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Global burden of colorectal cancer attributable to metabolic risks from 1990 to 2021, with predictions to 2046

Xiaoyue Zhang[1,2], Ziqing Xu[2,3], Lin Shang[4], Qian Yang[5], Hua Ye[2,3], Haiyan Liu[2,3], Yuanlin Zou[2,3], Yin Lu[2,3], Zhong Zheng[2,3], Meng Li[2,3], Peng Wang[2,3*] and Jicun Zhu[1*]

Abstract

Background Metabolic risks are significant factors associated with colorectal cancer. This study aimed to assess global, regional and national burden for CRC attributable to metabolic risks from 1990 to 2021 and to predict mortality by 2046.

Methods Data from the Global Burden of Disease Study 2021 were used to quantify deaths, disability-adjusted life years (DALYs), and age-standardized rates of CRC due to metabolic risk factors, disaggregated by sex, age, region, country/territory, and sociodemographic index (SDI). The average annual percentage change (AAPC) was used to analyze temporal trends from 1990 to 2021. Metabolic risks include high fasting plasma glucose (FPG) and high body mass index (BMI). Future mortality trends up to 2046 were forecast using age-period-cohort models.

Results Globally, CRC deaths attributable to metabolic risks increased 2.47-fold, rising from 73,443 in 1990 to 181,689 in 2021. The global age-standardized mortality rates (ASMRs) and age-standardized rates of DALYs (ASDRs) of CRC attributable to high FPG and ASDRs attributable to high BMI increased from 1990 to 2021. The ASMRs and ASDRs of males was higher than that of females, with increasing trends. Central Europe had the highest ASMRs and ASDRs of CRC attributable to metabolic risks in 2021. Most regions and countries showed increasing trends in ASMR and ASDR for CRC due to metabolic risks, with Andean Latin America, Southeast Asia, and Cabo Verde increasing the most. High-SDI regions had the largest burden of CRC attributable to metabolic risks, while burden of other SDI regions have been significantly increased. A positive association was observed between SDI and age-standardized rates (ASMR: $R_{FPG} = 0.803$, $R_{BMI} = 0.752$; ASDR: $R_{FPG} = 0.812$, $R_{BMI} = 0.756$). By 2046, the ASMR of CRC attributable to high FPG was projected to remain stable and the ASMR due to high BMI was expected to see a slightly increase.

Conclusion Colorectal cancer deaths and DALYs attributable to metabolic risk factors remain high, particularly in males and high-SDI regions. Further researches into the metabolic mechanisms of CRC and effective treatment strategies are needed.

Keywords Colorectal cancer, AAPC, Fasting plasma glucose, BMI, Burden, Prediction

*Correspondence:
Peng Wang
wangpeng1658@hotmail.com
Jicun Zhu
jicunzhu1101@163.com

Full list of author information is available at the end of the article

Background

Colorectal cancer (CRC) ranks third in incidence and second in mortality globally, with nearly 1.93 million new cases and 903,859 deaths in 2022 [1]. Globally, both the incidence and mortality of CRC continue to rise annually, with projections indicating that new cases could surpass 2.2 million and deaths 1.1 million by 2030 [2, 3]. The global burden of CRC varies significantly due to disparities in risk factor prevalence and prevention programs among different countries and regions [4].

Studies indicate that in addition to non-modifiable genetic factors [5, 6], modifiable factors such as unhealthy diet, smoking, alcohol use, physical inactivity, high fasting plasma glucose (FPG), and high body mass index (BMI) also significantly influence the development and advancement of CRC [7, 8]. Specifically, metabolic risks like high FPG and BMI are notable contributors to cancer progression and are potentially preventable. The relationship between metabolism and cancer is well-established, with aberrant metabolic processes being a key characteristic of cancer development [9, 10].

Metabolic risks had the highest percentage increase in deaths of cancer among all risk factors between 2000 and 2021 [11]. In 2019, over 400,000 deaths of cancer were linked to high FPG and high BMI globally [12, 13]. A cohort study indicated the relationship between metabolic factors and heightened CRC risk [14]. Specifically, in 2019, the proportion of CRC cases attributable to high FPG levels rose to 9.1%, while that attributed to high BMI increased to 7.8% [15]. Although the burden of CRC and its risk factors have been well estimated [15–17], there has not been a study addressing the global burden of CRC specifically attributed to metabolic risks.

