5 (91 to 115.6)	−6.2 (−16.6 to 6.4)
High-income Asia Pacific	335 708 (279 075 to 404 674)	117.1 (95.4 to 141.6)	−6.6 (−11.3 to −1.5)	5642 (4463 to 6652)	1 (0.8 to 1.1)	−76.9 (−79.3 to −74.7)	87 700 (75 518 to 97 867)	21.4 (18.6 to 24.1)	−72.1 (−75.5 to −69.3)
Australasia	15 950 (13 143 to 19 216)	39.6 (32 to 48)	−43.5 (−48.9 to −37.6)	505 (414 to 594)	0.9 (0.7 to 1)	−81.4 (−84.2 to −78.3)	7291 (6272 to 8342)	14.7 (12.7 to 16.6)	−80.9 (−83.1 to −78.3)
Western Europe	267 120 (222 158 to 318 412)	40 (32.5 to 48.3)	−30.2 (−34.5 to −26)	13 345 (11 615 to 14 955)	1.2 (1.1 to 1.4)	−69.6 (−71.8 to −65.4)	197 466 (179 439 to 215 617)	22.4 (20.7 to 24.3)	−69.3 (−71.3 to −65.9)
Southern Latin America	27 349 (22 907 to 32 304)	35.4 (29.5 to 42)	−15.9 (−20 to −11.5)	1312 (1141 to 1499)	1.5 (1.3 to 1.8)	−52.6 (−58.7 to −45.6)	25 363 (22 556 to 28 729)	31.2 (27.8 to 35.3)	−55.2 (−60.8 to −48.8)
High-income North America	541 480 (466 230 to 632 345)	100.6 (86.7 to 116.5)	−21.7 (−26 to −16.7)	5698 (5040 to 6154)	0.9 (0.8 to 0.9)	−68 (−69.7 to −65.9)	119 406 (108 526 to 131 585)	20.7 (18.7 to 22.8)	−62 (−64.1 to −59.5)
Caribbean	28 403 (24 106 to 33 183)	56.3 (47.7 to 66.2)	−23 (−26.1 to −19.8)	1759 (1476 to 2092)	3.4 (2.9 to 4.1)	−48.9 (−56.2 to −40.4)	44 111 (36 238 to 53 543)	87.4 (71.3 to 106.6)	−50.4 (−58.9 to −40.9)
Andean Latin America	25 932 (22 164 to 30 509)	43.4 (37.3 to 50.6)	−35.4 (−38.6 to −32.1)	1620 (1297 to 2004)	3 (2.4 to 3.7)	−63.3 (−70.7 to −51.5)	33 763 (27 058 to 41 817)	59.1 (47.4 to 73.4)	−69.4 (−76 to −59.5)
Central Latin America	80 456 (68 954 to 94 070)	33 (28.5 to 38.5)	−37.7 (−39.7 to −35.7)	7857 (6819 to 9139)	3.5 (3 to 4.1)	−62.9 (−67.3 to −57.3)	161 366 (139 617 to 188 762)	68 (58.6 to 79.3)	−64.8 (−69.4 to −59)
Tropical Latin America	115 939 (96 300 to 140 459)	47.3 (39.6 to 57.1)	−70 (−71.4 to −68.6)	5286 (4772 to 5823)	2.3 (2 to 2.5)	−62.5 (−65.4 to −57.5)	122 912 (114 129 to 132 708)	50.5 (46.8 to 54.6)	−65.4 (−67.9 to −62.1)
North Africa, and Middle East	522 218 (424 465 to 637 549)	91.1 (75.3 to 109.9)	−12.4 (−16.4 to −8.1)	9604 (7925 to 11 651)	2.6 (2.1 to 3.1)	−55.7 (−63.3 to −46.7)	266 067 (217 521 to 323 933)	56.4 (46.8 to 67.8)	−58.2 (−65.5 to −49.4)
South Asia	2 520 121 (2 085 276 to 3 013 098)	156.6 (130.6 to 187)	−43.6 (−45.3 to −41.8)	74 929 (63 470 to 89 532)	5.9 (5 to 7.1)	−66.9 (−73.2 to −59.2)	2 098 566 (1 792 974 to 2 479 691)	140 (119.9 to 165)	−69.6 (−74.8 to −62.7)
Central sub-Saharan Africa	97 138 (81 817 to 115 774)	116.5 (99.9 to 135.4)	−1.8 (−4.9 to 1.5)	2998 (2139 to 3997)	5.8 (3.6 to 8.3)	−30.5 (−46.7 to −10.4)	111 625 (82 300 to 149 232)	145.9 (105.7 to 193.2)	−37.4 (−51.1 to −16.6)
Eastern sub-Saharan Africa	298 069 (247 371 to 359 431)	103.9 (88.9 to 121.3)	−16.8 (−18.5 to −15.2)	7324 (4936 to 9942)	4.1 (2.6 to 5.9)	−43.6 (−60.4 to −30.1)	282 485 (206 782 to 367 085)	114.5 (78.3 to 153)	−46.4 (−62.6 to −32.4)
Southern sub-Saharan Africa	57 827 (47 764 to 69 641)	82.9 (69.2 to 98)	−2 (−4.2 to 0.4)	2513 (2241 to 2852)	4.9 (4.4 to 5.5)	−10.6 (−33.3 to 25.1)	69 784 (59 574 to 81 798)	112.2 (98.3 to 128.5)	−18.8 (−41.6 to 15)
Western sub-Saharan Africa	461 063 (379 646 to 552 951)	132.3 (113 to 154.3)	−6.1 (−7.2 to −4.9)	12 672 (9247 to 16 901)	6.7 (5.1 to 8.6)	−28.7 (−44.4 to −10.9)	474 887 (341 306 to 667 446)	166.1 (122.3 to 221)	−31.6 (−47 to −12.3)

