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Worldwide burden and cross-regional health inequalities of high BMI-attributable colorectal cancer by gender from 1990 to 2021, with predictions through 2041

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Abstract

Purpose To analyze the worldwide, regional, and national burden and trends of colorectal cancer (CRC) attributable to high body mass index (BMI) by gender from 1990 to 2021 and to forecast the burden through 2041.

Methods Data on deaths and disability-adjusted life years (DALYs) of CRC attributable to high BMI were obtained from the Global Burden of Disease (GBD) Study 2021. Disparities and trends in CRC due to high BMI burden were analyzed globally and regionally, with stratification by gender and age subgroups. An autoregressive integrated moving average (ARIMA) model was employed to project the future burden through 2041.

Results In 2021, the global age-standardized mortality rate (ASMR) and age-standardized DALYs rate (ASDR) of CRC attributable to high BMI were estimated at 1.17 [95% uncertainty interval (UI): 0.51 to 1.87] and 27.33 (95% UI: 11.80 to 43.37) per 100,000 population, respectively. Both metrics showed a modest increase from 1990 to 2021. During this period, the population attributable fraction (PAF) of CRC deaths due to high BMI increased steadily. Similarly, the PAF of CRC DALYs caused by high BMI also showed a continuous rise. High socio-demographic index (SDI) regions, Central Europe and countries such as Hungary and Slovakia, recorded the highest ASMR and ASDR in 2021. Projections indicate that the global ASMR will decrease by 1%, while the ASDR will increase by 4.23% by 2041.

Conclusion The global burden of CRC attributable to high BMI remains substantial and is projected to persist, with considerable regional and national variability. These findings emphasize the need for targeted public health interventions and policies to address this preventable risk factor.

Keywords Colorectal cancer, High BMI, Global burden of disease, Disability-adjusted life years

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Introduction

Colorectal cancer (CRC) remains a leading cause of morbidity and mortality worldwide, accounting for substantial global health and economic burdens [1]. In 2020, CRC was the third most commonly diagnosed cancer and the second leading cause of cancer-related deaths, with an estimated 1.9 million new cases and 935,000 deaths globally [2]. Despite improvements in screening and treatment, CRC continues to impose substantial economic and healthcare costs, particularly in high Human Development Index (HDI) countries where incidence rates remain elevated [3].

Among the many risk factors implicated in the etiology of CRC, high body mass index (BMI) has emerged as a significant modifiable determinant [4, 5]. Obesity is known to promote chronic low-grade inflammation, insulin resistance, and alterations in gut microbiota, all of which are closely linked to colorectal carcinogenesis [6–9]. The prevalence of high BMI has nearly tripled since 1975, with over 1.9 billion adults classified as overweight and more than 650 million as obese as of 2016 [10]. This global epidemic poses a critical challenge to CRC prevention and control efforts [11].

Quantifying the burden of CRC attributable to high BMI is essential for public health strategies aimed at reducing obesity-related health disparities [12, 13]. Previous studies have explored the link between high BMI and CRC. However, few have examined recent trends across time and regions or income levels. The Global Burden of Disease (GBD) study 2021 provides a unique opportunity to address this gap, offering high-resolution data on disease burden and risk factors from 1990 to 2021 at global, regional, and national levels [14].

This study aims to analyze the global, regional, and national burden of CRC attributable to high BMI from 1990 to 2021. By leveraging GBD data, we seek to elucidate trends in mortality and disability-adjusted life years (DALYs) associated with high BMI-related CRC, identify disparities across regions with stratification by gender and age subgroups, and highlight the need for targeted interventions. Understanding these patterns is critical for guiding health policies, allocating resources, and designing effective prevention strategies to mitigate the dual epidemics of high BMI and CRC.

Method

Data source

The data utilized in this study originated from the GBD Study 2021, an extensive international collaborative research initiative. This project systematically assessed age- and sex-specific mortality for 288 causes, prevalence and years lived with disability (YLDs) for 371 diseases and injuries, and comparative risks associated with 88 risk factors across 204 countries, territories, and 811 subnational locations spanning the period from 1990 to 2021 [14]. The GBD 2021 team collected raw data from civil registries, vital statistics, hospital databases, and household surveys. These data were analyzed to estimate the burden of CRC more accurately [15]. To ensure consistency, DisMod-MR version 2.1 was applied to correct biases in the primary data, producing standardized prevalence estimates stratified by age, sex, geographical location, and year. All estimates of deaths and DALYs attributable to high BMI were extracted directly from the GBD 2021 database, which provides 95% uncertainty interval (UI) based on 1000 draws from the posterior distribution of a Bayesian meta-regression model. These UIs reflect variability in data sources, modeling assumptions, and estimation procedures. Wider UIs typically indicate greater uncertainty in underlying data quality, sparse primary data, or heterogeneity across populations [16]. Through the Global Health Data Exchange (GHDx) platform (http://ghdx.healthdata.org/gbd-results-tool) [14], data on CRC deaths and DALYs attributable to high BMI, along with additional metrics such as age-standardized mortality rate (ASMR) and age-standardized DALYs rate (ASDR), were retrieved for 204 countries and territories during 1990 to 2021. These metrics were further categorized by sex, age group, GBD region, and socio-demographic index (SDI) quintile [17].

Definitions

The impact of high BMI was estimated in the GBD 2021 study by comparing actual health outcomes to hypothetical outcomes based on historical exposure scenarios. High BMI was defined as a BMI greater than 25 kg/m^2 for individuals aged 20 years and older. BMI is calculated as a person's weight in kilograms divided by the square of their height in meters. Detailed information about data selection and inputs has been previously provided [18]. DALYs, which represents the sum of healthy life-years lost between disease onset and mortality, was used to assess the burden of disease [19]. Additionally, an analysis was conducted to examine the correlation between disease burden and SDI. The SDI is a composite indicator used in the GBD study to measure a region's development status. It is calculated as the geometric mean of three rescaled components: income per capita, average educational attainment among individuals aged 15 years or older, and total fertility rate under the age of 25. SDI values range from 0 to 1, with higher values indicating higher levels of socio-demographic development. Based on SDI, countries and regions are categorized into five groups based on their SDI values: high SDI (≥ 0.80), high-middle SDI (≥ 0.69 and < 0.80), middle SDI (≥ 0.61 and < 0.69), low-middle SDI (≥ 0.45 and < 0.61), and low SDI (< 0.45) [20].

Metric of disease burden

We estimate the burden of CRC due to high BMI based on metrics including deaths number, DALYs ASDR, and ASMR categorized by geographic location, SDI, sex, and age group. The age-standardized rate (ASR) is the calculation of mortality and DALYs rates that takes into account the age distribution of a standard population [21]. ASR enables accurate comparisons of total mortality and DALYs rates across different regions and time periods by eliminating the impact of population age composition on these rates. All rates are presented per 100,000 individuals to mitigate the influence of age distribution within populations [22]. Instead of utilizing the current global population size in 2021, we employed the weight based on the standard global population of GBD study 2021.The population attributable fraction (PAF) of high BMI for CRC was obtained directly from the GBD 2021 database through the GHDx. PAF represents the proportion of CRC burden (in terms of deaths and DALYs) that can be attributed to high BMI, based on comparative risk assessment modeling [23]. We utilized the estimated annual percentage change (EAPC) to evaluate trends of ASR over a specified time period. Moreover, the EAPC was calculated by linear regression model: $y = \alpha + \beta x + \varepsilon$, where y is the ln(ASMR) or ln(ASDR), x is the calendar year, ε is the error term, and β is the trend of the ASR. The exact calculation was $EAPC = 100\ (exp(\beta) - 1)$. The linear regression model was used to calculate the 95% confidence interval (CI). In cases where both the EAPC and its corresponding 95% CI were greater than zero, the ASR was classified as exhibiting an increasing trend. Conversely, if they were less than zero, it indicated a decreasing trend. Otherwise, when neither of these conditions were met, the ASR was considered stable [24].

Prediction

We applied the autoregressive integrated moving average (ARIMA) model to predict the future burden of high BMI-attributable CRC. The general form of the ARIMA(p, d, q) model is:

$$Y_t = \varphi_1 Y_{t-1} + \cdots + \varphi_p Y_{t-p} + \varepsilon_t - \theta_1 \varepsilon_{t-1} - \cdots - \theta_q \varepsilon_{q-1}$$

Where Y_t represents the differenced series at time t, φ_i and θ_j are the coefficients of the autoregressive and moving average terms, respectively, and ε_t is a white noise error term. The series was differenced to achieve stationarity, as required for ARIMA modeling. In the ARIMA(p, d, q) model, p is the order of the autoregressive term, d is the number of differences required to achieve stationarity, and q is the order of the moving average term. These parameters were determined based on autocorrelation function (ACF) and partial autocorrelation function (PACF) plots. Model selection was guided by Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC) [25]. Residual diagnostics confirmed that residuals approximated white noise and followed a normal distribution. Residual diagnostics confirmed that the residuals of each model approximated white noise and followed a normal distribution. Six separate ARIMA models were developed for ASMR and ASDR, stratified by sex (male, female, and both sexes). The optimal (p, d, q) parameters and corresponding AIC and BIC values for each model are summarized in Table S1 [26].

Statistical analysis and software

Spearman's correlation analysis was performed to analyze the relationship between the SDI and ASR in 2021. All statistical analyses and visualizations were conducted using R software (version 4.3.3). The following R packages were used in this study: "ggplot2" for data visualization, "forecast" for ARIMA model construction and prediction, "dplyr" and "tidyr" for data manipulation, stats for regression analyses and correlation tests. A probability (p) value < 0.05 was considered statistically significant.

Result

Global trends of CRC attributable to high BMI

In 2021, it was estimated that CRC deaths and DALYs attributable to high BMI globally amounted to 99,268 (95% UI = 42,956.3 to 157,948.8) and 2,364,664.2 (95% UI = 1,021,593.6 to 3,752,340.4), respectively. Between 1990 and 2021, the number of CRC-related deaths linked to high BMI increased by 139%, rising from 41,535.8 (95% UI = 17,665.6 to 67,379) to 99,268 (95% UI = 42,956.3 to 157,948.8). Likewise, the DALYs attributed to high BMI grew by 133%, from 1,015,042.1 (95% UI = 429,787.2 to 1,631,973.8) to 2,364,664.2 (95% UI = 1,021,593.6 to 3,752,340.4). In 2021, the ASMR and ASDR were 1.17 (95% UI = 0.51 to 1.87) and 27.33 (95% UI = 11.8 to 43.37) per 100,000 population, respectively. Both the ASMR and ASDR associated with CRC due to high BMI showed slight increases, with EAPC of 0.001% (95% CI = -0.04 to 0.04) and 0.12% (95% CI = 0.08 to 0.16), respectively, from 1990 to 2021 (Tables 1 and 2; Fig. 1A, B). Additionally, in 2021, the PAF for deaths and DALYs due to high BMI in CRC were 9.51% (95% UI = 4.07 to 14.81%) and 9.69% (95% UI = 4.17 to 15.08%), reflecting increases of 30.6% and 37.5%, respectively, compared to 1990 (Fig. 1C, D).