The Global Burden of Disease (GBD) study included 371 diseases and 88 associated risk factors, offering data support to explore and clarify the epidemiological characteristics of CRC [11, 18]. We obtained detailed numbers, percentages, and rates of death and disability-adjusted life years (DALYs) of CRC due to metabolic risks from GBD 2021. Our analysis focused on exploring the temporal trends in CRC burden, elucidating influences of sex, age, geographic location, and socio-demographic index (SDI) on CRC deaths and DALYs. Additionally, we conducted forecasting to anticipate future trends, providing valuable insights for enhancing CRC prevention strategies.

Methods

Data sources

GBD 2021 estimates 371 diseases and 88 related risk factors at the global, regional, and national level. In this study, we identified two metabolic risk factors for CRC: "high fasting plasma glucose" and "high body-mass index". Then, "Colon and rectum cancer" was selected in the list of "Neoplasms".

Data on mortality, DALYs, age-standardized mortality rates (ASMRs) and age-standardized DALYs rates (ASDRs) for CRC were extracted from the GBD results tool (https://vizhub.healthdata.org/gbd-results/). These metrics were analyzed across 21 GBD regions and 204 countries/territories from 1990 to 2021, including information stratified by sex, age, and risk factors of CRC.

For SDI, 204 countries and territories were categorized into 5 grades: high, high middle, middle, low middle, and low. This classification was calculated based on the fertility rate of individuals under 25 years, educational attainment for those over 15 years and per capita income [19].

Definition of disease and risk factors

CRC was identified using the following international classification of diseases, tenth edition (ICD10) codes: C18-C19.0, C20, C21-C21.8, Z12.1-Z12.13, Z85.03-Z85.048, Z86.010.

In the GBD 2021, high BMI for adults (ages 20+) is defined as BMI greater than 20 to 23 kg/m^2, and high FPG was defined as any level above the theoretical minimum-risk exposure level (4.9–5.3 mmol/L) [11].

Statistical analyses

Death, DALYs, and their age-standardized rates (ASRs) were the main index to evaluate the burden of CRC. Rates were expressed in units per 100,000 person-years, and age-standardized rates were calculated using the GBD world population standard [20]. For each measure, a 95% uncertainty interval (UI) was reported. The Joinpoint model (Joinpoint 5.2.0, the National Cancer Institute) was used to calculate the average annual percentage changes (AAPC) and their 95% confidence intervals (CIs) to identify changes in time trends [21]. The two-tailed t-test was employed for statistical inference, and the null hypothesis of true AAPC was 0. *P*-value was determined by Monte Carlo methods, and the overall asymptotic significance level was maintained through a Bonferroni correction [22]. The Nordpred package in R software was used to predict the number of deaths and age-standardized mortality from 2022 to 2046, which used age-period-cohort analysis to predict disease trends. The correlation between SDI and ASMR as well as ASDR was evaluated using the Pearson test, and the expected relationship was determined through the locally weighted regression (LOESS) model. All analyses and visualizations were performed using R 4.3.1 and Joinpoint 5.2.0, with a significance threshold set at $P < 0.05$.

Table 1 Global burden of colorectal cancer attributable to high fasting plasma glucose in 1990 and 2021 and corresponding AAPC from 1990 to 2021