DALYs, disability-adjusted life years; UI, uncertainty interval; SDI, socio-demographic index.

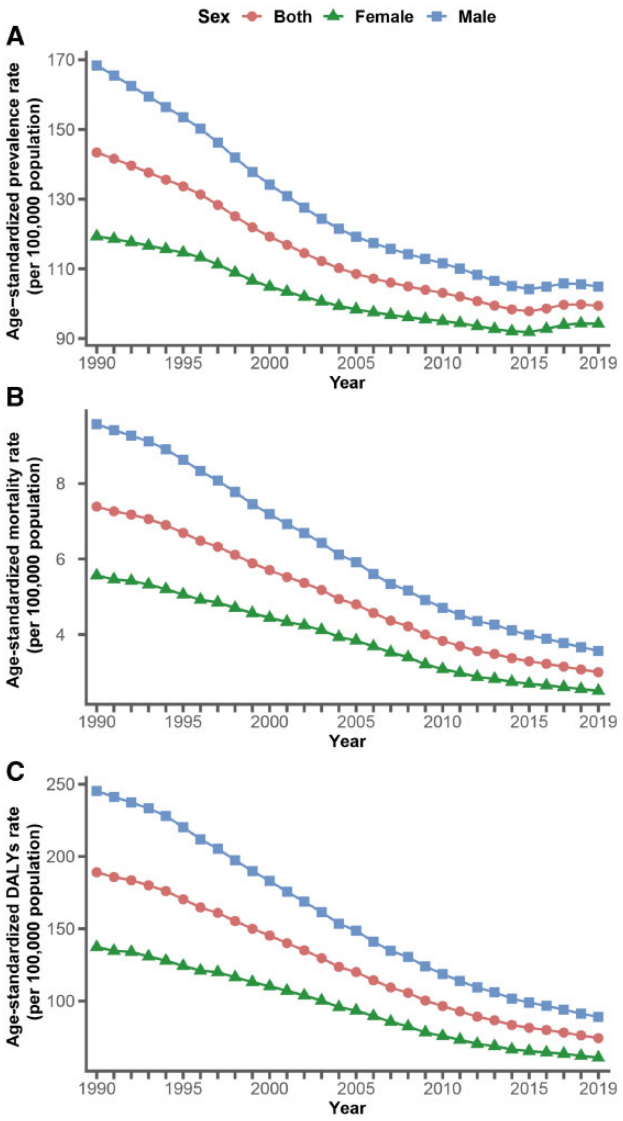

Figure 1 Age-standardized prevalence (A), mortality (B) and DALYs (C) rates of peptic ulcer disease from 1990 to 2019 by sex at the global level.

DALYs, disability-adjusted life years.