Geographical variations in CRC attributable to high BMI

In 2021, regions with high SDI reported the highest number of deaths (36,529.9, 95% UI = 15,670.3 to 58,138.7) and DALYs (775,808.6, 95% UI = 337,834.3 to 1,225,933.9) due to high BMI. In contrast, regions with low SDI showed the lowest figures for both CRC-related deaths (1,567.5, 95% UI = 614.9 to 2,540.4) and DALYs (47,046.6, 95% UI = 18,740.2 to 75,740.4). Furthermore, high SDI regions

Table 1 Global burden of colorectal cancer deaths attributable to high BMI in 1990 and 2021, and the estimated annual percentage change (EAPC) in ASMR from 1990 to 2021

Characteristics	1990			2021			1990–2021 EAPC (95% CI)
	Number of cases (95% UI)	PAF (%) (95% UI)	ASMR per 100,000 population (95% UI)	Number of cases (95% UI)	PAF (%) (95% UI)	ASMR per 100,000 population (95% UI)	
Global	41535.8(17665.6 to 67379)	7.28(3.06 to 11.62)	1.14(0.48 to 1.86)	99,268(42956.3 to 157948.8)	9.51(4.07 to 14.81)	1.17(0.51 to 1.87)	0.001 (-0.04 to 0.04)
Sex							
Female	22586.3(9702.9 to 36765)	0.8(0.34 to 1.26)	1.11(0.48 to 1.81)	48292.5(20914.4 to 76782.2)	1.04(0.45 to 1.62)	1.04(0.45 to 1.65)	-0.37 (-0.42 to -0.31)
Male	18949.5(7914.9 to 30723.2)	0.66(0.27 to 1.06)	1.17(0.49 to 1.9)	50975.5(21914.4 to 81236.5)	0.88(0.37 to 1.37)	1.33(0.57 to 2.13)	0.39 (0.36 to 0.42)
SDI regions							
High SDI	21852.2(9256.4 to 35533.2)	8.99(3.86 to 14.29)	1.96(0.83 to 3.19)	36529.9(15670.3 to 58138.7)	10.86(4.69 to 17.01)	1.68(0.73 to 2.66)	-0.64 (-0.69 to -0.59)
High-middle SDI	13679.9(5864.9 to 22167.7)	7.99(3.42 to 12.66)	1.44(0.61 to 2.33)	32966.4(14288.4 to 52368.1)	10.7(4.59 to 16.85)	1.67(0.72 to 2.66)	0.4 (0.32 to 0.48)
Middle SDI	4237.3(1566.5 to 6974.5)	4.01(1.52 to 6.46)	0.43(0.16 to 0.7)	21653.8(9249.9 to 34503.1)	7.88(3.29 to 12.4)	0.82(0.35 to 1.32)	2.13 (2.11 to 2.16)
Low-middle SDI	1244.5(472.1 to 1981.8)	3.68(1.42 to 5.94)	0.21(0.08 to 0.33)	6391.2(2689.5 to 10103.4)	7.01(2.94 to 10.99)	0.45(0.19 to 0.71)	2.72 (2.65 to 2.79)
Low SDI	442.3(161.4 to 737)	2.86(1.05 to 4.65)	0.2(0.07 to 0.33)	1567.5(614.9 to 2540.4)	4.92(1.98 to 7.76)	0.32(0.12 to 0.52)	1.5 (1.38 to 1.62)
GBD regions							
Andean Latin America	134.4(54.9 to 221.2)	7.81(3.21 to 12.54)	0.67(0.28 to 1.12)	672.4(287.4 to 1130.6)	11.64(5 to 18.38)	1.15(0.49 to 1.93)	1.81 (1.69 to 1.94)
Australasia	560.6(233.2 to 893.9)	9.71(4.14 to 15.59)	2.41(1 to 3.83)	1123.4(476.3 to 1796.5)	13.58(5.87 to 21.35)	2.01(0.85 to 3.2)	-0.78 (-0.86 to -0.71)
Caribbean	243.8(101.8 to 387.5)	7.03(2.91 to 11.12)	0.97(0.4 to 1.54)	841.4(355.2 to 1385)	10.67(4.66 to 16.97)	1.55(0.66 to 2.56)	1.68 (1.62 to 1.73)
Central Asia	488.2(201.6 to 783.8)	10.1(4.29 to 16.11)	1.04(0.43 to 1.68)	768.9(328.8 to 1215.1)	12.5(5.45 to 19.71)	0.96(0.41 to 1.53)	0.1 (-0.03 to 0.22)
Central Europe	3627.9(1590.1 to 5836.5)	11.29(4.88 to 18.08)	2.46(1.08 to 3.96)	6940.6(3093 to 11133.3)	13.38(5.89 to 21.18)	3.03(1.35 to 4.85)	0.56 (0.42 to 0.69)
Central Latin America	529.6(223.4 to 852.8)	9.43(4 to 15.05)	0.67(0.28 to 1.07)	3148.9(1402.9 to 5105.4)	13.72(6.12 to 21.6)	1.26(0.56 to 2.06)	2.11 (2.04 to 2.19)
Central Sub-Saharan Africa	50.4(18.9 to 86.2)	3.39(1.29 to 5.5)	0.23(0.09 to 0.39)	254.1(96.4 to 437.8)	6.91(2.81 to 10.8)	0.49(0.18 to 0.83)	2.41 (2.24 to 2.57)
East Asia	3773(1309.3 to 6405.9)	3.05(1.03 to 5.09)	0.45(0.16 to 0.77)	20370.8(8474.7 to 33798.9)	7.08(2.93 to 11.31)	0.96(0.4 to 1.59)	2.41 (2.34 to 2.48)
Eastern Europe	5381(2332 to 8579.2)	10.74(4.65 to 16.9)	1.92(0.83 to 3.06)	9051.6(3878.4 to 14440.4)	14.06(6.26 to 22.04)	2.53(1.09 to 4.04)	0.72 (0.6 to 0.84)
Eastern Sub-Saharan Africa	208.5(73.4 to 349.5)	2.68(0.93 to 4.25)	0.28(0.1 to 0.46)	773.8(295.2 to 1284.4)	4.84(1.92 to 7.59)	0.48(0.18 to 0.8)	1.62 (1.52 to 1.72)
High-income Asia Pacific	1424.9(521.3 to 2304.2)	4(1.46 to 6.5)	0.73(0.27 to 1.17)	4240(1633.5 to 6743.7)	5.26(2.08 to 8.36)	0.83(0.32 to 1.31)	0.32 (0.27 to 0.36)
High-income North America	8084.1(3450.1 to 13011.4)	10.93(4.68 to 17.27)	2.27(0.97 to 3.65)	12769.3(5673.4 to 19869.6)	14.88(6.69 to 23.18)	1.95(0.87 to 3.03)	-0.66 (-0.76 to -0.55)
North Africa and Middle East	1341.1(566 to 2184.2)	9.5(4.04 to 14.96)	0.83(0.35 to 1.35)	5636.8(2450.7 to 8982.3)	15.09(6.81 to 23.18)	1.31(0.58 to 2.1)	1.7 (1.54 to 1.85)
Oceania	14.7(5.9 to 24.5)	8.88(3.81 to 14.31)	0.51(0.21 to 0.85)	43.5(18 to 70.3)	11.39(5.08 to 17.68)	0.59(0.25 to 0.96)	0.51 (0.42 to 0.6)
South Asia	516.9(173.4 to 827.3)	2.05(0.7 to 3.28)	0.09(0.03 to 0.14)	3042.7(1182.3 to 4777.4)	4.55(1.8 to 7.27)	0.2(0.08 to 0.32)	2.81 (2.76 to 2.86)
Southeast Asia	652.6(220.7 to 1050.3)	2.64(0.94 to 4.22)	0.25(0.08 to 0.4)	4057.3(1623 to 6569.2)	5.11(2.09 to 8.07)	0.62(0.25 to 1)	3.04 (2.93 to 3.15)

Table 1 (continued)

Characteristics	1990			2021			1990–2021
	Number of cases (95% UI)	PAF (%) (95% UI)	ASMR per 100,000 population (95% UI)	Number of cases (95% UI)	PAF (%) (95% UI)	ASMR per 100,000 population (95% UI)	EAPC (95% CI)
Southern Latin America	932.7(403 to 1520.7)	10.4(4.49 to 16.72)	2.07(0.89 to 3.36)	2235.2(992.4 to 3641.5)	13.88(6.09 to 21.96)	2.52(1.12 to 4.11)	0.9 (0.73 to 1.08)
Southern Sub-Saharan Africa	197.2(83.5 to 310)	8.87(3.79 to 13.7)	0.77(0.33 to 1.22)	807.9(341.4 to 1269.9)	13.18(5.87 to 20.55)	1.49(0.63 to 2.34)	2.32 (2.06 to 2.58)
Tropical Latin America	699.2(289.8 to 1135.9)	8.63(3.64 to 13.87)	0.8(0.33 to 1.29)	3629.8(1533.5 to 5850.4)	12.35(5.24 to 19.67)	1.42(0.6 to 2.29)	1.87 (1.76 to 1.98)
Western Europe	12481.1(5253.1 to 20401.8)	9.15(3.91 to 14.69)	2.11(0.89 to 3.45)	18025.5(7622.6 to 29686.3)	11.51(4.95 to 18.36)	1.77(0.75 to 2.9)	-0.65 (-0.71 to -0.59)
Western Sub-Saharan Africa	193.8(76.5 to 312.9)	4.67(1.83 to 7.32)	0.24(0.09 to 0.38)	834(336.3 to 1365.1)	8.08(3.36 to 12.6)	0.47(0.19 to 0.75)	2.39 (2.33 to 2.45)

UI: Uncertainty interval, *CI*: Confidence interval, *EAPC*: Estimated Annual Percentage Change, *SDI*: Socio-demographic index, ASMR: Age-standardised mortality rate, *PAF*: Population attributable fraction

exhibited the highest ASMR (1.68, 95% CI = 0.73 to 2.66 per 100000 population) and ASDR (40, 95% CI = 17.48 to 62.93 per 100000 population) (Tables 1 and 2). From 1990 to 2021, the ASMR and ASDR in low, low-middle, middle, and high-middle SDI regions steadily increased, while those in high SDI regions declined (Fig. 2A, B). Additionally, regions with higher SDI exhibited a higher PAF of CRC deaths and DALYs due to high BMI, with a consistent upward trend in PAF observed across all SDI regions from 1990 to 2021 (Fig. 2C, D). Geographically, East Asia had the highest number of CRC-related deaths (20,370.8, 95% UI = 8,474.7 to 33,798.9) and DALYs (529,351.9, 95% UI = 219,132.7 to 886,681.3) in 2021 linked to high BMI. Conversely, South Asia recorded the lowest, while Central Europe had the highest ASMR and ASDR (0.2 and 3.03 deaths vs. 5.67 and 68.94 DALYs per 100000 population, respectively). Between 1990 and 2021, Australasia experienced the largest reductions in ASMR and ASDR, whereas Southeast Asia saw the most significant increases, with changes of -0.78% (95% CI = -0.86 to -0.71%) vs. 3.04% (95% CI = 2.93 to 3.15%) and − 0.94% (95% CI = -1.02 to -0.85%) vs. 2.84% (95% CI = 2.72 to 2.97%), respectively (Tables 1 and 2).

