Global disease burden linked to diet high in red meat and colorectal cancer from 1990 to 2019 and its prediction up to 2030

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Abstract
Numerous studies have already identified an association between excessive consumption of red meat and colorectal cancer (CRC). However, there has been a lack of detailed understanding regarding the disease burden linked to diet high in red meat and CRC. Our objective was to evaluate global, regional, and national mortality rates and disability-adjusted Life years (DALYs) related to this diet. We also considered factors such as sex, age, the socio-demographic index (SDI), and evaluated the cross-national inequalities. Furthermore, we utilized DALYs data from 204 countries and regions to gauge cross-country inequalities of CRC by calculating the slope index of inequality and concentration index as standard indicators of absolute and relative inequalities. Our data was derived from the Global Burden of Disease (GBD) Study 2019. The results show that globally, the ASMR and ASDR related to CRC due to diet high in red meat have decreased, with EAPCs of -0.32% (95% CI -0.37 to -0.28) and -0.18% (95% CI -0.25 to -0.11). Notably, the burden was higher among males and the elderly. The slope index of inequality rose from 22.0 (95% CI 18.1 to 25.9) in 1990 to 32.9 (95% CI 28.3 to 37.5) in 2019 and the concentration index fell from 59.5 (95% CI 46.4 to 72.6) in 1990 to 48.9 (95% CI 34.6 to 63.1) in 2019. We aim to offer evidence-based guidance for developing effective strategies that can mitigate the elevated CRC burden in certain countries.
Keywords: colorectal cancer, red meat, Global Burden of Disease, mortality, disability-adjusted life years, health inequality, epidemiology

1. Introduction

Colorectal cancer (CRC), also known as colorectal adenocarcinoma, primarily arises from the colon's glands and epithelial cells[1]. Worldwide, CRC is ranked third in cancer prevalence among males and second among females[2]. It is worth noting that more than half of the cases occur in more developed and industrialized countries[2, 3]. In these countries, CRC is the second most common tumor, with a lifetime incidence of 5%[4-6]. In regions with varying levels of economic development, there are significant differences in the 5-year survival rate of CRC. For instance, the overall 5-year survival rate in the United States is over 60%, whereas in developing countries, it is less than 40%[4].

The International Agency for Research on Cancer (IARC) defines red meat as unprocessed mammalian muscle meat[7, 8]. Dietary red meat, including beef, veal, pork, lamb, and mutton, provides us with several important essential nutrients[9, 10]. These essential nutrients comprise protein, essential amino acids, vitamins (including vitamin B12), minerals (including heme iron and zinc), and other micronutrients[11]. With the recent economic growth, the global demand for red meat has surged, in both developed and developing countries[12]. However, abundant evidence indicates that the diet high in red meat is associated with a range of health issues[13-15], including two major chronic diseases: cardiovascular disease and CRC[16-18]. A 1975 survey revealed a robust correlation (r=0.9) between per capita meat consumption and the incidence of CRC among women from 23 different countries[19]. Other research also reported that an increase in red meat consumption by 100 grams per day is associated with an 11%-51% greater risk of various cancer incidence and appears to be unrelated to any health benefits[20]. IARC has classified red meat consumption as a probable human carcinogen based on evidence related to CRC, pancreatic cancer, and prostate cancer (Group 2A)[8]. Recent guidelines recommend that the public should moderate their daily intake of red meat[21].

Previous Global Burden of Disease (GBD) studies predominantly emphasized the disease burden from high dietary red meat, rather than specifically addressing the CRC burden attributable to such consumption[22, 23]. Currently, no detailed report exists based on the GBD dataset focusing on the CRC burden from high global red meat consumption. Hence, we utilized data from GBD 2019 to determine the temporal trends in incidence and disability-adjusted life years (DALYs) at the global, regional, and national levels, stratified by sex, age, and SDI. We systematically summarized the global burden and health development status, including the unequal distribution of disease burden among countries, in order to provide evidence for policymakers. Given the public accessibility of the data, ethical approval and informed consent were not required for our study.

2.Materials and method

2.1Data source

The data from the Global Burden of Disease (GBD) for the year 2019 were used to estimate the incidence and burden of CRC. Data on CRC were sourced from various outlets, including hospital records, emergency department records, insurance claims, surveys, and the Global Vital Registration system.

The GBD data processing and model construction, which have been previously discussed in articles, were employed for this research[24, 25].

We extracted data from the Global Health Data Exchange website (http://ghdx.healthdata.org/gbd-results-tool) for the years 1990 to 2019, stratified by sex, age, and region. This data included CRC-related deaths, DALYs (Disability-Adjusted Life Years), age-standardized mortality rates (ASMR), and age-standardized DALY rates (ASDR).

Additionally, the relationship between SDI and the burden of disease were investigated. SDI is a composite index that considers a country's per capita income, average years of education, and fertility rate. It categorized 204 countries and regions into five groups: low SDI (<0.45), medium SDI (≥0.45 and <0.61), medium SDI (≥0.61 and <0.69), medium SDI (≥0.69 and <0.80), and high SDI (≥0.80)[26, 27].

High red meat consumption in the diet was defined as a daily intake of red meat (beef, pork, lamb, and goat, excluding poultry, fish, eggs, and all processed meats) exceeding 23g (ranging from 18g to 27g) as an optional level[28]. Detailed information about inclusion and exclusion criteria can be found in the preceding sections[25]. This research aimed to assess the incidence and burden of CRC while exploring its relationship with social demographic indices and diet high in red meat.

2.2. Statistical analyses

We analyzed the burden of CRC at the global national level. To account for demographic differences, we used age-standardized incidence rates (ASIR), mortality rates, and Disability-Adjusted Life Years (DALY) rates to better reflect actual incidence and mortality rates. All rates are expressed as per 100,000 people.

Additionally, estimated annual percentage changes (EAPC) were calculated using a linear regression equation: $y = \alpha + \beta x + \varepsilon$ (where y represents ln (ASMR or ASDR), and x represents the calendar year) to assess trends in ASMR and ASDR. The exact calculation is EAPC = 100 (exp(β) - 1)[29]. EAPC and its 95% confidence interval (CI) greater than 0 indicate an increasing trend in ASMR or ASDR over the years, while values lower than 0 indicate a decreasing trend. If EAPC is close to 0, it suggests stability[30].