(216 762 to 261 413) in 2019 globally. Meanwhile, the global age-standardized mortality rate also decreased by 59.4% (55.3 to 63.1) from 7.4 (6.9 to 7.9) per 100 000 population in 1990 to 3 (2.7 to 3.3) per 100 000 population in 2019 (Table 1), showing a steady decreasing pattern (Figure 1B). Among the 21 GBD regions, Oceania [7.2 (5.8 to 9)] and Western sub-Saharan Africa [6.7 (5.1 to 8.6)] revealed the highest age-standardized mortality rate of peptic ulcer disease per 100 000 population. In contrast, high-income North America [0.9 (0.8 to 0.9)] and Australasia [0.9 (0.7 to 1)] demonstrated the lowest age-standardized mortality rate in 2019 per 100 000 population (Table 1 and Supplementary Figure S1C, available as Supplementary data at *IJE* online). In addition, the largest decrease in the age-standardized mortality rate was reported in Australasia [−81.4% (−84.2 to −78.3)] between 1990 and 2019 (Table 1 and Supplementary Figure S1D, available as Supplementary data at *IJE* online). Among the 204 countries and territories, the age-standardized mortality rate of peptic ulcer disease ranged from 0.46 to 22.48 per 100 000 population in 2019. The highest age-standardized mortality rate was observed in Cambodia, Kiribati, Lao People's Democratic Republic and Timor-Leste (Figure 2B and Supplementary Table S4, available as Supplementary data at *IJE* online). From 1990 to 2019, the largest decrease in the age-standardized mortality rate was found in Bangladesh and an increase in the age-standardized mortality rate occurred only in Lithuania, Lesotho, Zimbabwe, Armenia, Russian Federation, Uzbekistan and Ukraine (Supplementary Figure S2B and Supplementary Table S4, available as Supplementary data at *IJE* online).

The DALYs burden of peptic ulcer disease

Globally, it was estimated 8 196 064 (7 581 035 to 8 965 447) of DALYs in 1990 and 6 029 510 (5 586 598 to 6 641 773) of DALYs in 2019 from peptic ulcer disease, with an age-standardized DALYs rate of 189 (175.5 to 205.6) in 1990 and 74.4 (69 to 81.9) in 2019 per 100 000 population, showing a sustained decreasing tendency [−60.6% (56.8 to 63.9)] from 1990 to 2019 (Table 1 and Figure 1C). The regions with the highest and lowest age-standardized DALYs rates of peptic ulcer disease in 2019 and the highest decrease in the age-standardized DALYs rate between 1990 and 2019 were the same as those reported for mortality burden of peptic ulcer disease in the above section (Table 1 and Supplementary Figure S1E and F, available as Supplementary data at *IJE* online). The national age-standardized DALYs rate of peptic ulcer disease in 2019 ranged from 9.88 to 512.71 per 100 000 population. Kiribati and Cambodia exhibited the highest age-standardized DALYs rate in 2019 (Figure 2C and Supplementary Table S5, available as Supplementary data at *IJE* online). From 1990 to 2019, the largest decrease in the age-standardized DALYs rate was found in Bangladesh and the age-standardized DALYs rate was observed to increase in the nations of Lithuania, Lesotho, Zimbabwe, Ukraine and Mozambique (Supplementary Figure S2C and Supplementary Table S5, available as Supplementary data at *IJE* online).

Age- and sex-related burden of peptic ulcer disease

Global age-standardized prevalence, mortality and DALYs rates were consistently higher in males than in females from 1990 to 2019 (Figure 1A–C). However, females in