Country-level burden of CRC attributable to high BMI

In 2021, at the national level, China reported the highest number of CRC-related deaths and DALYs attributable to high BMI, with 19,417.6 (95% UI = 8,052.9 to 32,452.4) deaths and 507,316.5 (95% UI = 209,263.9 to 853,770) DALYs, respectively. The USA followed, with 11,401.7 (95% UI = 5,070 to 17,660.9) deaths and 268,295.7 (95% UI = 122,072.8 to 412,890.8) DALYs. The Russian Federation ranked third, with 6,486.1 (95% UI = 2,777 to 10,321.1) deaths and 147,445.8 (95% UI = 63,131.2 to 233,862.5) DALYs. In the same year, Hungary and Slovakia experienced the highest ASMR and ASDR of CRC due to high BMI, whereas Bangladesh recorded the lowest values for both rates. The countries exhibiting the most substantial increases in ASMR were Viet Nam, Lesotho, and Cabo Verde, with EAPC of 4.65% (95% CI = 4.49 to 4.81%), 4.48% (95% CI = 3.96 to 5%), and 4.42% (95% CI = 4.04 to 4.79%), respectively. Similarly, Viet Nam, Lesotho, and Zimbabwe also had the greatest rises in ASDR, with EAPC of 4.74% (95% CI = 4.54 to 4.94%), 4.7% (95% CI = 4.15 to 5.25%), and 4.11% (95% CI = 3.45 to 4.78%), respectively. Meanwhile, Austria showed the sharpest decline in both ASMR and ASDR, with EAPC of -1.86% (95% CI = -1.92 to -1.8) and − 1.88% (95% CI = -1.94 to -1.82), respectively (Figs. 3 and 4; Tables S2, S3).

Global CRC burden attributable to high BMI by sex and age

Sex-based disparities continue to influence the global burden of CRC associated with high BMI. In 2021, the number of CRC-related deaths and DALYs was higher in males than in females, with values of 50,975.5 (95% UI = 21,914.4 to 81,236.5) vs. 48,292.5 (95% UI = 20,914.4 to 76,782.2) and 1,268,890.8 (95% UI = 544,821.7 to 2,022,284.6) vs. 1,095,773.4 (95% UI = 474,289.9 to 1,727,956), respectively (Table 1). The ASMR for CRC linked to high BMI was also higher in males, with values of 1.33 (95% UI = 0.57 to 2.13) per 100,000 population compared to 1.04 (95% UI = 0.45 to 1.65) per 100,000 population in females. Similarly, the ASDR was higher in males [31.09 (95% UI = 13.36 to 49.47) vs. 23.96 (95% UI = 10.36 to 37.75)]. From 1990 to 2021, the EAPCs in ASMR and ASDR attributable to high BMI were 0.39% (95% CI = 0.36 to 0.42%) and 0.48% (95% CI = 0.45 to 0.51%) for males, while for females, the EAPCs were − 0.37% (95% CI = -0.42 to -0.31%) and − 0.26% (95% CI = -0.31 to -0.2%), respectively (Tables 1 and 2; Fig. 1A, B). Despite these trends, the PAFs of CRC deaths and DALYs attributable to high BMI were higher in females (10.44% and 10.71%, respectively) than in males (8.77% and 8.97%) in 2021 (Fig. 1C, D).

Table 2 Global burden of colorectal cancer dalys attributable to high BMI in 1990 and 2021, and the estimated annual percentage change (EAPC) in ASDR from 1990 to 2021

Characteristics	1990			2021			1990–2021 EAPC (95% CI)
	Number of cases (95% UI)	PAF (%) (95% UI)	ASMR per 100,000 population (95% UI)	Number of cases (95% UI)	PAF (%) (95% UI)	ASMR per 100,000 population (95% UI)	
Global	1015042.1(429787.2 to 1631973.8)	7.05(2.95 to 11.25)	25.54(10.83 to 41.2)	2364664.2(1021593.6 to 3752340.4)	9.69(4.17 to 15.08)	27.33(11.8 to 43.37)	0.12 (0.08 to 0.16)
Sex							
Female	525776.2(225045.6 to 849419.9)	0.78(0.33 to 1.23)	24.73(10.59 to 39.99)	1095773.4(474289.9 to 1727956)	1.07(0.47 to 1.66)	23.96(10.36 to 37.75)	-0.26 (-0.31 to -0.2)
Male	489265.9(202595.5 to 796350.9)	0.64(0.26 to 1.04)	26.42(10.97 to 42.88)	1268890.8(544821.7 to 2022284.6)	0.9(0.38 to 1.4)	31.09(13.36 to 49.47)	0.48 (0.45 to 0.51)
SDI regions							
High SDI	490182.6(210224.6 to 788176.6)	9.17(3.93 to 14.6)	44.94(19.27 to 72.19)	775808.6(337834.3 to 1225933.9)	11.57(5.06 to 18.06)	40(17.48 to 62.93)	-0.48 (-0.52 to -0.43)
High-middle SDI	346229.2(147488.9 to 559452.8)	7.84(3.35 to 12.47)	34.2(14.56 to 55.28)	769289.9(332395 to 1220597.7)	10.87(4.68 to 17.06)	39.23(16.94 to 62.34)	0.31 (0.24 to 0.37)
Middle SDI	125727.8(46880.4 to 206617.4)	4(1.54 to 6.42)	11.03(4.1 to 18.13)	584511.4(248469.1 to 929607.8)	8.21(3.46 to 12.92)	21.01(8.93 to 33.45)	2.1 (2.07 to 2.14)
Low-middle SDI	37581.2(14269 to 60129.2)	3.69(1.42 to 5.95)	5.52(2.1 to 8.81)	184447.8(77501.9 to 290094.4)	7.2(3.03 to 11.28)	11.87(5 to 18.73)	2.69 (2.63 to 2.76)
Low SDI	13400.1(4984 to 22374.7)	2.96(1.1 to 4.8)	5.28(1.94 to 8.78)	47046.6(18740.2 to 75740.4)	5.22(2.11 to 8.23)	8.17(3.23 to 13.2)	1.33 (1.22 to 1.45)
GBD regions							
Andean Latin America	3674.5(1506.5 to 5995.5)	8.36(3.51 to 13.48)	16.83(6.89 to 27.44)	16947.4(7443.7 to 28548.2)	12.44(5.4 to 19.52)	28(12.28 to 47.21)	1.67 (1.55 to 1.79)
Australasia	13424.1(5579.5 to 21236)	10.05(4.31 to 16.13)	58.17(24.18 to 91.85)	23565.4(10170 to 37480.5)	14.14(6.15 to 22.17)	46.65(20.18 to 74.39)	-0.94 (-1.02 to -0.85)
Caribbean	6308.4(2656.5 to 10111.5)	7.54(3.13 to 11.91)	23.81(10 to 38.23)	20386.2(8687.1 to 33782.8)	11.33(5.04 to 17.97)	37.94(16.17 to 62.94)	1.66 (1.61 to 1.71)
Central Asia	14011.6(5760.4 to 22453.1)	9.98(4.26 to 15.88)	28.36(11.66 to 45.42)	21393.2(9092.7 to 33879.8)	12.57(5.5 to 19.87)	24.46(10.4 to 38.7)	-0.22 (-0.32 to -0.13)
Central Europe	87450.4(38342.3 to 140810.9)	11.4(4.94 to 18.23)	57.78(25.32 to 93)	148738.2(66397.2 to 238495.6)	13.67(6.02 to 21.61)	68.94(30.82 to 110.6)	0.48 (0.34 to 0.61)
Central Latin America	14473.4(6123.9 to 23291)	9.69(4.13 to 15.49)	16.13(6.82 to 25.96)	84536.9(37821.8 to 134896.2)	14.22(6.39 to 22.22)	32.79(14.66 to 52.33)	2.32 (2.25 to 2.4)
Central Sub-Saharan Africa	1494.1(554.6 to 2559.9)	3.41(1.3 to 5.55)	5.96(2.23 to 10.14)	7638.1(2874.6 to 13167.7)	6.98(2.86 to 10.9)	12.19(4.62 to 21.03)	2.34 (2.19 to 2.5)
East Asia	113878.4(39419.4 to 193735.9)	3.08(1.05 to 5.15)	11.93(4.13 to 20.29)	529351.9(219132.7 to 886681.3)	7.41(3.1 to 11.78)	24.42(10.09 to 40.83)	2.31 (2.21 to 2.41)
Eastern Europe	137909.2(59625 to 219010.6)	10.77(4.68 to 16.97)	48.61(20.98 to 77.14)	208723.8(90209.9 to 331586.2)	14.24(6.34 to 22.29)	60(25.94 to 95.33)	0.45 (0.31 to 0.58)
Eastern Sub-Saharan Africa	6358.8(2271.4 to 10621.8)	2.82(1.01 to 4.47)	7.52(2.67 to 12.61)	23026.2(8703.5 to 37649)	5.18(2.06 to 8.18)	11.97(4.57 to 19.8)	1.33 (1.23 to 1.43)
High-income Asia Pacific	36685.6(13456.3 to 59450.7)	4.2(1.53 to 6.84)	17.92(6.55 to 28.98)	80601.4(31642.1 to 127988.1)	5.6(2.2 to 8.95)	19.32(7.65 to 30.53)	0.13 (0.09 to 0.18)
High-income North America	185196.9(80214.1 to 295439.6)	11.48(4.96 to 18.12)	54.48(23.66 to 86.76)	296819.6(135095.2 to 460708.7)	15.56(7.08 to 23.86)	49.52(22.63 to 76.52)	-0.42 (-0.5 to -0.33)
North Africa and Middle East	39567.7(16500.5 to 65046.5)	9.65(4.11 to 15.23)	21.25(8.93 to 34.73)	156482.3(66565 to 247801.8)	15.47(7.02 to 23.58)	31.83(13.68 to 50.63)	1.46 (1.32 to 1.6)
Oceania	470.6(193.9 to 787.7)	9.15(3.96 to 14.75)	13.6(5.52 to 22.78)	1362(562.2 to 2191.1)	11.7(5.24 to 18.12)	15.48(6.43 to 25.08)	0.44 (0.37 to 0.52)
South Asia	16693.8(5702.8 to 26476.2)	2.12(0.73 to 3.38)	2.47(0.83 to 3.93)	91500.2(35883 to 144388.5)	4.8(1.91 to 7.62)	5.67(2.22 to 8.92)	2.74 (2.69 to 2.78)
Southeast Asia	20952.7(7310.9 to 33667.9)	2.85(1.04 to 4.53)	7.05(2.42 to 11.33)	119340.4(48437.4 to 193338.9)	5.51(2.24 to 8.7)	16.64(6.73 to 26.92)	2.84 (2.72 to 2.97)
Southern Latin America	22071.6(9492.6 to 36141.3)	10.7(4.58 to 17.21)	47.48(20.42 to 77.6)	50169.6(22345.7 to 81467.6)	14.36(6.34 to 22.44)	58.65(26.14 to 95.15)	0.95 (0.8 to 1.11)