Furthermore, to explore the factors affecting the EAPC of the CRC burden related to a diet high in red meat, we also assessed the correlation between the age-standardized indicator of diet high in red meat in 1990 and SDI in 2019 with EAPC at the national level using the Spearman rank test.

We used the concentration index (CI) and the slope index to quantify the health inequalities. The slope index of inequality and concentration index, are two standard indicators of absolute inequality and relative inequality， respectively[31].The slope index of inequality is calculated by regressing the national DALYs ratio for all age groups on a relative positional scale associated with SDI, defined as the midpoint of the population cumulative range ranked by SDI[32]. Heteroscedasticity is explained by a weighted regression model. The concentration index is calculated by numerically integrating the area under the Lorenz concentration curve, which is fitted using the cumulative scores of DALYs and the cumulative relative distribution of the population based on SDI[33]. All statistical analyses were performed with R software (version 4.2.3).

3.Result

3.1. Global spatial and temporal colorectal cancer burden attributable to diet high in red meat

Globally, in 1990 and 2019, approximately 0.026 million and 0.052 million deaths from CRC were linked to a diet high in red meat. The male-to-female ratio for these deaths was around 1.3 and 1.5, respectively, for CRC. During this period, there was a rapid increase in deaths and DALYs associated with diet high in red meat. However, the ASMR and ASDR showed little change, with EAPC in ASMR for females being less than 0, and greater than 0 for males (Table 1, 2; Figure 1).

Table 1. Deaths of colon and rectum cancer attributable to diet high in red meat in 1990 and 2019 for both sexes and all locations, with EAPC from 1990 and 2019.

location	Deaths cases in 1990	ASMR per 100 000 in 1990	Deaths cases in 2019	ASMR per 100 000 in 2019	EAPC (1990–2019)
Global					
Both	26087 (6690 to 50231)	0.71 (0.18 to 1.38)	52811 (13598 to 100688)	0.66 (0.17 to 1.26)	-0.32% (-0.37 to -0.28)
Female	12951 (3302 to 24856)	0.64 (0.16 to 1.23)	22760 (5663 to 44004)	0.52 (0.13 to 1.01)	-0.83% (-0.88 to -0.78)
Male	13136 (3427 to 25156)	0.81 (0.21 to 1.56)	30051 (7627 to 57328)	0.83 (0.21 to 1.59)	0.07% (0.01 to 0.12)
Region					
High SDI	14063 (3944 to 25419)	1.34 (0.38 to 2.42)	18849 (4893 to 35349)	0.97 (0.26 to 1.79)	-1.29% (-1.37 to -1.21)
High-middle SDI	8864 (2276 to 17225)	0.87 (0.22 to 1.7)	18793 (5033 to 35132)	0.93 (0.25 to 1.74)	0.09% (0.01 to 0.17)
Middle SDI	2278 (297 to 5662)	0.23 (0.03 to 0.59)	11723 (2560 to 23587)	0.49 (0.1 to 0.99)	2.95% (2.77 to 3.12)
Low-middle SDI	649 (122 to 1497)	0.12 (0.02 to 0.27)	2826 (617 to 5904)	0.22 (0.05 to 0.45)	2.38% (2.28 to 2.48)
Low SDI	221 (32 to 565)	0.1 (0.01 to 0.26)	598 (98 to 1464)	0.12 (0.02 to 0.3)	0.81% (0.72 to 0.9)
Central Sub-Saharan Africa	27 (5 to 67)	0.13 (0.02 to 0.32)	61 (10 to 150)	0.12 (0.02 to 0.3)	-0.18% (-0.51 to 0.15)
East Asia	2851 (408 to 6970)	0.34 (0.05 to 0.84)	16498 (4056 to 31569)	0.82 (0.2 to 1.58)	3.6% (3.35 to 3.86)
Eastern Europe	2995 (772 to 5768)	1.07 (0.28 to 2.07)	2708 (468 to 5947)	0.79 (0.14 to 1.72)	-1.91% (-2.21 to -1.62)
Eastern Sub-Saharan Africa	88 (10 to 231)	0.12 (0.01 to 0.32)	241 (27 to 626)	0.16 (0.02 to 0.4)	0.9% (0.79 to 1.02)
Andean Latin America	36 (4 to 92)	0.18 (0.02 to 0.47)	154 (17 to 392)	0.28 (0.03 to 0.71)	1.81% (1.68 to 1.95)
High-income Asia Pacific	910 (87 to 2421)	0.47 (0.05 to 1.25)	2196 (275 to 5546)	0.47 (0.06 to 1.14)	-0.25% (-0.35 to -0.15)
High-income North America	4798	1.36	6386	1.02	-1.21%

location	Deaths cases in 1990	ASMR per 100 000 in 1990	Deaths cases in 2019	ASMR per 100 000 in 2019	EAPC (1990–2019)
	(1332 to 8719)	(0.38 to 2.44)	(1712 to 11567)	(0.28 to 1.82)	(-1.33 to -1.09)
Caribbean	83 (8 to 220)	0.33 (0.03 to 0.87)	209 (20 to 560)	0.4 (0.04 to 1.08)	0.9% (0.79 to 1.01)
Australasia	630 (276 to 959)	2.72 (1.19 to 4.15)	888 (367 to 1387)	1.75 (0.74 to 2.71)	-1.8% (-1.97 to -1.63)
Central Europe	1538 (322 to 3190)	1.06 (0.22 to 2.23)	2862 (699 to 5678)	1.33 (0.33 to 2.61)	1.04% (0.92 to 1.17)
Central Latin America	189 (24 to 461)	0.24 (0.03 to 0.58)	807 (130 to 1946)	0.34 (0.05 to 0.84)	1.38% (1.33 to 1.42)
Central Asia	271 (70 to 524)	0.57 (0.14 to 1.11)	389 (98 to 756)	0.56 (0.14 to 1.11)	0.39% (-0.13 to 0.91)
North Africa and Middle East	301 (29 to 820)	0.18 (0.02 to 0.5)	882 (86 to 2352)	0.22 (0.02 to 0.57)	0.76% (0.51 to 1.02)
Oceania	6 (1 to 16)	0.22 (0.03 to 0.59)	15 (2 to 41)	0.24 (0.03 to 0.64)	0.11% (-0.02 to 0.24)
South Asia	267 (70 to 583)	0.05 (0.01 to 0.12)	947 (228 to 2161)	0.07 (0.02 to 0.16)	0.84% (0.71 to 0.97)
Southeast Asia	406 (51 to 1036)	0.17 (0.02 to 0.42)	1822 (220 to 4550)	0.31 (0.04 to 0.77)	2.15% (2.08 to 2.21)
Southern Latin America	896 (376 to 1387)	2 (0.82 to 3.09)	1768 (705 to 2777)	2.1 (0.84 to 3.3)	0.15% (0.06 to 0.23)
Southern Sub-Saharan Africa	83 (11 to 211)	0.32 (0.04 to 0.84)	209 (30 to 498)	0.4 (0.06 to 0.95)	1.01% (0.84 to 1.18)
Tropical Latin America	388 (78 to 834)	0.45 (0.09 to 0.98)	2403 (890 to 3925)	1 (0.36 to 1.64)	3.02% (2.41 to 3.64)
Western Europe	9232 (2731 to 16476)	1.59 (0.48 to 2.82)	11104 (2953 to 20565)	1.16 (0.32 to 2.11)	-1.33% (-1.44 to -1.22)
Western Sub-Saharan Africa	92 (10 to 244)	0.11 (0.01 to 0.3)	262 (29 to 684)	0.16 (0.02 to 0.41)	1.35% (1.23 to 1.48)