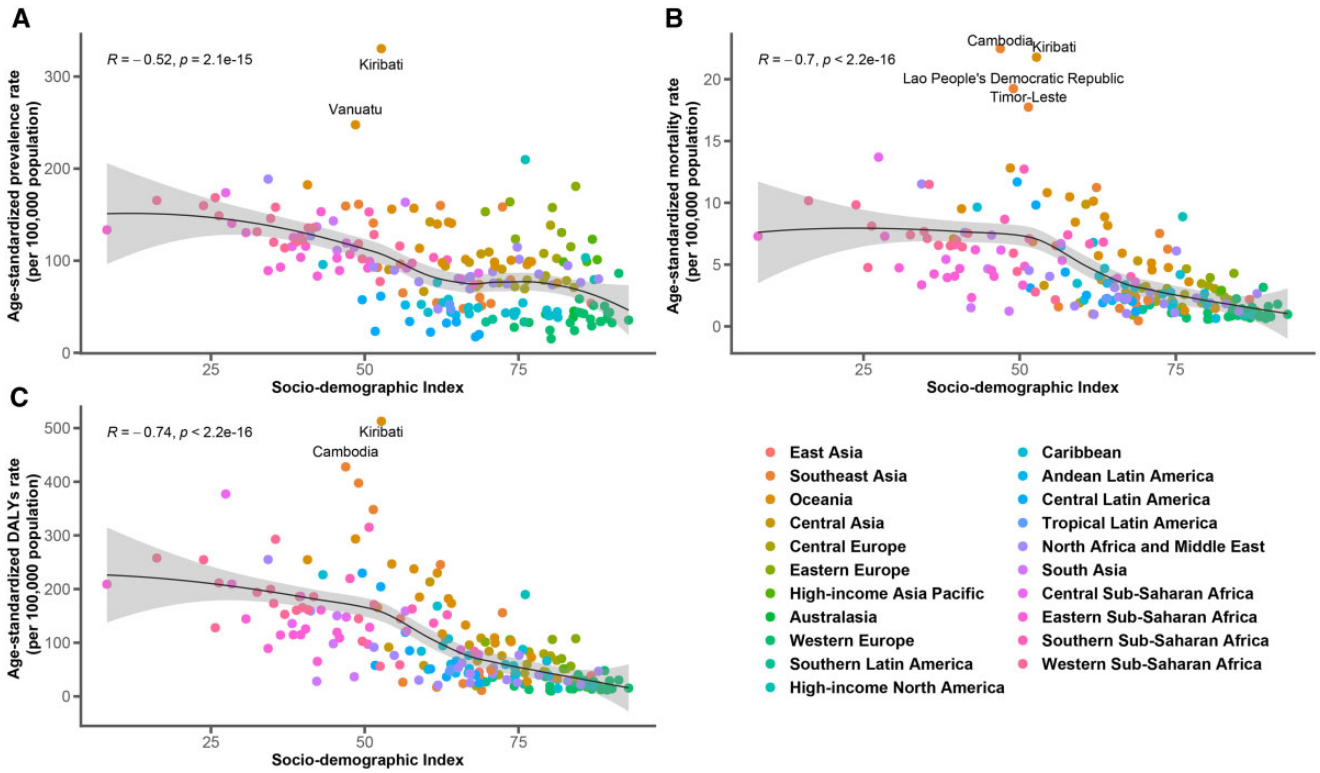

Figure 2 Correlation of the age-standardized prevalence (A), mortality (B) and DALYs (C) rates of peptic ulcer disease in 2019 with different SDI in 204 countries and territories.

DALYs, disability-adjusted life years; SDI, socio-demographic index.

the low SDI quintile had a higher age-standardized prevalence rate of peptic ulcer disease than males from 1990 to 2019 (Figure 3). All regions apart from South Asia, Western sub-Saharan Africa, Central sub-Saharan Africa, High-income North America, and North Africa and Middle East had higher age-standardized prevalence rates among males than among females in 2019 (Supplementary Figure S1A, available as Supplementary data at *IJE* online). Although the burden of peptic ulcer disease decreased from 1990 to 2019 for both males and females globally, an increased age-standardized prevalence rate from 1990 to 2019 was found for females in Eastern Europe, Southern sub-Saharan Africa, Western sub-Saharan Africa and Central sub-Saharan Africa (Supplementary Figure S1B, available as Supplementary data at *IJE* online). The highest increases in the age-standardized prevalence, mortality, and DALYs rates for females were reported in Eastern Europe (Supplementary Figure S1B, S1D, S1F, available as Supplementary data at *IJE* online). The prevalence rate increased gradually with age, peaking at age 80 to 84 years, and then showed a mild decrease over age 85 years in 2019 (Figure 4A). Overall, mortality and DALYs rates of peptic ulcer disease increased with age, reaching their highest level in the 85 plus years age group, with a dramatic increase in the mortality rate in the group aged over 85 years (Figure 4B-C). Moreover, the prevalence, mortality, and DALYs rates were higher in males than in females in the older age groups (25 plus years). However, females in lower age groups (under 25 years) had a higher prevalence rate than males (Figure 4A).

The burden of peptic ulcer disease by SDI

The patterns of disease burden due to peptic ulcers varied substantially according to SDI quintiles. The age-standardized prevalence rate showed a decreasing tendency from 1990 to 2015 in all SDI quintiles and then a mild increase from 2015 to 2019 in the middle SDI quintile. Moreover, the highest decrease in the age-standardized prevalence rate was reported in the low-middle SDI quintile [−41.7% (−43.5 to −39.8)]. Additionally, the low and low-middle SDI quintiles had the highest age-standardized prevalence rate from 1990 to 2019, whereas the lowest age-standardized prevalence rate was found in the high SDI quintile before 2005 and in the middle SDI quintile from 2005 to 2019 (Table 1 and Figure 5A). For the age-standardized mortality and DALYs rates, gradual decreasing trends were observed among all SDI quintiles from 1990 to 2019. But the low SDI quintile had the lowest decrease in the age-standardized mortality [−51.7% (−59.3