Table 2 (continued)

Characteristics	1990			2021			1990–2021 EAPC (95% CI)
	Number of cases (95% UI)	PAF (%) (95% UI)	ASMR per 100,000 population (95% UI)	Number of cases (95% UI)	PAF (%) (95% UI)	ASMR per 100,000 population (95% UI)	
Southern Sub-Saharan Africa	5488.2(2315.6 to 8602.3)	9.02(3.84 to 13.98)	18.78(7.96 to 29.48)	21915.4(9192.3 to 34323)	13.2(5.89 to 20.58)	35.73(15.05 to 55.83)	2.36 (2.1 to 2.62)
Tropical Latin America	19341.4(8091.7 to 31333.8)	8.86(3.75 to 14.29)	19.74(8.2 to 31.96)	94304.1(39800.4 to 150657.5)	12.67(5.42 to 20.09)	36.04(15.2 to 57.63)	1.89 (1.79 to 2)
Western Europe	264280.1(111569 to 431654.1)	9.39(4.01 to 15.14)	46.8(19.73 to 76.51)	344,976(147806.6 to 564627.8)	11.85(5.08 to 18.89)	39.08(16.77 to 63.51)	-0.67 (-0.74 to -0.6)
Western Sub-Saharan Africa	5310.9(2112.9 to 8558.9)	4.82(1.91 to 7.58)	5.71(2.26 to 9.23)	22,886(9127.6 to 37858.8)	8.26(3.42 to 12.93)	10.79(4.35 to 17.69)	2.2 (2.14 to 2.25)

UI: Uncertainty interval, *CI*: Confidence interval, *EAPC*: Estimated Annual Percentage Changes, *SDI*: Socio-demographic index, *DALYs*: disability-adjusted life years, *ASDR*: Age-standardised DALYs rate, *PAF*: Population attributable fraction

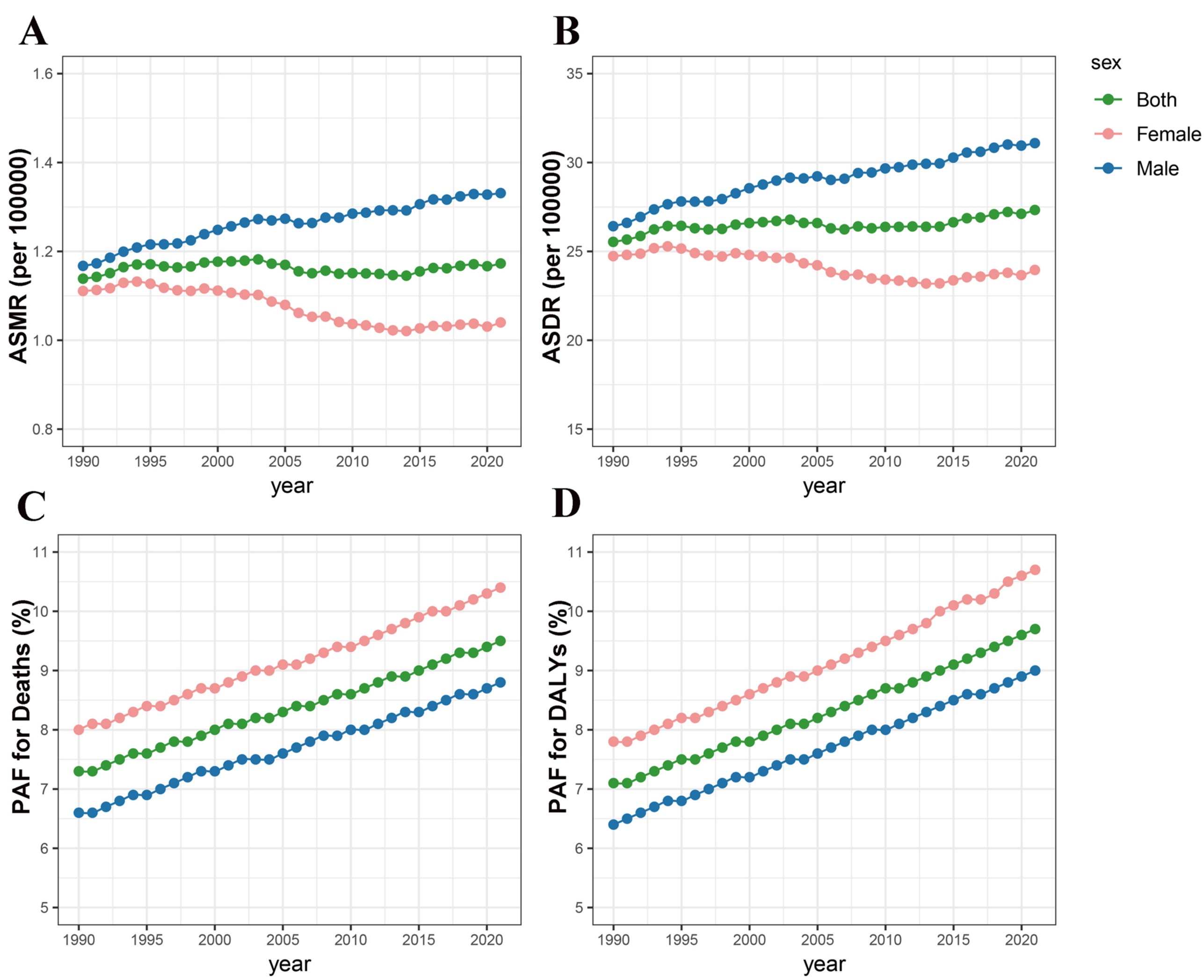

Fig. 1 Trends in global ASMR, ASDR, PAF for deaths and DALYs of colorectal cancer attributable of high BMI by sex, from 1990 to 2021. ASMR **(A)** ASDR **(B)** Percent of Deaths **(C)** Percent of DALYs **(D)**. *ASDR* Age-standardized DALYs rate, *ASMR* Age-standardized mortality rate, *BMI* body-mass index, *PAF*: Population attributable fraction, *DALYs* disability-adjusted life years

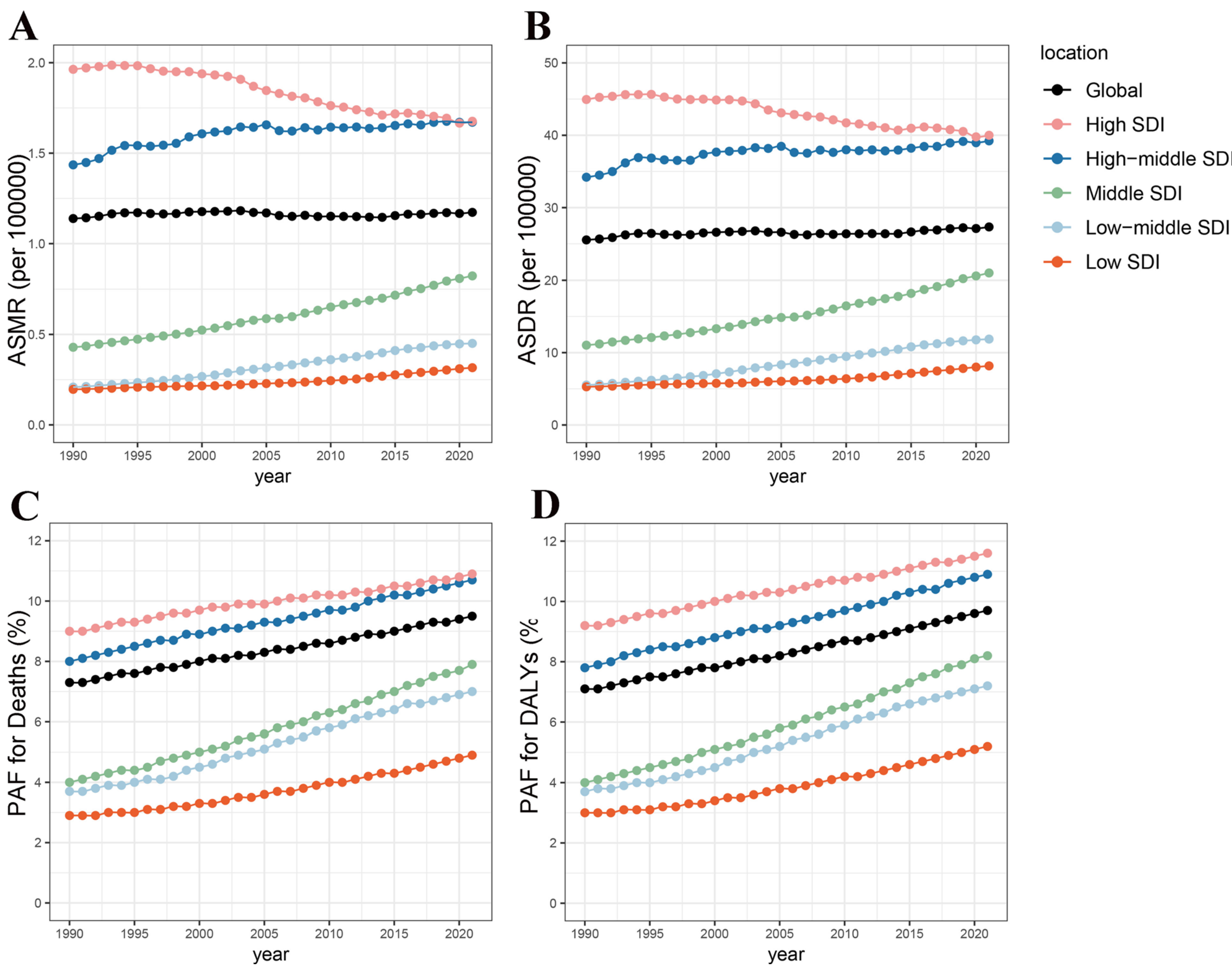

Fig. 2 Trends in global ASMR, ASDR, PAF for deaths and DALYs of colorectal cancer attributable of high BMI by SDI quintiles, from 1990 to 2021. ASMR **(A)** ASDR **(B)** Percent of Deaths **(C)** Percent of DALYs **(D)**. *ASDR* Age-standardized DALYs rate, *ASMR* Age-standardized mortality rate, *BMI* body-mass index, *PAF*: Population attributable fraction, *DALYs* disability-adjusted life years

When comparing male and female subgroups across different age groups, we observed that in individuals under 80 years, the number of deaths and DALYs due to CRC attributable to high BMI was higher in males. Conversely, in those aged 80 years and older, these metrics were higher in females (Fig. 5A, B). Furthermore, the PAFs of CRC deaths and DALYs attributable to high BMI remained consistently higher in females across all age groups (Fig. 5C, D). Between 1990 and 2021, the rates of mortality and DALYs for CRC attributable to high BMI increased with age, exhibiting a significant rise after age 50, with an accelerated increase after age 80 (Fig. 6A, B). The highest number of deaths occurred in individuals aged 70–74 years, while the greatest burden of DALYs was observed in those aged 65–69 years (Fig. 6C, D).