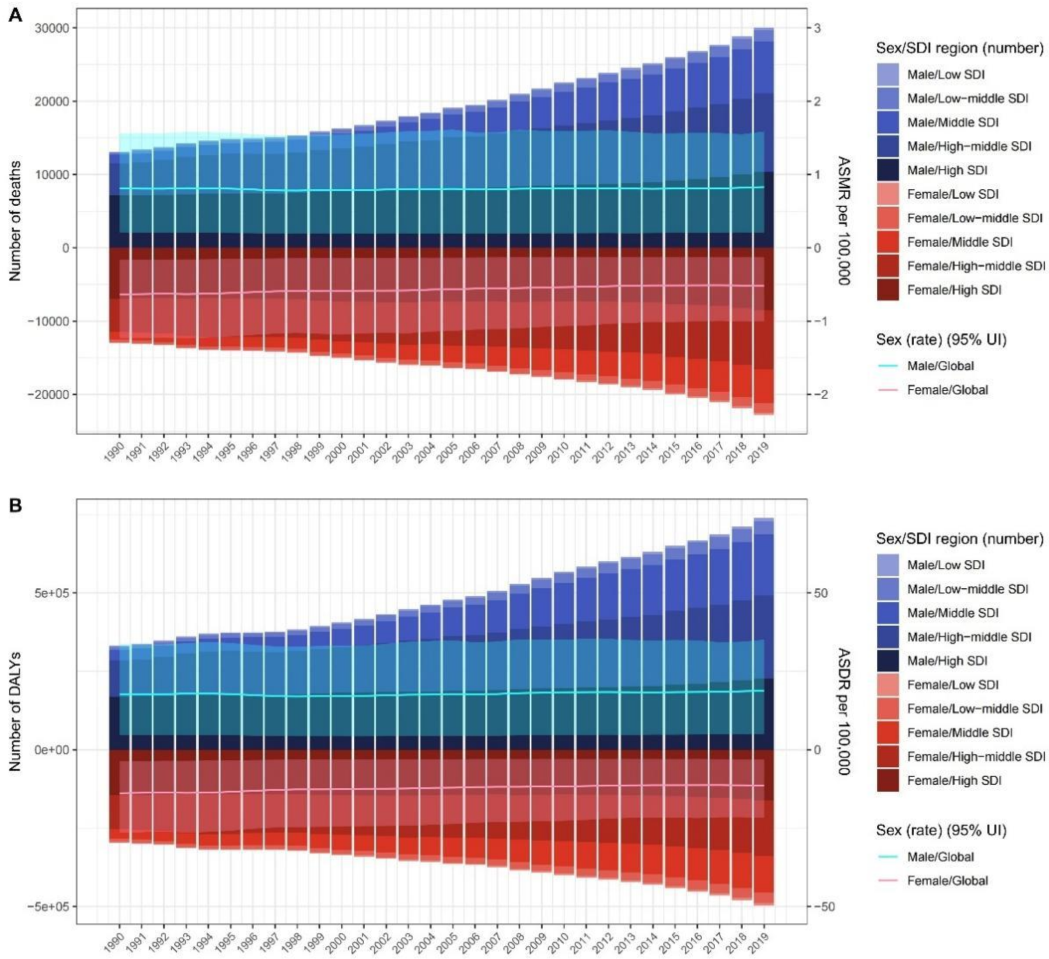

Figure 1. The burden of colorectal cancer deaths (A) and DALYs (B) due to diet high in red meat from 1990 to 2019 by sex and SDI region. The bar is the number of colorectal cancer deaths and DALYs attributable to diet high in red meat. The line with 95% UI represents ASMR and ASDR attributable to diet high in red meat. ASMR, age-standardized mortality rate; DALYs, disability-adjusted life-years; ASDR, age-standardized DALY rate; UI, uncertainty interval; SDI, sociodemographic index.

Table 2. DALYs of colon and rectum cancer attributable to diet high in red meat in 1990 and 2019 for both sexes and all locations, with EAPC from 1990 and 2019.