Location	1990		2021		AAPC	
	ASMR (/10^5) (95%UI)	ASDR (/10^5) (95%UI)	ASMR (/10^5) (95%UI)	ASDR (/10^5) (95%UI)	ASMR (95%CI)	ASDR (95%CI)
Global	0.89 (0.45, 1.34)	18.46 (9.27, 28.03)	0.98 (0.51, 1.49)	20.31 (10.46, 30.81)	0.31* (0.19, 0.43)	0.31* (0.19, 0.43)
Female	0.76 (0.38, 1.15)	15.49 (7.76, 23.35)	0.77 (0.39, 1.16)	15.59 (7.97, 23.67)	0.03 (-0.09, 0.15)	0.02 (-0.11, 0.14)
Male	1.07 (0.54, 1.61)	22.12 (11.05, 33.38)	1.25 (0.64, 1.90)	25.76 (13.05, 39.44)	0.50* (0.38, 0.62)	0.50* (0.40, 0.60)
SDI levels						
Low SDI	0.34 (0.16, 0.53)	7.46 (3.65, 11.66)	0.44 (0.22, 0.69)	9.27 (4.47, 14.31)	0.92* (0.78, 1.05)	0.72* (0.61, 0.83)
Low-middle SDI	0.30 (0.15, 0.46)	6.86 (3.48, 10.53)	0.52 (0.26, 0.79)	11.71 (5.82, 17.78)	1.82* (1.71, 1.93)	1.77* (1.70, 1.83)
Middle SDI	0.61 (0.29, 0.93)	13.39 (6.53, 20.72)	0.77 (0.40, 1.20)	16.92 (8.68, 26.32)	0.80* (0.61, 0.99)	0.77* (0.61, 0.94)
High-middle SDI	0.97 (0.49, 1.48)	20.94 (10.47, 32.11)	1.17 (0.61, 1.80)	24.87 (12.71, 38.46)	0.65* (0.46, 0.84)	0.57* (0.38, 0.77)
High SDI	1.33 (0.69, 1.99)	27.71 (14.10, 41.57)	1.33 (0.67, 1.99)	27.65 (14.20, 41.32)	-0.01 (-0.07, 0.06)	-0.03 (-0.15, 0.09)

Abbreviations: *UI*, uncertainty interval; *CI*, confidence interval; ASMR, age-standardized mortality rate; ASDR, age-standardized disability-adjusted life-year rate; AAPC, average annual percentage change; SDI, socio-demographic index; ∗ $P < 0.05$

Table 2 Global burden of colorectal cancer attributable to high body-mass index in 1990 and 2021 and corresponding AAPC from 1990 to 2021

Location	1990		2021		AAPC	
	ASMR (/10^5) (95%UI)	ASDR (/10^5) (95%UI)	ASMR (/10^5) (95%UI)	ASDR (/10^5) (95%UI)	ASMR (95%CI)	ASDR (95%CI)
Global	1.14 (0.48, 1.86)	25.54 (10.83, 41.20)	1.17 (0.51, 1.87)	27.33 (11.80, 43.37)	0.10 (-0.03, 0.22)	0.22* (0.09, 0.36)
Female	1.11 (0.48, 1.81)	24.73 (10.59, 39.99)	1.04 (0.45, 1.65)	23.96 (10.36, 37.75)	-0.21* (-0.30, -0.12)	-0.10 (-0.24, 0.05)
Male	1.17 (0.49, 1.90)	26.42 (10.97, 42.88)	1.33 (0.57, 2.13)	31.09 (13.36, 49.47)	0.44* (0.32, 0.56)	0.54* (0.41, 0.67)
SDI levels						
Low SDI	0.20 (0.07, 0.33)	5.28 (1.94, 8.78)	0.32 (0.12, 0.52)	8.17 (3.23, 13.20)	1.57* (1.48, 1.66)	1.43* (1.35, 1.51)
Low-middle SDI	0.21 (0.08, 0.33)	5.52 (2.10, 8.81)	0.45 (0.19, 0.71)	11.87 (5.00, 18.73)	2.53* (2.41, 2.66)	2.52* (2.41, 2.63)
Middle SDI	0.43 (0.16, 0.70)	11.03 (4.10, 18.13)	0.82 (0.35, 1.32)	21.01 (8.93, 33.45)	2.13* (2.01, 2.26)	2.10* (1.98, 2.23)
High-middle SDI	1.44 (0.61, 2.33)	34.20 (14.56, 55.28)	1.67 (0.72, 2.66)	39.23 (16.94, 62.34)	0.52* (0.31, 0.73)	0.46* (0.22, 0.70)
High SDI	1.96 (0.83, 3.19)	44.94 (19.27, 72.19)	1.68 (0.73, 2.66)	40.00 (17.48, 62.93)	-0.52* (-0.67, -0.38)	-0.39* (-0.55, -0.24)