Factors associated with the burden of CRC attributable to high BMI

A nonlinear "S"-shaped association between ASMR and SDI was observed. Specifically, ASMR increased sharply when SDI exceeded 0.25 and then gradually declined as SDI surpassed 0.75. Regionally, the highest CRC ASMR linked to high BMI was observed in Central Europe, Southern Latin America, and Eastern Europe. Conversely, the lowest CRC ASMR associated with high BMI was found in South Asia, Southeast Asia, and Central Sub-Saharan Africa (Fig. 7A). A similar trend was noted between ASDR and SDI (Fig. 7B). In 2021, across 204 countries and territories, the relationship between CRC ASMR due to high MBI and SDI was initially increased and then decreased as SDI rose (Fig. 7C). The trend of ASDR was similar to ASMR in 204 countries and territories (Fig. 7D).

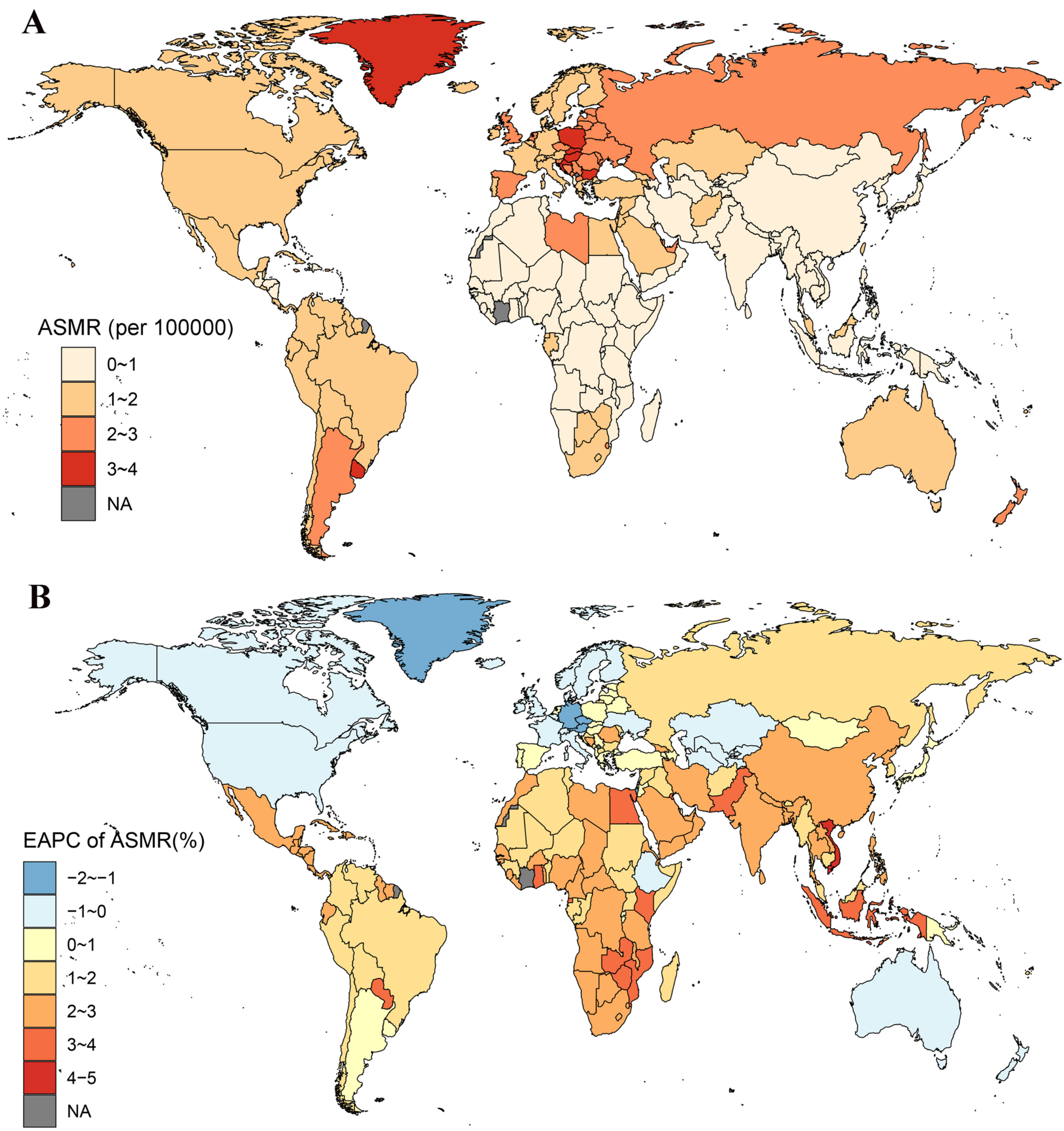

Fig. 3 Age-standardized mortality rate (ASMR) **(A)** and estimated annual percentage change (EAPC) **(B)** of colorectal cancer attributable of high body-mass index in 204 countries and territories

Projected CRC burden attributable to high BMI

The global ASMR for CRC attributable to high BMI is projected to decline by 1% by 2041, reaching an estimated rate of 1.16 per 100,000 population (Fig. 8A). In contrast, the ASDR for CRC attributable to high BMI is expected to increase by 4.23% by 2041, reaching 28.5 per 100,000 population (Fig. 8B). Between 2021 and 2041, the ASMR in males is expected to remain higher than in females. Specifically, the ASMR for males in 2041 is projected to rise by 7.94%, reaching 1.44 per 100,000 population. On the other hand, the ASMR in females is anticipated to remain nearly constant at 1.05 per 100,000 population, similar to the 2021 level (Fig. 8A). The projected ASDR for males in 2041 is expected to increase by 9.7%, reaching 34.1 per 100,000 population. In contrast, the ASDR

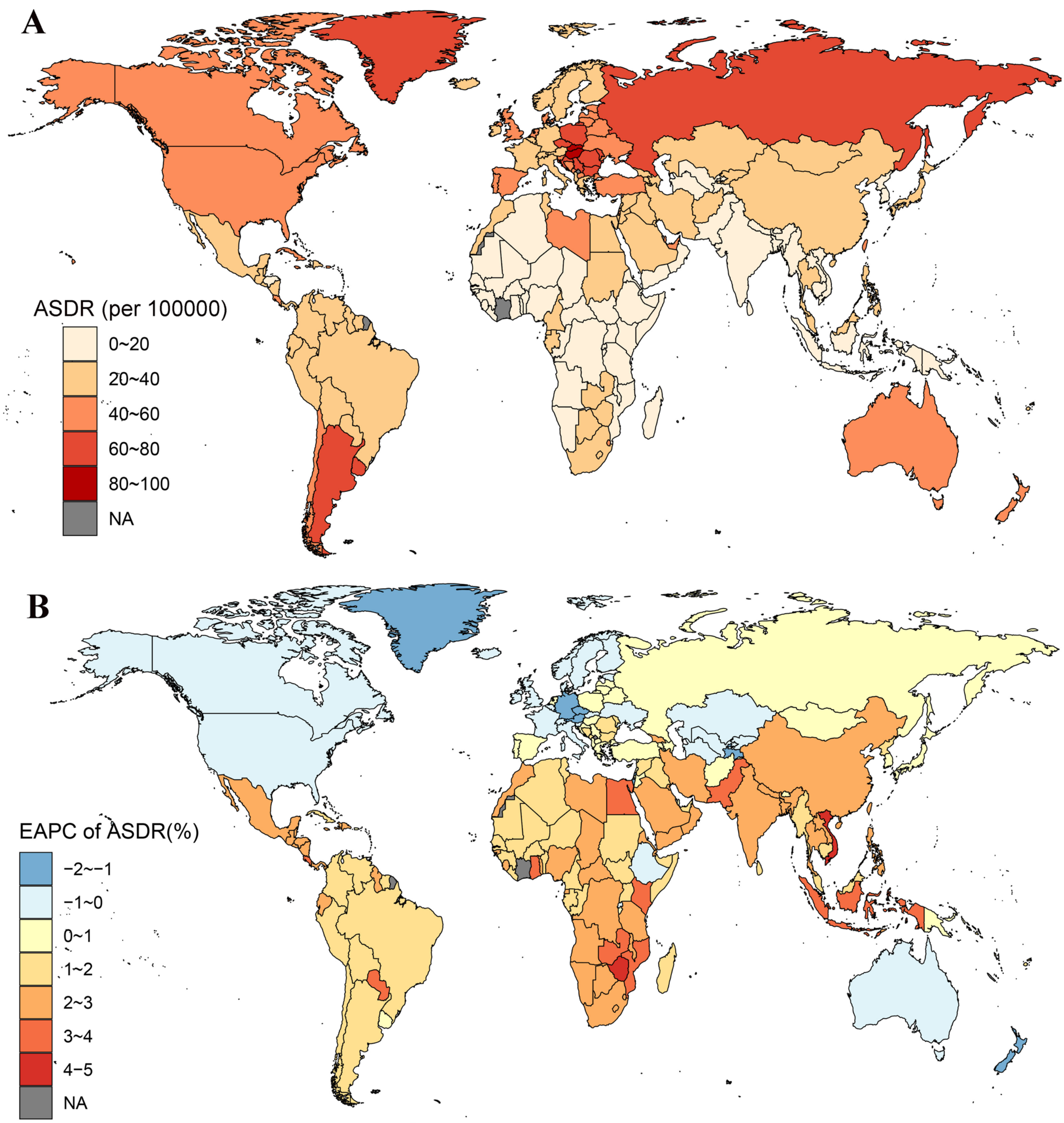

Fig. 4 Age-standardized DALYs rate (ASDR) **(A)** and estimated annual percentage change (EAPC) **(B)** of colorectal cancer attributable to high body-mass index in 204 countries and territories. *DALYs* disability-adjusted life years

for females is predicted to remain stable at 24 per 100,000 population in 2041, consistent with the 2021 (Fig. 8B).