location		DALYs in 1990	ASDR per 100 000 in 1990	DALYs in 2019	ASDR per 100 000 in 2019	EAPC (1990–2019)
Global						
	Both	627834 (165197 to 1192278)	15.63 (4.08 to 29.8)	1234678 (332704 to 2306844)	14.95 (4.02 to 27.99)	-0.18% (-0.25 to -0.11)
	Female	296273 (76863 to 562565)	13.86 (3.6 to 26.4)	496397 (132360 to 944785)	11.43 (3.05 to 21.75)	-0.77% (-0.84 to -0.71)
	Male	331561	17.73	738281	18.83	0.24%

location	DALYs in 1990	ASDR per 100 000 in 1990	DALYs in 2019	ASDR per 100 000 in 2019	EAPC (1990–2019)
	(88528 to 627390)	(4.67 to 33.68)	(198240 to 1373853)	(5.03 to 35.12)	(0.16 to 0.32)
Region					
High SDI	314924 (92479 to 557564)	30.93 (9.16 to 54.6)	389921 (108477 to 703495)	22.76 (6.57 to 40.43)	-1.2% (-1.27 to -1.12)
High-middle SDI	221808 (58212 to 422210)	20.29 (5.29 to 38.8)	440051 (124026 to 802903)	21.86 (6.2 to 39.94)	0.09% (-0.01 to 0.19)
Middle SDI	65863 (8875 to 161394)	5.77 (0.75 to 14.25)	311976 (73750 to 608407)	11.96 (2.77 to 23.44)	3% (2.82 to 3.19)
Low-middle SDI	18653 (3612 to 42686)	2.83 (0.54 to 6.52)	75490 (17505 to 155025)	5.22 (1.19 to 10.78)	2.39% (2.29 to 2.49)
Low SDI	6319 (893 to 16233)	2.43 (0.35 to 6.21)	16780 (2643 to 41401)	2.92 (0.47 to 7.18)	0.73% (0.64 to 0.82)
Central Sub-Saharan Africa	796 (141 to 1950)	3.15 (0.57 to 7.77)	1771 (274 to 4466)	2.92 (0.46 to 7.19)	-0.17% (-0.48 to 0.14)
East Asia	83024 (12430 to 200519)	8.61 (1.25 to 20.89)	436252 (115075 to 813024)	20.8 (5.44 to 38.62)	3.72% (3.44 to 3.99)
Eastern Europe	77518 (20849 to 145612)	27.49 (7.36 to 51.58)	62825 (11277 to 137394)	18.92 (3.42 to 41.18)	-2.2% (-2.53 to -1.88)
Eastern Sub-Saharan Africa	2553 (286 to 6777)	3.04 (0.35 to 8)	6912 (738 to 18081)	3.71 (0.41 to 9.69)	0.79% (0.68 to 0.91)
Andean Latin America	912 (96 to 2357)	4.18 (0.44 to 10.82)	3690 (443 to 9188)	6.43 (0.76 to 16.05)	1.8% (1.66 to 1.93)
High-income Asia Pacific	22154 (2126 to 59218)	10.88 (1.05 to 29.1)	41772 (5719 to 101560)	10.94 (1.65 to 25.79)	-0.2% (-0.32 to -0.08)
High-income North America	110891 (32929 to 193179)	32.99 (9.96 to 57.08)	144668 (42179 to 251558)	25.35 (7.51 to 43.92)	-1.08% (-1.19 to -0.96)
Caribbean	1956 (185 to 5166)	7.39 (0.7 to 19.52)	4608 (437 to 12277)	8.91 (0.85 to 23.75)	0.87% (0.75 to 0.98)
Australasia	14698 (6625 to 22077)	63.82 (28.97 to 95.77)	18262 (7951 to 28011)	39.61 (17.84 to 60.29)	-1.91% (-2.08 to -1.74)
Central Europe	37988 (8506 to 76660)	25.72 (5.77 to 51.88)	63016 (16256 to 122005)	31.44 (8.24 to 60.21)	0.99% (0.84 to 1.14)

location	DALYs in 1990	ASDR per 100 000 in 1990	DALYs in 2019	ASDR per 100 000 in 2019	EAPC (1990–2019)
Central Latin America	5030 (675 to 11890)	5.5 (0.72 to 13.21)	20610 (3627 to 48284)	8.47 (1.47 to 19.89)	1.59% (1.54 to 1.65)
Central Asia	8019 (2143 to 15197)	15.9 (4.21 to 30.17)	10914 (2929 to 21059)	13.59 (3.49 to 26.08)	-0.19% (-0.7 to 0.33)
North Africa and Middle East	8526 (802 to 23203)	4.5 (0.43 to 12.31)	23444 (2225 to 62629)	4.98 (0.48 to 13.24)	0.51% (0.25 to 0.77)
Oceania	187 (23 to 484)	5.47 (0.66 to 14.24)	454 (49 to 1206)	5.65 (0.59 to 15.03)	-0.02% (-0.14 to 0.1)
South Asia	7509 (2045 to 16221)	1.23 (0.32 to 2.67)	24347 (5853 to 55572)	1.66 (0.4 to 3.79)	0.86% (0.73 to 0.99)
Southeast Asia	11633 (1431 to 29882)	4.08 (0.51 to 10.45)	49492 (5926 to 123345)	7.56 (0.91 to 18.86)	2.1% (2.04 to 2.17)
Southern Latin America	20605 (9149 to 31548)	44.3 (19.61 to 67.88)	38064 (16077 to 58942)	46.7 (19.81 to 72.14)	0.17% (0.1 to 0.24)
Southern Sub-Saharan Africa	2216 (302 to 5423)	7.39 (0.98 to 18.32)	5485 (878 to 12736)	9.1 (1.4 to 21.36)	1.09% (0.91 to 1.27)
Tropical Latin America	10572 (2212 to 22079)	10.65 (2.16 to 22.52)	61167 (23985 to 97095)	24.61 (9.58 to 39.24)	3.15% (2.49 to 3.81)
Western Europe	198617 (60793 to 339982)	36.14 (11.18 to 61.52)	210073 (59872 to 372018)	25.63 (7.6 to 44.82)	-1.42% (-1.51 to -1.34)
Western Sub-Saharan Africa	2429 (262 to 6498)	2.61 (0.29 to 6.94)	6853 (714 to 18052)	3.39 (0.37 to 8.86)	1.16% (1.04 to 1.28)

On a global scale, regions with high SDI had the most deaths related to diet high in red meat (0.018 million) in 2019, while high-middle SDI regions had the highest DALYs (0.44 million), together accounting for over 35% of cases worldwide. However, the highest ASMR and ASDR were observed in high SDI regions. Over the years, ASMR and ASDR increased in low, low-middle, middle, and high-middle SDI regions, with middle and low-middle SDI regions experiencing a faster increase compared to low and high-middle SDI regions. In contrast, high SDI regions had a significant decrease in ASMR [EAPC -1.29% (95% CI: -1.37 to -1.21)] and ASDR [EAPC -1.2% (95% CI: -1.27 to -1.12)] (Table 1, 2).