Abbreviations: *UI*, uncertainty interval; *CI*, confidence interval; ASMR, age-standardized mortality rate; ASDR, age-standardized disability-adjusted life-year rate; AAPC, average annual percentage change; SDI, socio-demographic index; ∗ $P < 0.05$

Results

Burden at the global level

Globally, CRC due to metabolic risks caused 181,689 (95% UI: 85,383 to 283,351) deaths in 2021, which was 2.47-fold higher than 73,443 (95% UI: 33,719 to 115,437) in 1990. Over the past 32 years, the ASMR attributable to high FPG lightly increased (AAPC = 0.31 [95% CI: 0.19, 0.43]), while the trend of ASMR attributable to high BMI was not statistically significant. Similarly, the ASDRs attributable to high FPG and high BMI lightly increased (FPG: AAPC = 0.31 [95% CI: 0.19, 0.43]; BMI: AAPC = 0.22 [95% CI: 0.09, 0.36]) (Tables 1 and 2). For males, both ASMRs and the ASDRs attributable to high FPG and high BMI all showed increasing trends, while the increasing trend was only observed in the ASMR attributable to high BMI for females (Fig. 1).

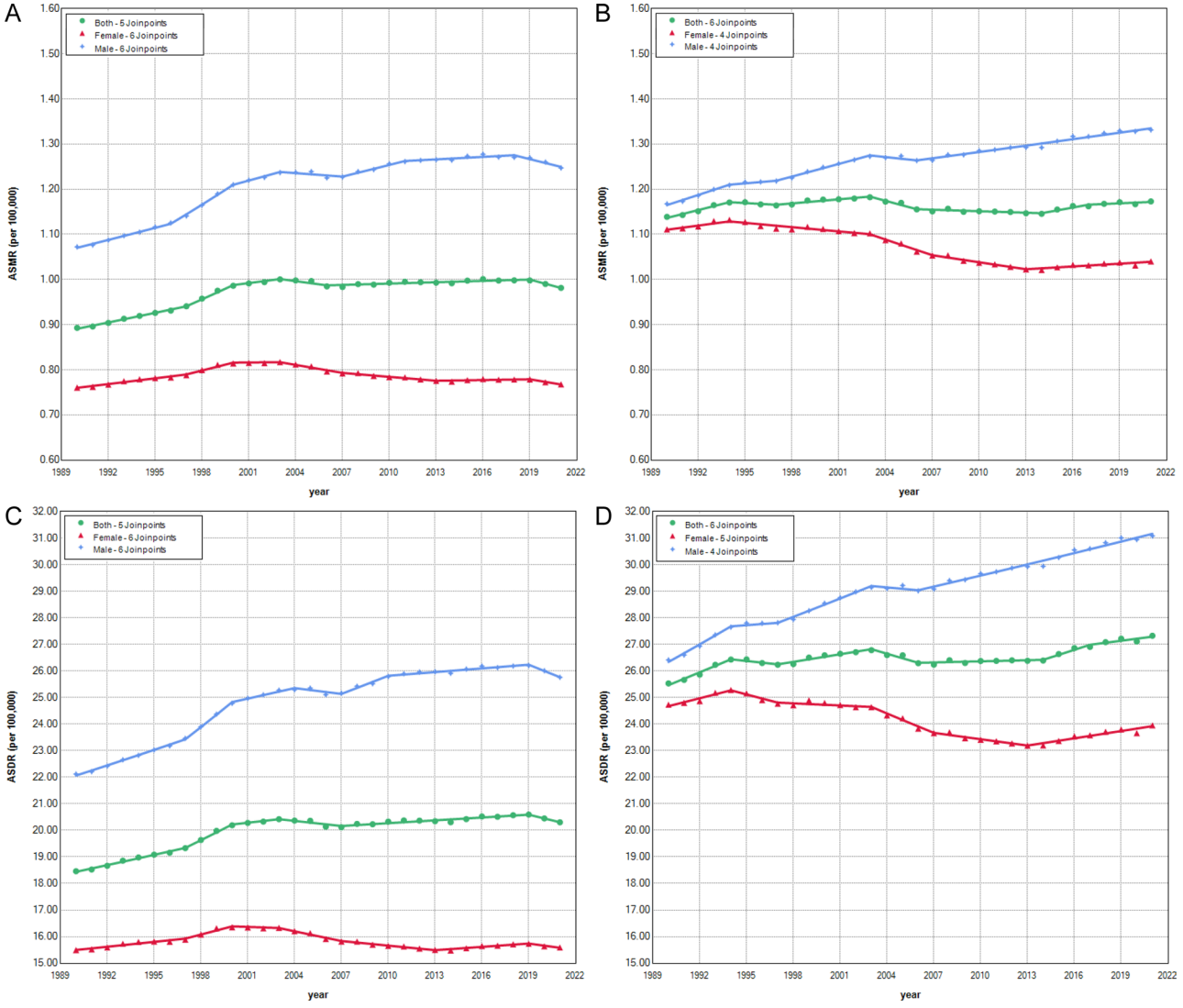

Fig. 1 Global trends of ASMR and ASDR for CRC attributable to metabolic risk factors by sex from 1990 to 2021. (**A**): Global trends in ASMR of CRC attributable to high FPG. (**B**): Global trends in ASMR of CRC attributable to high BMI. (**C**): Global trends in ASDR of CRC attributable to high FPG. (**D**): Global trends in ASDR of CRC attributable to high BMI. Abbreviations: CRC, colorectal cancer; ASMR, age-standardized mortality rate; ASDR, age-standardized DALY rate; DALY, disability-adjusted life year; FPG, fasting plasma glucose; BMI, body-mass index; $*P < 0.05$