Discussion

Escalating global burden of CRC attributable to high BMI and underlying mechanisms

Our study reveals a concerning escalation in the global burden of CRC associated with high BMI. Our findings indicate that nearly 100,000 annual deaths worldwide linked to CRC attributable to high BMI in recent years, more than double the number in 1990. Notably, the PAFs of CRC deaths and DALYs due to high BMI have shown a consistent upward trend. These findings underscore high BMI as an increasingly significant risk factor for CRC-related mortality, consistent with prior studies that have identified obesity as a critical public health threat

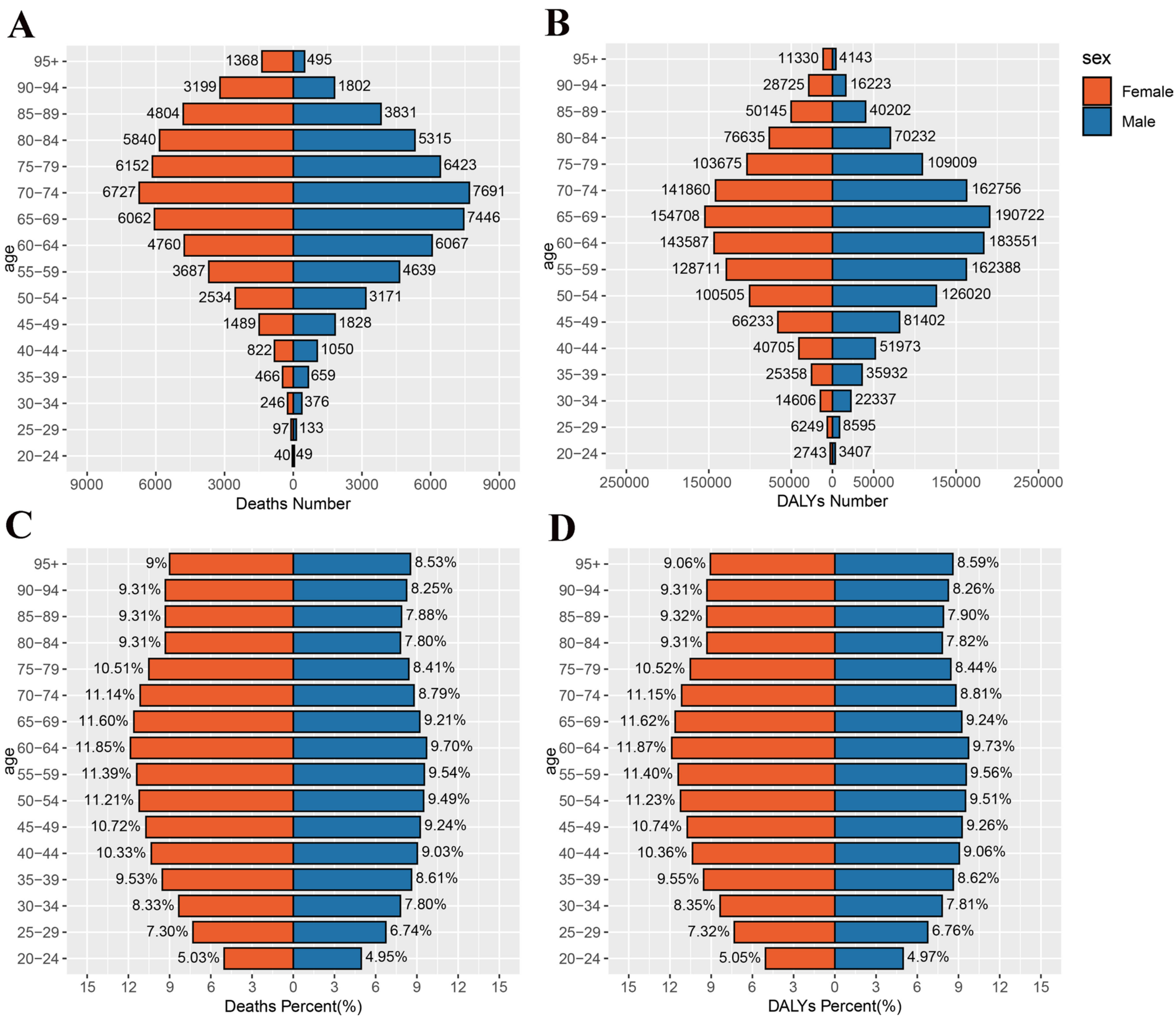

Fig. 5 Stratification analysis of deaths and DALYs of colorectal cancer attributable to high body-mass by age and sex in 2021; Deaths number **(A)** DALYs number **(B)** Deaths percent **(C)** DALYs percent **(D)**. *DALYs* disability-adjusted life years

globally [27, 28]. Several reasons may explain this situation. Firstly, the global economic boom has increased the availability and consumption of high-calorie diets, leading to a rapid increase in obesity, particularly in regions with high SDI [18, 29, 30]. Secondly, in most parts of the world, sedentary jobs and lifestyles have become more prevalent, further contributing to the obesity epidemic [31, 32]. Thirdly, in addition to the epidemiological associations, several biological mechanisms have been proposed to explain the link between elevated BMI and CRC. Obesity promotes chronic low-grade inflammation and insulin resistance, which may create a pro-tumorigenic microenvironment. Elevated levels of insulin and insulin-like growth factors (IGFs) can stimulate colorectal epithelial cell proliferation and inhibit apoptosis [33]. Adipose tissue also secretes adipokines such as leptin and adiponectin, which are known to modulate inflammatory pathways and cellular metabolism [34]. Furthermore, obesity is associated with dysbiosis of the gut microbiota, which may affect mucosal immunity and carcinogenesis [35]. Emerging evidence also suggests that obesity can influence epigenetic regulation and immune surveillance in the tumor microenvironment. These mechanistic pathways offer promising targets for risk stratification and therapeutic intervention, and merit further investigation in translational studies. Additionally, obesity may complicate surgical procedures and postoperative recovery in CRC patients, further impacting treatment outcomes and survival rates [36].

While this study focuses on the burden of CRC attributable specifically to high BMI, it is important to recognize that several other lifestyle factors—such as smoking,

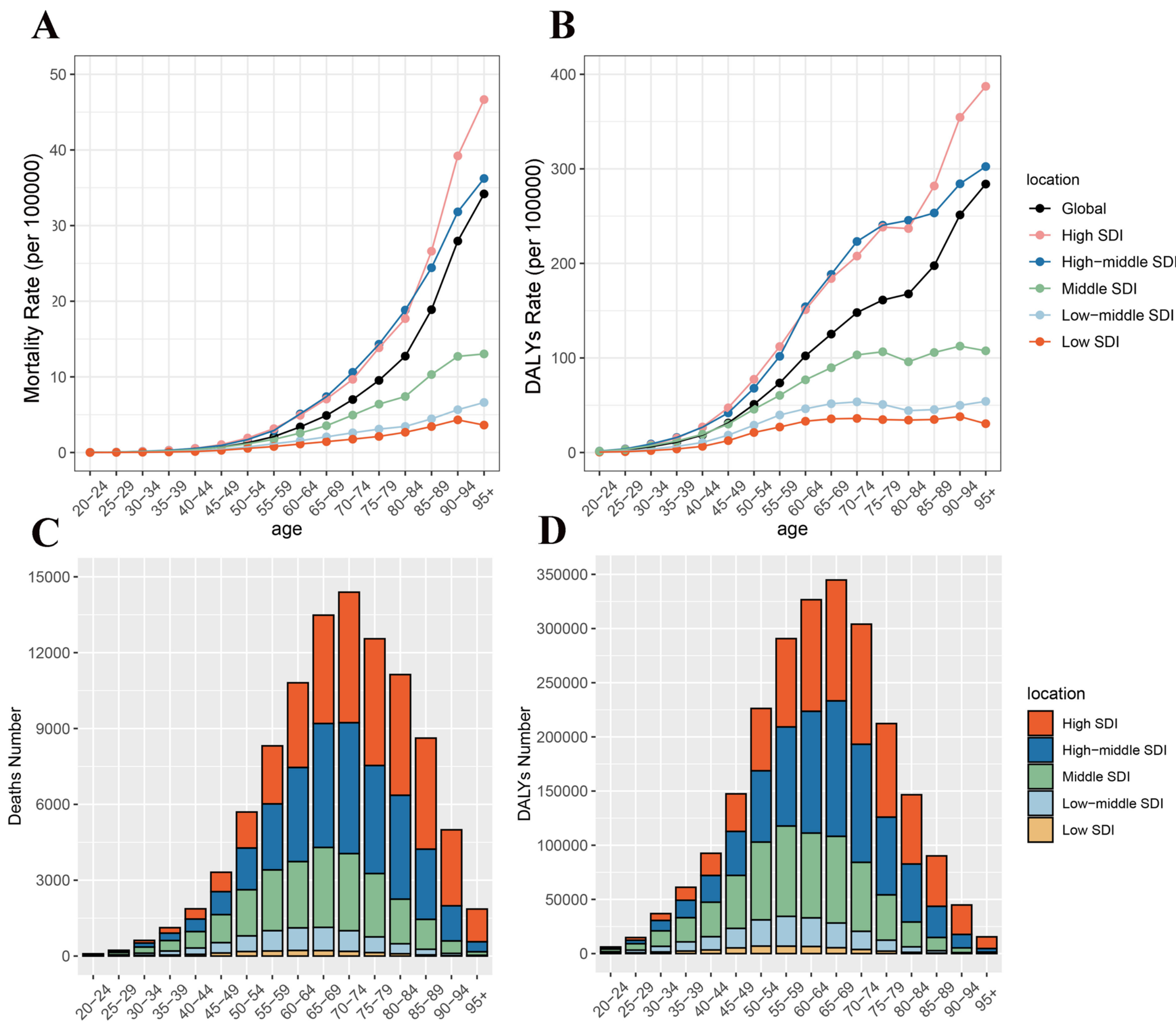

Fig. 6 Stratification analysis of deaths and DALYs of colorectal cancer attributable to high body-mass by age and SDI regions in 2021; Mortality rate **(A)** DALYs rate **(B)** Deaths number **(C)** DALYs number **(D)**. *DALYs* disability-adjusted life years

alcohol consumption, physical inactivity, and poor dietary patterns—are also well-established contributors to CRC risk [37]. These risk factors often co-exist with obesity and may act synergistically, further compounding the disease burden. For example, smoking and alcohol use have been shown to increase the risk of CRC through both inflammatory and genetic mechanisms, and individuals with sedentary lifestyles are more likely to develop obesity as well as CRC [38]. Although the GBD framework models risk factors separately, the potential interaction and co-occurrence of these exposures may influence our estimates. Future studies should consider integrated lifestyle risk profiles to better understand the complex etiologies of CRC. The wide UIs observed for some estimates, such as global CRC deaths attributable to high BMI in 2021, suggest considerable variability in source data and potential limitations in data completeness, particularly in low- and middle-income countries. Nonetheless, the central trends and directionality of the burden remain consistent across regions and over time, supporting the robustness of the overall conclusions.