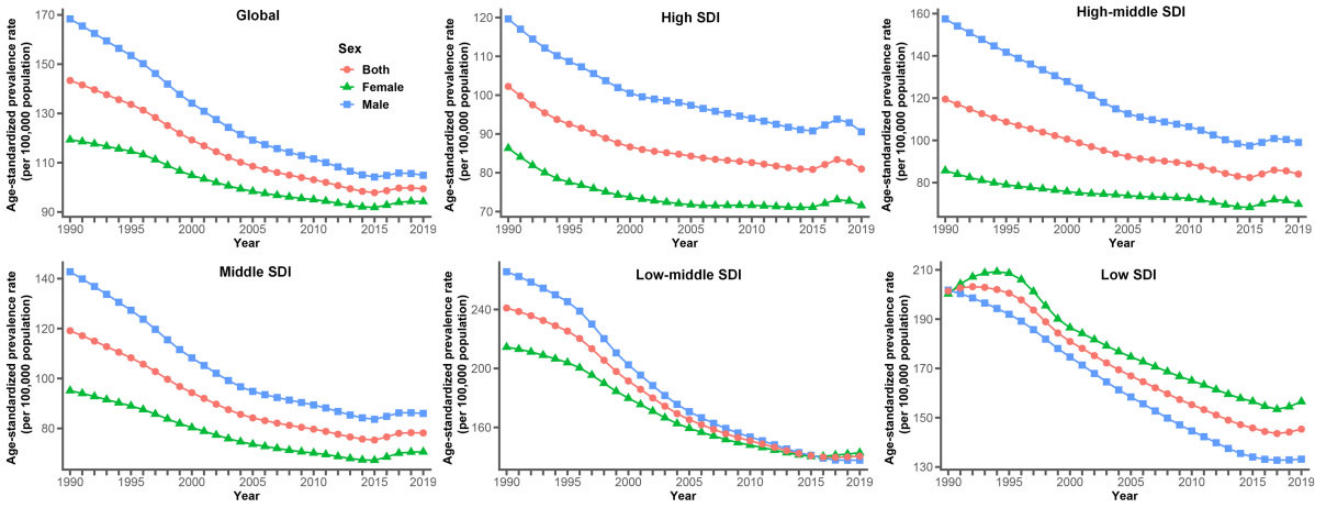

Figure 3 Age-standardized prevalence rate of peptic ulcer disease from 1990 to 2019 by sex and SDI quintile.

SDI, socio-demographic index.

to −42.8)] and DALYs [−54.7% (−61.6 to −47.5)] rates. The highest age-standardized mortality and DALYs rates were seen in the low and low-middle SDI quintiles, whereas the lowest were in the high SDI quintile from 1990 to 2019 (Table 1 and Figure 5B and C).

Moreover, moderate negative correlations were found between SDI and age-standardized prevalence ($R = -0.52$, $P < 0.05$), mortality ($R = -0.7$, $P < 0.05$) and DALYs ($R = -0.74$, $P < 0.05$) rates of peptic ulcer disease in 2019 (Figure 2A–C). We further investigated the change in disease burden for 204 countries and territories from 1990 to 2019 by SDI levels and discovered negative relationships between SDI and changes in the age-standardized mortality ($R = -0.5$, $P < 0.05$) and DALYs ($R = -0.47$, $P < 0.05$) rates (Supplementary Figure S2B and C, available as Supplementary data at *IJE* online). However, this relationship was not observed between the SDI and change in the age-standardized prevalence rate ($R = -0.091$, $P = 0.2$) (Supplementary Figure S2A, available as Supplementary data at *IJE* online).

Discussion

Our study is the first to report comprehensive estimates of prevalence for peptic ulcer disease by sex and age group at global, regional and national levels over 30 years. Based on GBD 2019, we observed that the prevalence of peptic ulcer disease has been increasing since 1990, reaching 8.1 million in 2019. However, the age-standardized prevalence rate decreased by 30.7% from 143.4 in 1990 to 99.4 in 2019 per 100 000 population. The increase in prevalence and the decrease in the age-standardized prevalence rate could be mainly explained by the population growth and worldwide ageing and in most of the countries from 1990 to 2019. Furthermore, the decrease in the global age-standardized prevalence rate from 1990 to 2019 may be attributed to the parallel decrease in *H. pylori* infections[16] observed since 1994 when the National Institutes of Health guidelines started recommending the use of antibiotics for the treatment of patients with peptic ulcers.[23] The use of NSAIDs, including aspirin, is another common factor that increases risk by two to four times for peptic ulcers and their complications.[6,24] Although NSAIDs are still some of the most widely prescribed drugs in the world, more rational use of NSAIDs might decrease the risk of peptic ulcer disease and its complications.[25] Meanwhile, widespread and evidence-based use of proton-pump inhibitors and histamine$_2$ receptor antagonists has probably also contributed to a rapid decline in the prevalence of peptic ulcer disease and its related complications over the past three decades.[13] Surprisingly, the largest decrease in the age-standardized prevalence occurred in Tropical Latin America, including Brazil and Paraguay, from 1990 to 2019. This phenomenon might be due to combretaceae, a popular medical plant in Brazil and Paraguay, having anti-*H. pylori* and antiulcer action.[26,27]