In 2021, more males under 85 years of age died from CRC due to high FPG compared to females, and more males under 80 years of age succumbed to CRC due to high BMI than females among those years of age.

Mortality rates exhibited a positive correlation with age, with people over 95 years had the highest rates for both sexes. Mortality rates for CRC due to high FPG were greater in males than in females in all age groups, while mortality rates due to high BMI were higher in females than in males aged over 95 years (Fig. 2).

Burden at the regional and national levels

Among the 21 GBD regions, High-income North America and North Africa and Middle East had the highest proportion of CRC deaths and DALYs attributable to metabolic risk factors in 2021(Fig. 3).

In 2021, the Central Europe recorded the highest ASMR of CRC attributable to high FPG (ASMR = 2.16/100,000 [95% UI: 1.11, 3.25]), and the lowest ASMR occurred in South Asia (ASMR = 0.39/100,000 [95% UI: 0.19, 0.59]) (Supplementary Table S1). Regarding ASMR of CRC attributable to high BMI, Central Europe had the highest rate (ASMR = 3.03/100,000 [95% UI: 1.35, 4.85]), which was nearly 15 times higher than in South Asia (ASMR = 0.20/100,000 [95% UI: 0.08, 0.32]) (Supplementary Table S2). The highest ASDR of CRC attributable to high FPG and high BMI also occurred in Central Europe.

The Andean Latin America was observed the highest increase in ASMR of CRC attributable to high FPG