Interestingly, our findings demonstrate a rising ASDR yet a slightly declining ASMR from 1990 to 2021, which may reflect complex interactions between high BMI-related biological mechanisms and advancements in CRC management. For instance, chronic low-grade inflammation, insulin resistance, and dysbiosis associated with high BMI likely contribute to earlier onset and more aggressive forms of CRC, leading to increased YLDs and hence a higher ASDR [5, 9]. Meanwhile, improvements in early detection, surgical techniques, and adjuvant therapies may have reduced mortality rates, partially offsetting

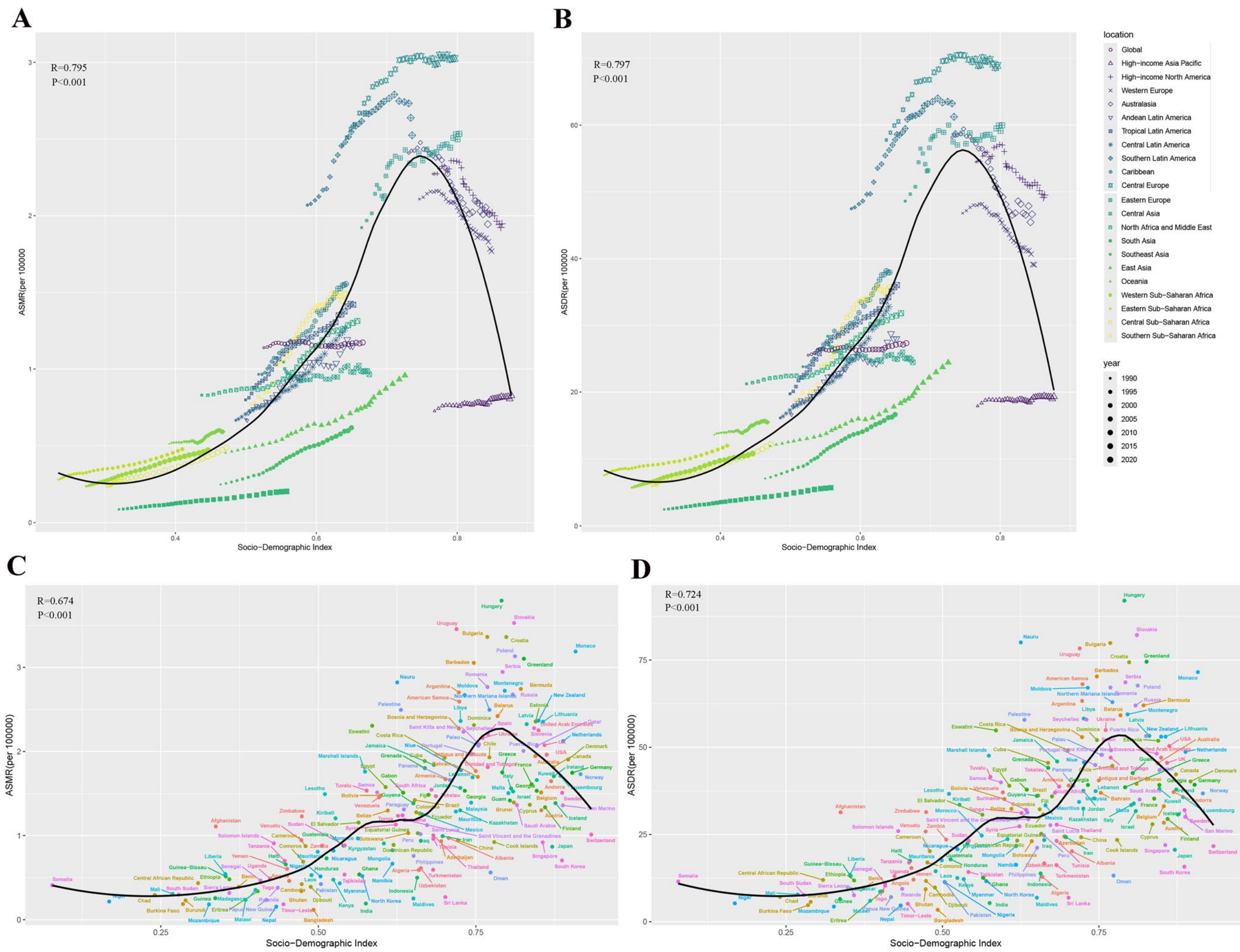

Fig. 7 Correlation between high body-mass index-attributable colorectal cancer in ASMR or ASDR and SDI between 1990 and 2021; ASMR **(A)** and ASDR **(B)** in 21 GBD regions, ASMR **(C)** and ASDR **(D)** in 204 nations. *ASMR* age-standardized mortality rate, *ASDR* age-standardized DALYs rate, *GBD* global burden of disease study, *DALYs* disability-adjusted life years

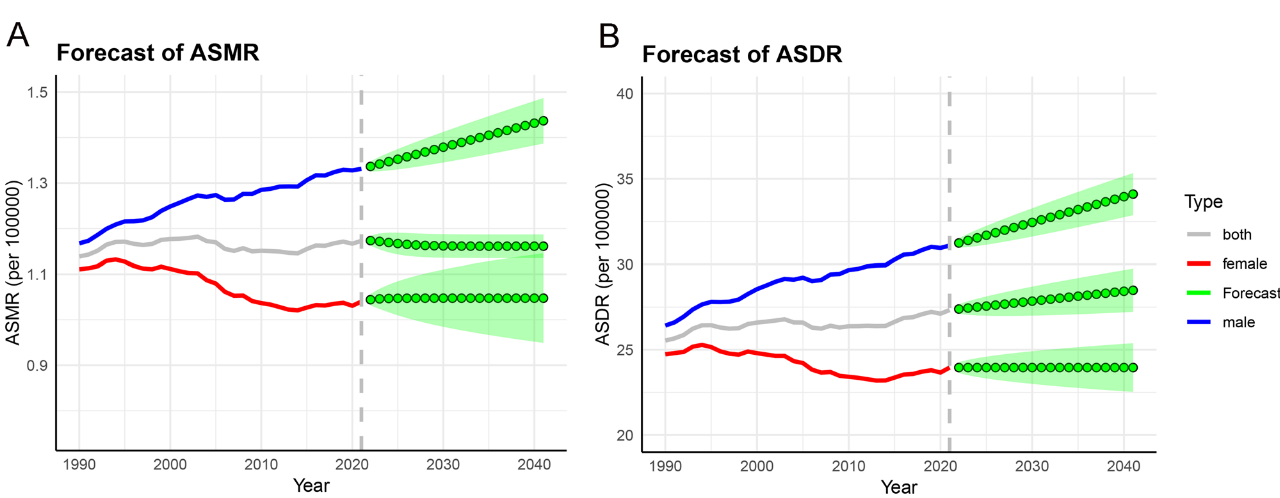

Fig. 8 Forecasts of age-standardized mortality rate (ASMR) **(A)** and age-standardized DALYs rate (ASDR) **(B)** of high body-mass index-attributable colorectal cancer, stratified by sex, over the next 20 years using the ARIMA model. *ARIMA* autoregressive integrated moving average, *DALYs* disability-adjusted life years

the lethality of high BMI-attributable CRC [39]. Additionally, high BMI-related comorbidities may delay optimal treatment or reduce treatment tolerance, resulting in prolonged disease courses without immediate fatality—further contributing to the growing DALYs burden [40].

Cross-regional disparities driven by socioeconomic and healthcare inequities

Our analysis revealed substantial regional disparities in the CRC burden attributable to high BMI. Regions with higher SDI exhibited higher ASMR and ASDR of CRC due to high BMI. Moreover, in high-middle to low SDI regions, regions with higher SDI exhibited faster increase of ASMR and ASDR. Contrarily, high SDI regions experienced a decline in these metrics. This pattern was similar to that of overall CRC. These trends may reflect variations in healthcare systems, public health policies, and socioeconomic development [41]. High SDI regions benefit from advanced healthcare infrastructure, improved CRC screening, and early diagnosis, contributing to declining CRC mortality rates [42]. Moreover, heightened public awareness and government interventions targeting obesity and CRC prevention may further mitigate disease burden. In contrast, the rapid rise in obesity and limited healthcare resources in upper-middle SDI regions may account for the accelerated increase in ASMR and ASDR [43].

Regional disparities in the burden of CRC attributable to high BMI are shaped by a complex interplay of sociocultural, economic, and healthcare system factors that extend beyond differences in screening coverage alone. In high-SDI regions, the decline in CRC mortality despite rising high BMI prevalence may reflect the mitigating effects of robust healthcare infrastructure, widespread CRC screening programs (e.g., colonoscopy, FIT), and early access to multidisciplinary care [44]. Public health initiatives—such as taxation of sugar-sweetened beverages, front-of-package labeling, and obesity awareness campaigns—have also played a role in curbing CRC risk by promoting healthier lifestyles [45]. Conversely, in low- and middle-SDI regions, a combination of rapid urbanization, dietary westernization (characterized by increased intake of processed foods, red meat, and sugary drinks), and physical inactivity—often influenced by cultural norms, especially among women—has contributed to rising obesity and CRC risk [13]. Compounding these behavioral risks, weaker healthcare infrastructure, limited access to timely diagnosis and treatment, and inadequate investment in cancer screening programs hinder effective disease control. In some cultures, excess body weight may even be perceived as a sign of health or prosperity, diminishing public and policy urgency for intervention [53]. Additionally, low health literacy and limited public health outreach further reduce awareness of the link between obesity and cancer. These region-specific mechanisms help explain why high BMI contributes disproportionately to CRC burden in certain settings and underscore the need for tailored, culturally sensitive strategies that account for both local risk environments and systemic health disparities.

While data quality limitations in low-middle or low-SDI regions are an acknowledged challenge—particularly due to incomplete cancer surveillance and death registration systems—the GBD study has implemented a series of robust strategies to address these gaps. In particular, the DisMod-MR 2.1 modeling framework plays a key role in synthesizing data from diverse sources, adjusting for known biases, and ensuring internal consistency across estimates of incidence, prevalence, mortality, and disability [17]. These methods have significantly improved the reliability of estimates, even in data-sparse settings. Although some degree of uncertainty may still remain in regions with extremely limited input data, the overall quality and comparability of GBD estimates have been substantially enhanced through these methodological advances [15]. Therefore, while caution is warranted when interpreting trends from low-middle or low-SDI regions, the GBD framework provides a sound and scientifically rigorous basis for global and cross-regional comparisons [46].