Deaths due to gastric and duodenal ulcers are usually associated with perforation into the peritoneal cavity or bleeding without effective control.[15] Previous epidemiological investigations in European and non-European countries revealed a marked decline in mortality from gastric and duodenal ulcers.[14,15] A previous analysis of peptic ulcer disease from 1990 to 2016 also indicated a decreased mortality rate in India.[17] This is supported by the present data.

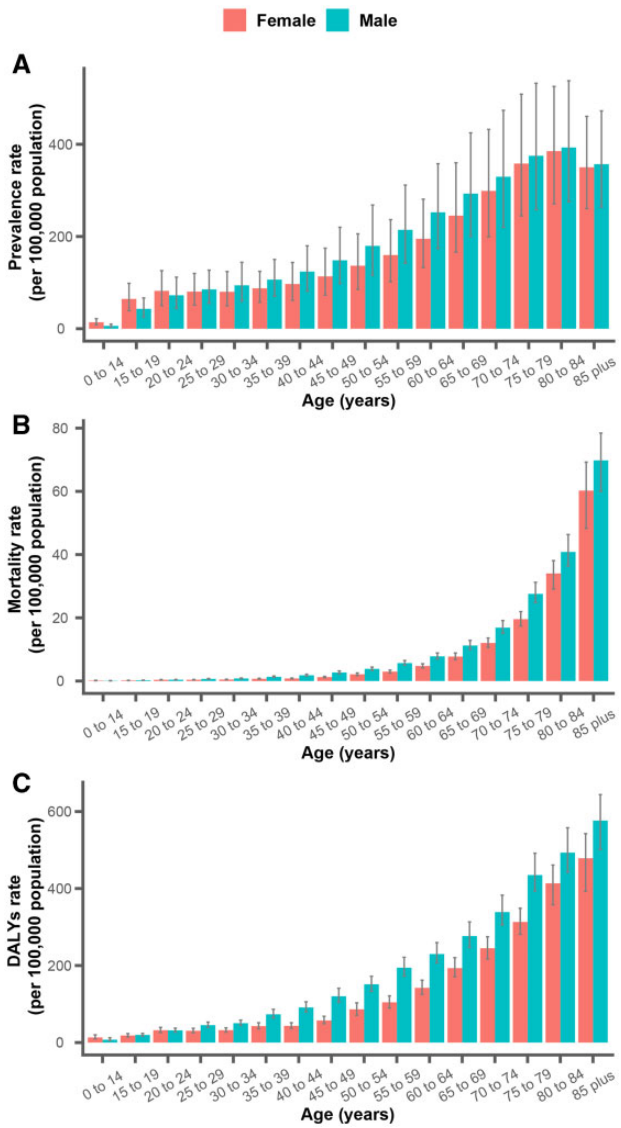

Figure 4 Prevalence (A), mortality (B) and DALYs (C) rates of peptic ulcer disease by age and sex in 2019 at the global level.

DALYs, disability-adjusted life years.