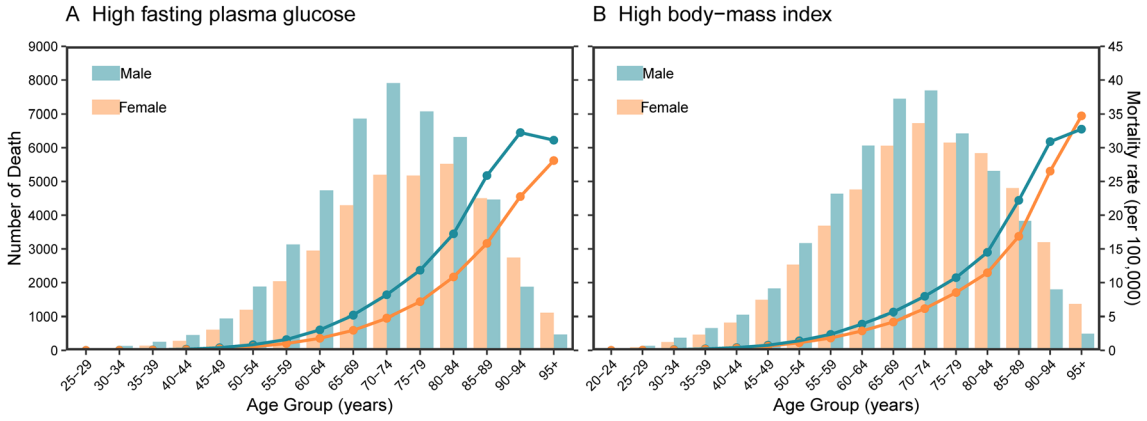

Fig. 2 Age-specific deaths and mortality rates of global colorectal cancer attributable to metabolic risk factors by sex and age in 2021. (**A**): Age-specific deaths and mortality rates of global colorectal cancer attributable to high FPG. (**B**): Age-specific deaths and mortality rates of global colorectal cancer attributable to high BMI. Abbreviations: FPG, fasting plasma glucose; BMI, body-mass index

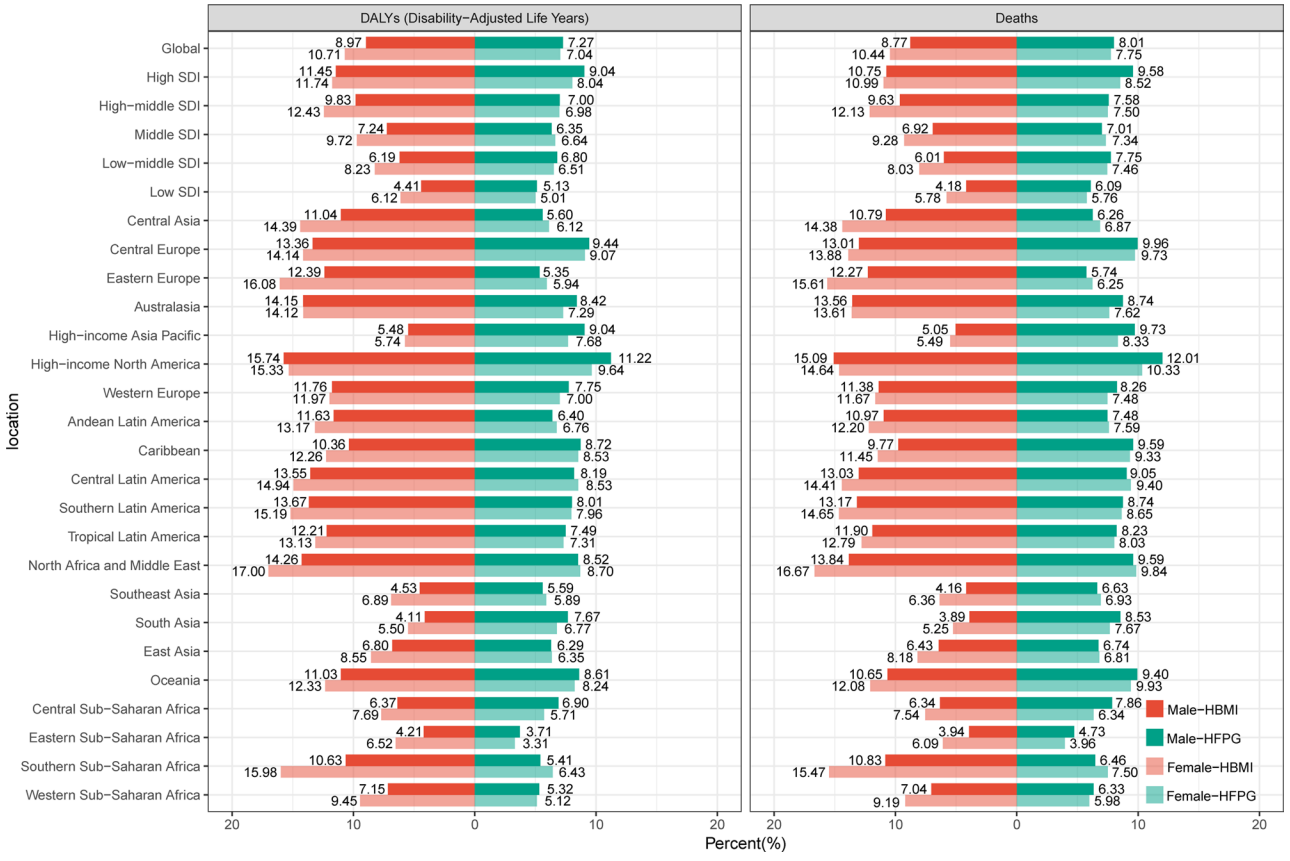

Fig. 3 The proportion of colorectal cancer deaths and DALYs attributable to metabolic risk factors globally by region and sex in 2021. Abbreviations: SDI, sociodemographic index; DALYs, disability-adjusted life years; HBMI, high body-mass index; HFPG, high fasting plasma glucose