At the regional level according to the Global Burden of Disease (GBD) classification, East Asia carried the heaviest burden in 2019, with 0.016 million deaths and 0.43 million DALYs worldwide. However, Australasia had the highest ASMR (1.75 per 100,000) and ASDR (39.61 per 100,000).

The most significant increase in ASMR and ASDR from 1990 to 2019 was observed in Tropical Latin America and East Asia, with Estimated Annual Percent Changes (EAPCs) exceeding 3 in both regions. On the other hand, Eastern Europe experienced the most substantial decrease in ASMR [EAPC -1.91% (95% CI: -2.21 to -1.62)] and ASDR [EAPC -2.2% (95% CI: -2.53 to -1.88)] (Table 1, 2).

At country level, China had the highest number of CRC deaths and DALYs attributed to a high red meat diet in 2019 (Table S1, S2). Argentina and Greenland had the highest ASMR and ASDR in 2019 (Figure 2A and B; Table S1, S2). However, the most substantial increase in ASMR and ASDR occurred in Equatorial Guinea, with EAPCs of 4.71% (95% CI: 4.27 to 5.14) and 4.31% (95% CI: 3.9 to 4.72), respectively (Figure S1; Table S1, S2).

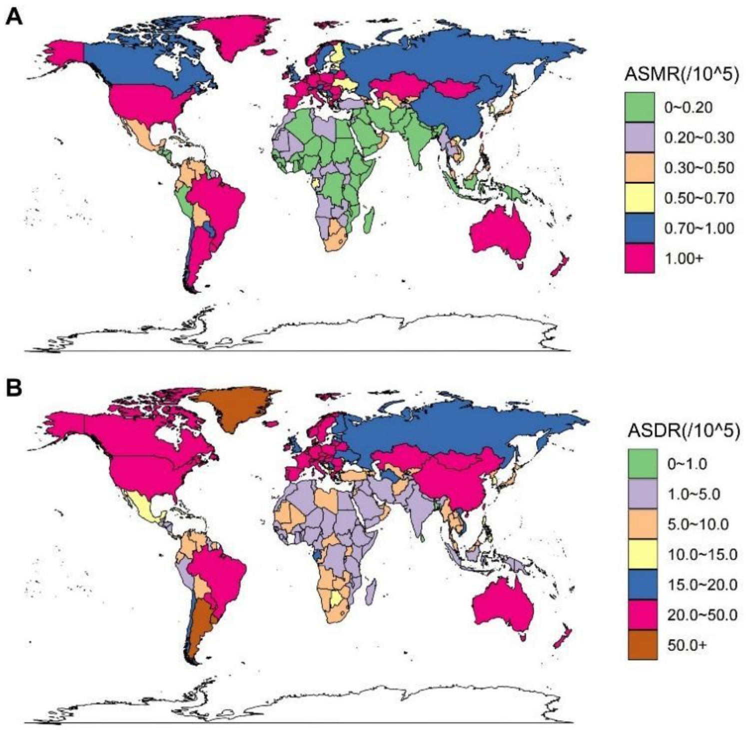

Figure 2. These maps show the ASMR (A) and ASDR (B) of colorectal cancer due to diet high in red meat per 100,000 people in 2019 in 204 countries and territories, for both sexes. ASMR, age-standardized mortality rate; ASDR, age-standardized DALY rate.

3.2. Global colorectal cancer burden attributable to diet high in red meat by age and sex

In 2019, the number of deaths from CRC attributed to diet high in red meat exhibited a synchronous pattern in males and females, first rising and then declining with age. The peak age of incidence was in the 70-74 years group (Figure S2). More deaths were observed in the 65-74 years age range, with a higher number of age-specific deaths in males compared to females (Figure S2). Consequently, the age-specific mortality rate in males was greater than that in females, and showed a rapid increase for both sexes (Figure 3A).

The age-specific number of colorectal cancer DALYs followed a similar pattern to that of deaths, but the peak point appeared in the 65-69 years age group, with more DALYs occurring in the 60-69 years age range (Figure S2). The age-specific number of CRC DALYs was significantly higher in males than in females (Figure S2). Correspondingly, the age-specific DALY rate in males was larger than that in females. The trend of the age-specific DALY rate resembled that of the mortality rate but declined in the 80-84 years age group (Figure 3B).

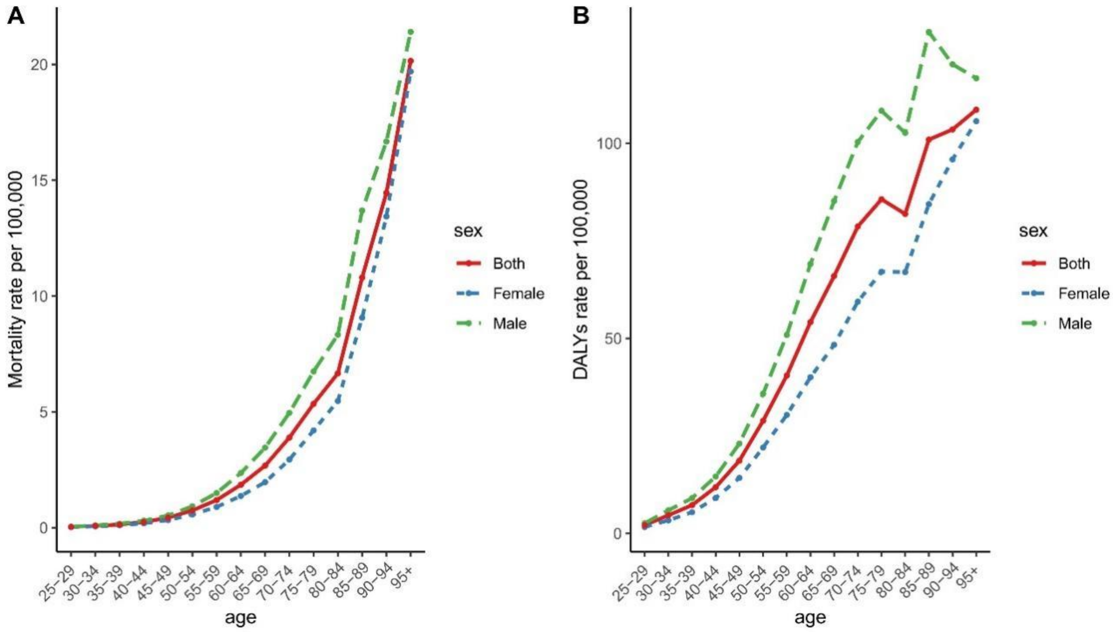

Figure 3. Age-specific rates of mortality (A) and DALYs (B) of colorectal cancer due to diet high in red meat by sex, 2019. DALYs, disability-adjusted life-years.