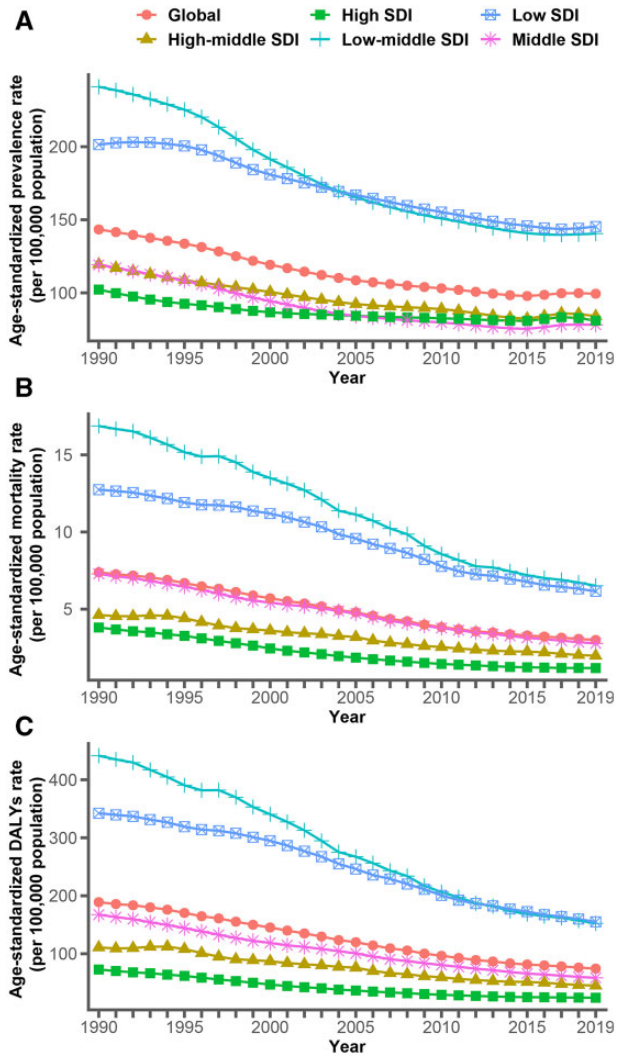

Figure 5 Age-standardized prevalence (A), mortality (B) and DALYs (C) rates of peptic ulcer disease from 1990 to 2019 by SDI quintile.

DALYs, disability-adjusted life years; SDI, socio-demographic index.

The estimated number of deaths decreased from 0.28 million in 1990 to 0.24 million in 2019 globally and the age-standardized mortality showed a substantial decrease (59.4%) from 1990 to 2019. This decline has persisted to the present and is seen in most countries. One reason might be earlier and more effective outpatient management for peptic ulcer disease, which has reduced the number of individuals with deteriorating conditions.[12] Additionally, although the widespread use of NSAIDs contributes substantially to the burden of complicated peptic ulcers,[28] some studies have found a reduced risk of gastric ulcer complications among *H. pylori*-infected patients taking NSAIDs.[29,30] This could be because *H. pylori* induces an increase in gastric mucosal prostaglandin E_2 levels that may partially reverse the mucosal toxicity of NSAIDs[31,32] or suppression of gastric acid secretion.[33] The use of endoscopic haemostasis and a multimodal and multidisciplinary care strategy for perforation may improve clinical outcomes and decrease the mortality of peptic ulcers.[34,35] Differences in the regional mortality of peptic ulcer disease should be noted. Oceania had the highest age-standardized mortality rate of peptic ulcer disease in 2019. Diet, environment and geographic distribution may partly explain this unusual finding in Oceania.[36–38] However, the specific and comprehensive underlying reasons deserve future investigations.

Peptic ulcer disease and its complications can influence individual daily activities, impair patients' quality of life and generate a heavy economic and social burden. About 40% of all ulcer patients in the USA have had to see a

physician five or more times within a year[4] and the total cost of peptic ulcer disease in the USA, incorporating both direct costs and loss of work productivity, has been estimated to be $5.65 billion per year.[4] A study in Netherlands found the per-patient costs of haemorrhage, perforation or a combination of both to be €12 000, €19 000 and €26 000, respectively.[5] In this study, we also observed 6.0 million DALYs due to peptic ulcer disease in 2019, even though there was a 60.6% decrease in the age-standardized DALYs rate from 1990 to 2019, which was more remarkable than the decline in the age-standardized prevalence rate, probably due to *H. pylori* eradication and more asymptomatic ulcer patients being diagnosed with endoscopy in recent years.[39,40]

The burden of peptic ulcer disease was also explored for different sex and age groups. It is well known that the prevalence of peptic ulcer disease increases sharply with age.[11] The current study demonstrated that the highest prevalence, mortality and DALYs rates of peptic ulcer disease in both females and males occurred at ages 80–84 and ≥85 years. From 1990 to 2019, the age-standardized prevalence, mortality and DALYs rates of peptic ulcer disease in males were higher than those in females. Epidemiological evidence indicates that higher *H. pylori* infection rates are associated with being male and increasing age.[41] Sex hormones also play a role in the sex differences of peptic ulcer disease. Several studies have found that female sex hormones have protective effects against peptic ulcer disease, such as increased mucus, phospholipid levels and bicarbonate secretion.[42] This implies that policies should focus on males and older populations globally. A previous study indicated that the male-to-female ratio for peptic ulcer disease was 7:1 among children (range, 5–18 years).[43] However, we found that females had a higher burden of peptic ulcer disease than males among those aged <25 years. The female population in Eastern Europe had the highest increase in the burden of peptic ulcer disease from 1990 to 2019. And females in the low SDI quintile had a higher age-standardized prevalence rate of peptic ulcer disease than males from 1990 to 2019. These unexpected discoveries for females need further research to understand their underlying causes, and appropriate policies and practices for prevention and treatment need to be developed.