with an AAPC of 2.16 (95% CI: 1.74, 2.57), followed by Southern Sub-Saharan Africa (AAPC = 1.95 [95% CI: 1.62, 2.27]). Australasia experienced the most significant decrease in ASMR (AAPC = − 0.63 [95% CI: −0.79, − 0.46]). Similar trends were observed for ASDR, with Andean Latin America and Southern Sub-Saharan Africa showing the most significant increases and Australasia showing the most significant decrease (Supplementary Table S1).

Southeast Asia exhibited the most significant increase in ASMR of CRC attributable to high BMI (AAPC = 3.01 [95% CI: 2.97, 3.06]), followed by South Asia (AAPC = 2.82 [95% CI: 2.65, 2.99]). Australasia had the most significant decrease (AAPC = − 0.60 [95% CI:

−0.79, − 0.41]). The trends of ASDR in these GBD regions were similar to that of ASMR (Supplementary Table S2).

Among countries, the burden of CRC attributable to high FPG showed wide range of variation in 2021. The ASMR ranged from 0.19/100,000 in Malawi to 2.62/100,000 in Barbados and the ASDR ranged from 3.84/100,000 in Mozambique to 53.69/100,000 in Hungary (Supplementary Table S3, Fig. S1A and S2A). Most countries showed increasing trends in ASMR and ASDR for CRC due to high FPG, with notable rises in Cabo Verde, Egypt, and Lesotho.

Regarding CRC burden attributable to high BMI, ASMR ranged from 0.12/100,000 in Bangladesh to 3.79/100,000 in Hungary, and ASDR ranged from 3.41/100,000 in Bangladesh to 92.03/100,000 in Hungary (Supplementary Table S4, Fig. S1B and S2B). Cabo Verde, Viet Nam, and Lesotho experienced the greatest increases in ASMR, and similar trends were also observed in the ASDR.

Burden at different SDI levels

In terms of SDI levels, the high-SDI regions showed the greatest proportion of deaths and DALYs for CRC due to high metabolic risks (Fig. 3). The ASMR and ASDR of CRC due to high metabolic risks consistently remained highest in high-SDI regions from 1990 to 2021 (Fig. 4).