Globally, the age-specific mortality rate has increased in the 25-49 years and over 95 years age groups for both sexes from 1990 to 2019, with the most rapid increase occurring in the 25-29 years age group (Figure 4A). In males, the age-specific mortality rate rose in the 25-59 years and over 85 years age groups from 1990 to 2019, but fell in the 65-84 years age group, with the most significant increases and decreases occurring in the 65-69 years and 70-74 years age groups, respectively (Figure 4A). Conversely, the age-specific mortality rates in females declined in most age groups (Figure 4A). The age-specific mortality rates increased in low, low-middle, and middle SDI regions from 1990 to 2019. In high SDI regions, the age-specific mortality rates dropped in the 35-89 years age range, followed by an increase in older age groups. In high-middle SDI regions, the age-specific mortality rates decreased in the 60-69 years age group and increased in relatively younger and older age groups (Figure 4B). The EAPCs in age-specific DALY rates exhibited a similar pattern to that in age-specific mortality rates (Figure S3).

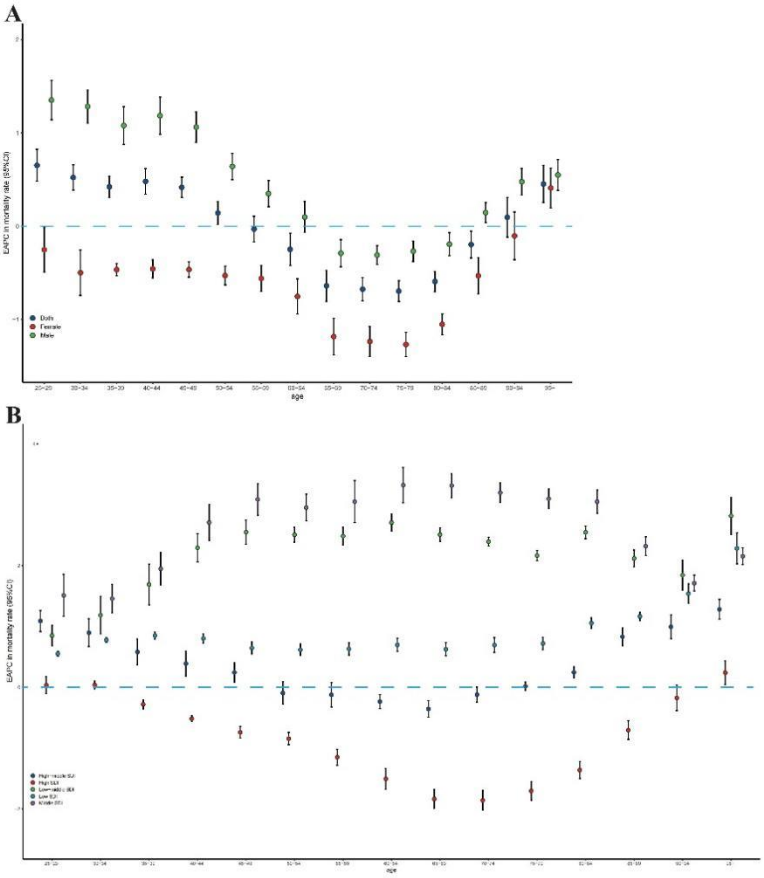

Figure 4. The age distribution of colorectal cancer due to a diet high in red meat trend in mortality rate from 1990 to 2019 by sex (A) and location (B). EAPC, estimated annual percentage change; SDI, sociodemographic index.

3.3. The association between SDI, global inequalities, and the burden of colorectal cancer burden attributable to diet high in red meat

In general, the ASMR displayed an inverted V-shaped correlation with the SDI, reaching its peak around an SDI value of approximately 0.75 (Figure 5A). The EAPC in ASMR exhibited a strong negative correlation with ASMR values in 1990 ($\rho = -0.551$, $P < 0.001$), particularly when ASMR was low (Figure 5B). Furthermore, the EAPC in ASMR showed a negative association with SDI values in 2019 ($\rho = -0.216$, $P < 0.001$), particularly for SDI values exceeding 0.75 (Figure 5C). Similar patterns were also evident when considering ASDR and their correlation with SDI, as well as the relationship between EAPC in ASDR and ASMR in 1990 and SDI in 2019 (Figure S2).