The "S"-shaped association between SDI and ASMR likely reflects a combination of epidemiological transition and differential capacity to respond to the growing burden of high BMI. In low-SDI countries, the burden may be underestimated due to limited diagnostic capacity and underreporting, giving the false impression of a low ASMR [45]. As countries transition into middle SDI levels, rapid urbanization and westernized diets lead to increased high BMI prevalence and consequently higher CRC incidence [42]. However, healthcare infrastructure often lags behind, with limited access to early CRC screening, diagnosis, and treatment, resulting in sharply rising mortality rates. In high-SDI regions, although high BMI prevalence remains high, robust cancer screening programs, effective public health campaigns, and better access to timely care contribute to a reversal in mortality trends [47]. This non-linear pattern underscores the importance of tailoring interventions to each country's level of socioeconomic development, focusing not only on obesity prevention but also on enhancing early detection and equitable access to care. As the GBD 2021 database primarily provides national-level estimates. This may limit the applicability of our findings in large, diverse countries (e.g., China, India, the U.S.) where significant within-country disparities likely exist. Future studies using high-resolution subnational data are needed to support more targeted public health strategies [17].

Gender- and age-specific patterns of high BMI-related CRC burden

Our findings reveal notable gender and age disparities in the burden of CRC attributable to high BMI, highlighting the need for tailored prevention strategies. Males consistently exhibit higher ASMR and ASDR compared to females. This may reflect sex-based differences in body fat distribution—men are more likely to accumulate visceral adipose tissue, which is metabolically active and pro-inflammatory, thereby increasing CRC risk through insulin resistance, hyperinsulinemia, and chronic low-grade inflammation [48]. Conversely, females tend to store fat subcutaneously, which may confer relatively less oncogenic risk. Moreover, estrogen has been shown to exert a protective effect against colorectal tumorigenesis, particularly before menopause, which might partially explain the lower CRC mortality in women despite increasing obesity rates [49]. Importantly, our analysis also shows that females bear a relatively higher proportional burden (i.e., PAF) of CRC due to high BMI in certain regions, particularly in low- and middle-income countries. This could be influenced by regional disparities in female obesity prevalence, limited access to early screening, and sociocultural barriers to care-seeking among women [38]. In terms of age differences, we observed a pronounced increase in high BMI-attributable CRC burden with advancing age. Both ASMR and ASDR begin to rise substantially after age 50, peaking in the 70–74 and 65–69 age groups, respectively. This trend likely reflects the cumulative biological impact of long-term excess adiposity, age-related immunosenescence, and declining metabolic resilience. Additionally, obesity-related comorbidities such as type 2 diabetes, metabolic syndrome, and fatty liver disease, which compound CRC risk, are more prevalent in older adults [4]. On the other hand, early-onset CRC (under age 50) is increasing globally, and while our study excluded individuals below 20 due to data limitations, the upward trend in the 20–49 age group underscores the need for earlier preventive strategies [47]. Collectively, these findings underscore the importance of integrating gender-sensitive and age-specific approaches into CRC prevention policies. For instance, public health strategies could prioritize weight management and CRC screening for older adults, while addressing sociocultural determinants of obesity and healthcare access among women. Furthermore, future research should explore sex- and age-specific biological pathways linking adiposity to colorectal carcinogenesis to support the development of more personalized interventions [50].

Future trends highlight increasing dalys despite stabilizing mortality

Contrary to the anticipated global decline in overall CRC mortality and disability, our projections indicate that the burden of CRC attributable to high BMI will persist or even worsen by 2041—particularly among males. While the global ASMR is expected to decline slightly by 1%, the ASDR is projected to rise by 4.23%, highlighting a shifting burden from mortality to morbidity. This divergence is more pronounced in males, with the ASMR and ASDR expected to increase by 7.94% and 9.7%, respectively, while female rates remain largely stable. Several factors may explain this trend. First, improvements in early detection and treatment, especially in high-SDI regions, may reduce CRC mortality while increasing survival rates—resulting in more individuals living with CRC-related disability [45]. Second, prolonged survival due to earlier diagnosis and medical advances may be accompanied by long-term treatment side effects or functional impairment, contributing to rising DALYs despite stable or declining mortality. Third, excess body weight may predispose patients to earlier-stage or slower-progressing disease, reducing fatality but increasing the burden of chronic illness. Lastly, population aging may lead to more individuals living longer with CRC, further elevating the DALYs burden [42]. These findings underscore the complex interplay between risk exposure, disease progression, and demographic transitions, and highlight the need for integrated strategies targeting both CRC prevention and long-term survivorship, especially in populations with rising obesity prevalence.

Strengths and limitations of the study and data sources

This study is the first to use the 2021 GBD database to comprehensively analyze the global burden of CRC attributable to high BMI from 1990 to 2021, incorporating multidimensional perspectives and providing predictive insights for the next 20 years. However, several inherent limitations of the GBD 2021 database may have affected the granularity and interpretability of our findings to some extent [30]. First, the database defines high BMI exposure uniformly as BMI > 25 kg/m^2, without further stratification by obesity class. This precluded our ability to assess dose-response relationships or to identify potential high-risk subgroups based on obesity severity. Second, the analysis was restricted to individuals aged 20 years and older, as GBD does not provide reliable estimates of high BMI-attributable colorectal cancer (CRC) burden in younger populations. Although early-onset CRC is an emerging concern globally, current evidence suggests that high BMI-attributable CRC cases in individuals under 20 remain extremely rare, and their exclusion is unlikely to substantially alter the overall conclusions [47]. Third, the absence of incidence data attributable to high BMI limits the ability to distinguish whether overweight and obesity primarily influence CRC initiation, progression, or mortality, thereby constraining the study's implications for early prevention strategies. Despite these limitations, the mortality and DALY estimates derived from the GBD data still provide valuable insights into the global and regional burden of overweight-attributable CRC. Future research integrating stratified BMI exposure levels, younger populations, and incidence data will be essential to refine our understanding of the relationship between adiposity and CRC development across the disease continuum. Fourth, data collection heterogeneity and potential errors, may introduce bias into our estimates. To address these limitations, future research should integrate data from additional epidemiological databases, such as SEER (Surveillance, Epidemiology, and End Results) and GLOBOCAN (Cancer's Global Cancer Observatory), to enhance representativeness [2, 51].

On the other hand, due to the observational and population-level nature of the GBD dataset, the present study cannot establish causality between high BMI and CRC outcomes. Although the GBD comparative risk assessment framework is grounded in systematic reviews and meta-analyses of epidemiological studies, residual confounding from unmeasured variables—such as dietary composition, physical activity levels, genetic susceptibility, and access to healthcare—may bias the estimated associations. Thus, the findings should be interpreted as associations at the population level [18]. Future prospective cohort studies and mechanistic research are warranted to clarify the causal pathways involved. Another limitation lies in the assumption of stationarity required by the ARIMA methodology of our prediction model. While differencing was applied to achieve stationarity, real-world healthcare data are often influenced by dynamic external factors, such as advancements in medical technologies, policy interventions, and behavioral changes in the population. These factors may introduce structural changes that are not captured in the historical time series, potentially affecting the reliability of long-term forecasts. Therefore, our projection results should be interpreted with caution, particularly when used for future planning in rapidly changing healthcare environments [26].

Implications for global CRC prevention and policy recommendations

Our findings underscore the need for urgent public health interventions to reduce high BMI-attributable CRC burden globally. To address this, we recommend implementing targeted prevention strategies at both the individual and population levels. First, nationwide anti-obesity campaigns should be launched to increase public awareness of the health risks associated with obesity, particularly its role in the development of CRC. These campaigns could focus on promoting healthier dietary choices, reducing consumption of processed foods and sugary drinks, and encouraging physical activity. Additionally, improving access to CRC screening is crucial for early detection and prevention. Health systems should ensure that populations at high risk of obesity-related CRC, including older adults and individuals in low- and middle-income countries, have access to affordable and timely screening services. From a policy perspective, governments could implement taxes on sugary foods and beverages, which have been shown to reduce consumption and promote healthier dietary habits. Furthermore, urban planning should focus on creating environments that encourage physical activity, such as the development of parks, pedestrian-friendly infrastructure, and spaces for recreational sports. These measures, when combined, can help reduce the burden of overweight and obesity and, in turn, the incidence of CRC.

Conclusion

In brief, our findings indicated that the ASMR and ASDR of CRC attributable to high BMI exhibited an modestly upward trend, while the percentage of them to overall CRC patients demonstrated a significant increase from 1990 to 2021 globally. The high SDI regions, Central Europe, and countries such as Hungary and Slovakia exhibited the highest ASMR and ASDR of CRC attributable to high BMI in 2021, while the high-middle SDI regions, Southeast Asia, and countries such as Viet Nam and LesothoIt showed the most rapid growth of ASMR and ASDR from 1990 to 2021. The PAFs of CRC deaths and DALYs due to high BMI were higher among females. The mortality and DALYs rates due to CRC attributable to high BMI increased with age, while the 65–74 age group experiences the highest number of them. It was predicted that the ASMR and ASDR of CRC attributable to high BMI would decline by 1% and increase by 4.23% until 2041. Our findings emphasize the critical role of CRC attributable to high BMI in the global disease burden and highlight the importance of addressing obesity and CRC through comprehensive, region-specific, and age-appropriate strategies to mitigate its impact on public health. In low-SDI regions, where healthcare infrastructure and surveillance systems are often limited, targeted strategies such as community-based obesity prevention programs, cost-effective CRC screening initiatives, and international collaboration for data system strengthening are urgently needed to reduce the future burden of high BMI-related CRC.

Abbreviations

ARIMA	Autoregressive integrated moving average
ACF	Autocorrelation function

AIC	Akaike Information Criterion
ASDR	Age-standardized DALYs rate
ASMR	Age-standardized mortality rate
ASR	Age-standardized rate
BIC	Bayesian Information Criterion
BMI	Body mass index
CI	Confidence interval
CRC	Colorectal cancer
DALYs	Disability-adjusted life years
EAPC	Estimated annual percentage change
GBD	Global burden of disease
GHDx	Global Health Data Exchange
GLOBOCAN	Cancer's Global Cancer Observatory
HDI	Human development index
IGFs	Insulin-like growth factors
PACF	Partial autocorrelation function
PAF	Population attributable fraction
SEER	Surveillance, Epidemiology, and End Results
SDI	Socio-demographic index
UI	Uncertainty interval
YLDs	Years lived with disability

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12876-025-03938-4.

Supplementary Material 1: Table S1 Optimal ARIMA Model Parameters and Corresponding AIC/BIC Values for Each Time Series.

Supplementary Material 2: Table S2 Global deaths burden of colorectal cancer attributable to high body-mass index in 1990 and 2021 with EAPC from 1990 to 2021 at countries/territories level, both sexes.

Supplementary Material 3: Table S3 Global DALYs burden of colorectal cancer attributable to high body-mass index in 1990 and 2021 with EAPC from 1990 to 2021 at countries/territories level, both sexes.

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Author contributions

J. Z., and J. Y. contributed to the study conception and design. The first draft of the manuscript was written by J. Y. and Data collection and analysis were performed by J. Z and J. Y. performed the visualization. J. Y. and provided the language help. All authors read and approved the final manuscript.

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Data availability

Publicly available datasets were analyzed in this study. The data can be found here: http://ghdx.healthdata.org/gbd-results-tool.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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