SDI is a social and economic indicator that reflects the level of education and income. In our study, we found negative correlations between age-standardized prevalence, mortality and DALYs rates of peptic ulcer disease and SDI for the 204 countries and territories. This means that the burden of disease was generally lower in countries with higher socio-economic development levels. The burden of peptic ulcer disease was observed to be the highest in low-middle and low SDI quintiles. Studies have shown that individuals with lower educational levels and socio-economic status are 5.5 and 6.6 times more likely to be infected with *H. pylori*, respectively.[44] An epidemiological survey has found that the infection rate of *H. pylori* among illiterate people is significantly higher than in literate people.[41] Besides educational level and socio-economic status, access to early diagnosis and high-quality healthcare and treatment should also be considered as factors impacting peptic ulcer disease.[13] Therefore, lower SDI countries and territories should be given more attention for the prevention, early diagnosis and treatment of peptic ulcer disease. Figure 2 showed that some countries in the middle SDI group (Cambodia, Lao People's Democratic Republic, Timor-Leste, Vanuatu and Kiribati) had particularly high burdens of peptic ulcer. The phenomenon might be caused by unsatisfied sanitation and hygiene, and high *H. pylori* prevalence in those countries.[45] Moreover, with the medical system developing, peptic ulcer diseases are more prone to being detected.

The present study was carried out with a standardized approach to describe the relative burden due to peptic ulcer disease at the global, regional and national levels between 1990 and 2019. However, several limitations should be considered.

First, as with all research based on GBD, the quality and quantity of input data are subject to potential biases influencing the accuracy and robustness of the GBD 2019 estimates, which can be partially overcome using DisMod-MR 2.1. A few countries and territories provided typical national data that caused the burden estimates of peptic ulcer disease to be reliant on modelled data rather than population-based data. More comprehensive health surveys are needed to acquire representative data in more countries in the future.

Second, endoscopy is considered to be the golden standard for the diagnosis of peptic ulcer disease. A prospective study on Chinese patients undergoing upper endoscopy screening as part of a routine health maintenance programme found that approximately two-thirds of those with peptic ulcer disease were asymptomatic.[39] Therefore, it is possible that the prevalence of peptic ulcer disease, especially chronic disease, in asymptomatic periods has been underestimated.

Third, gastric and duodenal ulcer disease data were mixed in the GBD 2019 database. Subtyping and temporal-spatial characteristics of peptic ulcer disease observed by endoscopy are needed in the future. Fourth, the risk factors for peptic ulcer include *H. pylori* infection, demography, environment, socio-economic factors, being male, being older, smoking, consuming alcohol, having psychological stress, using analgesic drugs and having

chronic medical conditions.[6,9–11] However, only smoking was identified as a risk factor in the GBD 2019 database. More health surveys with wider coverage of possible risk factors are needed in the future as well.

Conclusion

Our study showed a globally decreasing trend in the age-standardized prevalence, mortality and DALYs estimates for peptic ulcer disease from 1990 to 2019. However, across SDI quintiles, the low-middle and low SDI quintiles had the highest age-standardized prevalence, mortality and DALYs rates from 1990 to 2019. We also observed that males had a higher age-standardized prevalence rate of peptic ulcer disease than females, except in the age group <25 years in 2019 and in the low SDI quintile from 1990 to 2019. The findings emphasized the necessity for more efforts on the prevention, early diagnosis and treatment of peptic ulcer disease in low SDI and low-middle SDI groups of countries and those specific countries with the highest burden of peptic ulcer disease.

Ethics approval

This study did not require ethics approval.

Data availability

The data sets generated for this study can be found in the GBD at http://ghdx.healthdata.org/gbd-results-tool.

Supplementary data

Supplementary data are available at *IJE* online.

Author contributions

J.R. designed the study and drafted the manuscript. J.R., X.J. and J.L. extracted, collected and analysed the data. X.J., J.L., R.L., Y.G., J.Z., X.W. and G.W. provided important intellectual content and revised the manuscript. G.W. supervised the study. All authors approved the final version of the manuscript, including the authorship list.

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Conflict of interest

The authors declare no conflicts of interest.

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