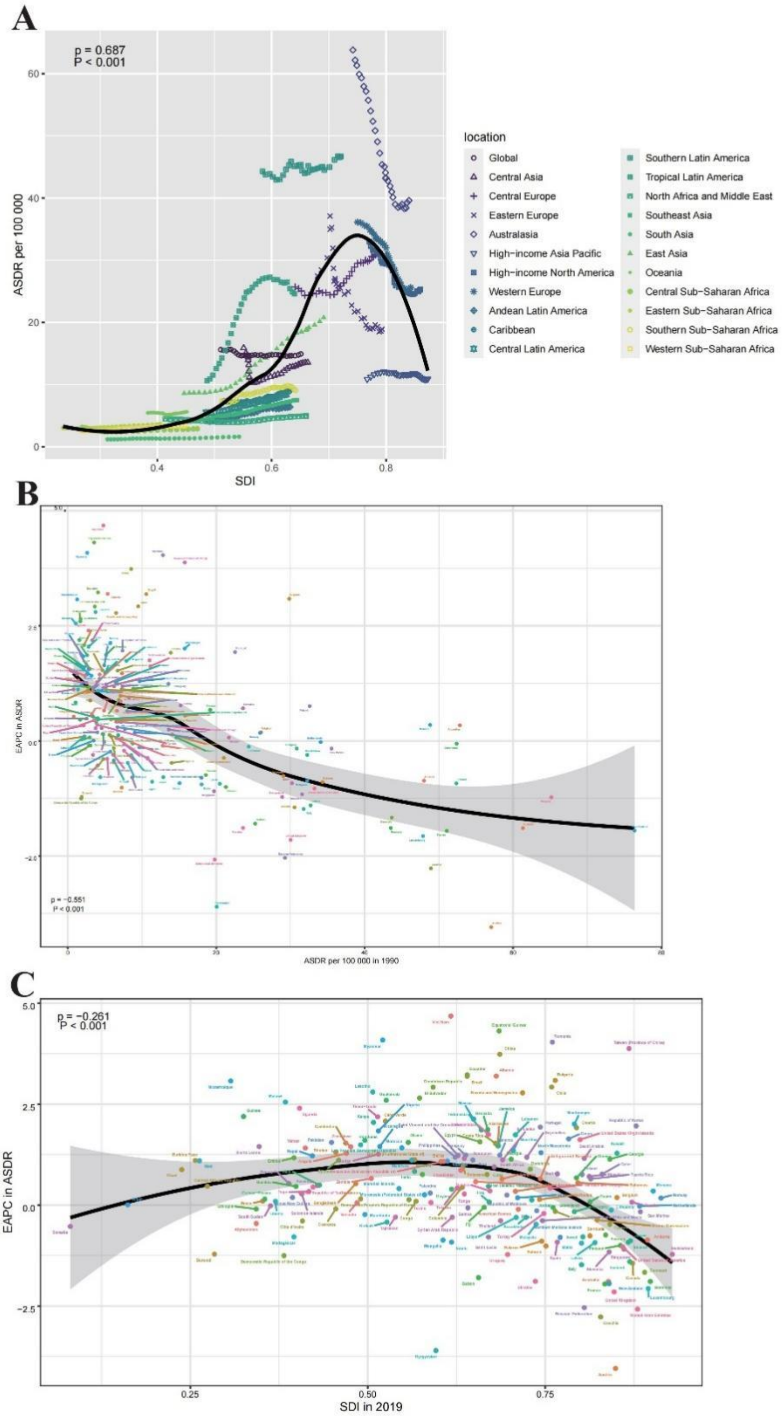

Figure 5. The correlation between colorectal cancer due to diet high in red meat in ASMR and SDI (A), between EAPC in ASMR and ASMR in 1990 (B), and between EAPC in ASMR and SDI in 2019 (C). EAPC, estimated annual percentage change; ASMR, age-standardized mortality rate; SDI, sociodemographic index.

In 1990 and 2019, 204 countries and territories experienced significant income-related inequalities in DALYs caused by CRC, the slope index of inequality in the DALYs rate between the highest and the lowest SDI country increased from 22.0 (95% CI 18.1 to 25.9) in 1990 to 32.9 (95% CI 28.3 to 37.5) in 2019 (Figure 6A; Table 3). The concentration index was 59.5 (95% CI 46.4 to 72.6) in 1990 and 48.9 (95% CI 34.6 to 63.1) in 2019 indicating that the burden was disproportionately concentrated in more-affluent countries (Figure 6B; Table 3).

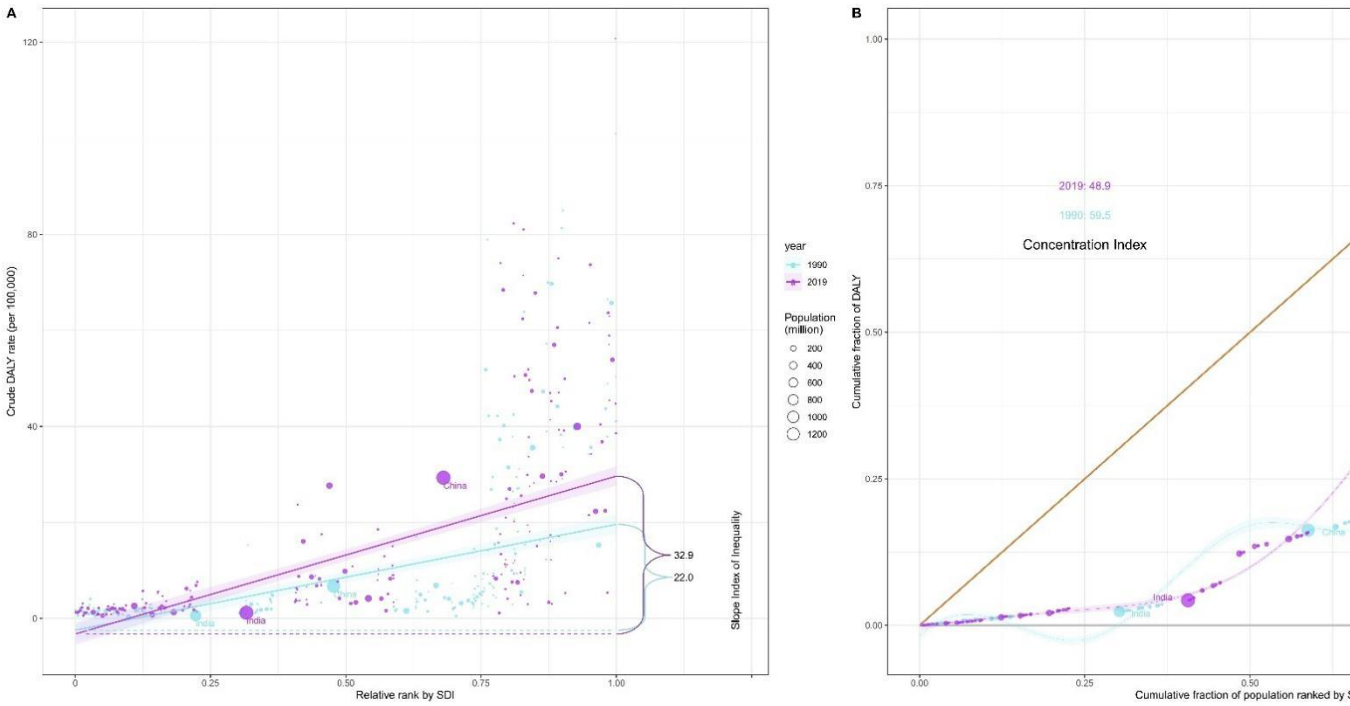

Figure 6. Income-related health inequality regression (A) and concentration curves (B) for DALYs of colorectal cancer due to diet high in red meat across 204 counties and territories, 1990 and 2019. DALYs, disability-adjusted life-years.

Table 3. Summary measures for cross-country inequalities related to SDI in DALYs of colorectal cancer burden attributable to diet high in red meat.

Diseases	Health inequality metrics	Year	Value	95% CI
colon and rectum cancer	Slope index of inequality	1990	22.0	28.3 to 37.5
		2019	32.9	18.1 to 25.9
	Concentration index	1990	59.5	46.4 to 72.6
		2019	48.9	34.6 to 63.1

4.Discussion

Our research analyzed the global burden of CRC caused by high red meat consumption in diets from 1990 to 2019, stratified by factors such as year, age, sex, region, and sociodemographic index. Our findings revealed a consistent global rise in mortality and DALYs rate linked to CRC due to elevated red meat consumption. This indicates that the burden it imposes remains a significant global public health concern.

In the 2019 report, there were over 50,000 reported cases of death, with the elderly being a high-risk group. Although the age-standardized death rate related to high red meat consumption in diets and CRC has declined from 1990 to 2019, the absolute number of fatalities has more than doubled. Population growth and age demographic shifts might account for this rise. Furthermore, the burden is closely related to socioeconomic development and how it is distributed unevenly. As high and high-middle SDI regions shoulder a greater burden, their ASDR and ASMR consistently decrease annually. Specifically, Western Europe has seen significant reductions in ASMR and ASDR. Conversely, there has been a concerning increase in low SDI regions, such as tropical Latin America. No doubt, economic growth has brought more affordable red meat and shifted the disease burden pattern in low and middle-income countries from infectious diseases, maternal and neonatal diseases, and nutritional diseases to non-communicable chronic diseases[24, 34], with CRC importantly of noteworthy. Additionally, the escalating male-to-female ratio in CRC-related deaths indicates that males are being affected to a greater extent. The reason for this may be that males are more likely to consume unprocessed red meat, leading to higher estimated intake levels[35]. Another hypothesis is that dietary-related effects may vary by sex due to hormonal differences between males and females, as well as the tendency for females to develop proximal tumors and males to develop distal and rectal tumors[36].

Meat processing, preservation, and high-temperature cooking can yield carcinogens such as HCAs, PAHs, and NOCs, which are implicated in the onset of several cancers[37-40]. Furthermore, red meat is a major source of heme iron. Many epidemiological and evidence-based studies have suggested a possible association between the intake of heme iron and the risk of various cancers, including colorectal cancer[41, 42]. Compared to low-income countries, high-income countries have a red meat consumption level that is approximately five times higher[43]. Despite the health inequality analysis indicating that the burden is disproportionately concentrated in wealthier countries, high-income countries have exhibited reduced red meat consumption over recent decades. This decline is primarily due to the development of relevant dietary guidelines and an increased level of compliance with these guidelines. Additionally, people are becoming more aware of the negative health effects of red meat consumption[44-46]. Another study has demonstrated the merit of public health initiatives that limit red meat intake in developed countries[47]. Therefore, high-income countries should emphasize the benefits of a healthy diet and use evidence-based intervention measures to educate and empower individuals to understand the risks associated with excessive red meat consumption[23, 48]. At the same time, although the burden in developing countries is relatively smaller, deaths related to CRC are rapidly increasing. From a nutritional perspective, animal-source foods (ASF) including red meat remain important in developing countries[43]. In these nations, it might not be necessary to completely avoid the consumption of red meat[12, 49, 50]. Most African countries are low-income or middle-income nations and their people do not consume red meat, even at potentially beneficial levels and this can contribute to severe nutritional deficiencies associated with a low life expectancy[51, 52]. For such countries, vigilance should not be relaxed, as paradoxically, excessive red meat consumption can eventually burden these nations[22]. Policymakers must remain cognizant of this risk.

Furthermore, though excessive red meat consumption is unhealthy, our study did not directly link it to CRC causality. We could only delineate the present burden and trends. Our study utilized data from GBD 2019, which primarily consists of national and regional data. The accuracy of our research hinges on the GBD study's data quality and volume. We lack individual-level data to support our findings. In addition, the highest consumers of red meat (the top 20% of red meat consumers) also have the highest body mass index, are more likely to smoke, engage in less physical activity, generally have lower levels of education and health literacy, consume smaller quantities of fruits and vegetables, and have higher daily calorie intake. Any or a combination of these residual confounding factors could potentially influence the association between red meat intake and colorectal cancer[16].

5.Conclusions

Although the ASIR and ASDR of CRC associated with diet high in red meat have decreased globally from 1990 to 2019, the absolute number of cases is still on the rise. The number of deaths has more than doubled since 1990, with a greater impact on males and older individuals. CRC linked to diet high in red meat exhibited significant income-related inequality, disproportionately burdening more affluent countries. However, in developing countries, including some countries in tropical Latin America and Africa, ASIR and ASDR related to cancer were higher. We hope that our research can provide insights for policymakers to tailor dietary guidelines, disease control, and prevention strategies based on the specific circumstances of different countries, especially for least developed countries with relatively lower economic levels.

Author Contributions

All authors contributed to the manuscript presented methodology, conceptualization, data analysis, and manuscript writing.

Funding

This project was supported by the Hainan Province Clinical Medical Center and the Key Research and Development Program of Hainan Province (ZDYF2021SHFZ087).

Institutional Review Board Statement

The study complied with the Helsinki Declaration and has been approved by the Medical Ethics Committee of Tongji Hospital.

Informed Consent Statement

The institutions responsible for conducting the surveys were obligated to obtain informed consent from the participants.

Data Availability Statement

The data is accessible through a public, open-access repository. All data is publicly available, and it can also be obtained upon request.

Conflicts of Interest

The authors declare no conflict of interest.

Abbreviations

CI: confidence interval; DALYs, disability-adjusted life years; EAPC: estimated annual percent change; GBD: disability-adjusted life years; SDI: sociodemographic index; UI: uncertainty interval; ASMR= age standardized mortality rate; ASDR= age-standardized disability adjusted life year rate; WHO: World Health Organization; CRC: colorectal cancer; HCA: heterocyclic amines; PAHs: polycyclic aromatic hydrocarbons; NOCs: N-nitroso compounds.

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