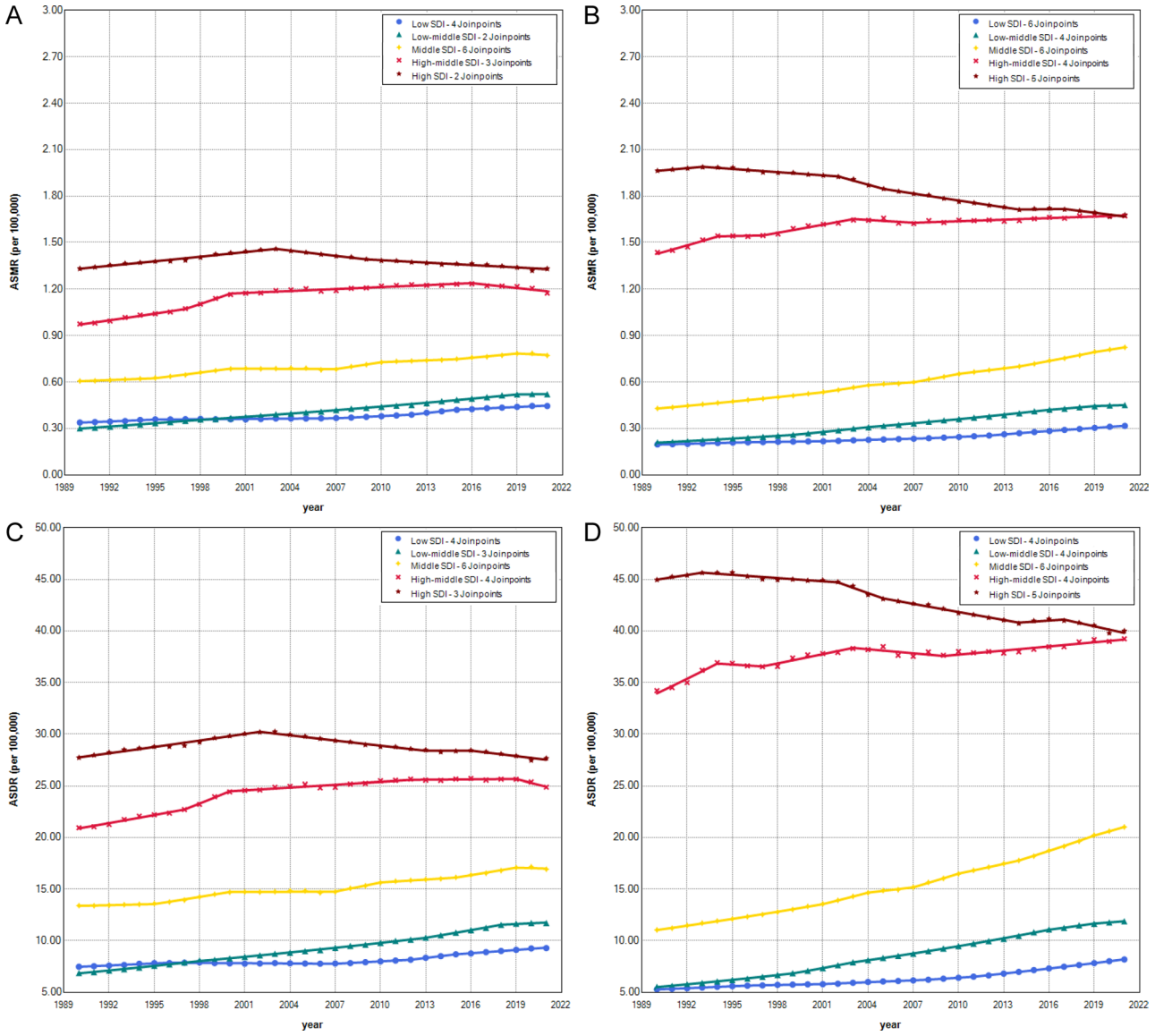

Fig. 4 Global trends of ASMR and ASDR for CRC attributable to metabolic risk factors by SDI from 1990 to 2021. (**A**): Global trends in ASMR of CRC attributable to high FPG. (**B**): Global trends in ASMR of CRC attributable to high BMI. (**C**): Global trends in ASDR of CRC attributable to high FPG. (**D**): Global trends in ASDR of CRC attributable to high BMI. Abbreviations: CRC, colorectal cancer; ASMR, age-standardized mortality rate; ASDR, age-standardized DALY rate; SDI, sociodemographic index; DALY, disability-adjusted life year; FPG, fasting plasma glucose; BMI, body-mass index; $*P < 0.05$

Since 1990, both ASMR and ASDR of CRC due to high metabolic risks have been significantly increased across all SDI regions except for high-SDI regions, where the largest increases were observed in low-middle SDI regions (Tables 1 and 2). In high-SDI regions, only ASMR and ASDR for CRC attributed to high BMI showed significant decreases, with AAPCs of −0.52 (95% CI: −0.67, −0.38) and −0.39 (95% CI: −0.55, −0.24), respectively.

Furthermore, ASMRs due to high metabolic risks of each region from 1990 to 2021 exhibited relationships with SDI, which showed downward trends until SDI value reached about 0.75. Similar patterns were noted in the relationship between SDI and ASDRs. The correlation coefficients for ASMR and ASDR due to high FPG were about 0.803 ($P<0.01$) and 0.812 ($P<0.01$), respectively. For high BMI, the coefficients were about 0.752 ($P<0.01$) for ASMR and 0.756 ($P<0.01$) for ASDR. In Central Europe and Southern Latin America, ASMR and ASDR for CRC due to high metabolic risks were much higher than expected (Fig. 5). For countries, the burden of CRC due to high FPG was notably high in Barbados and Hungary. Hungary and Slovakia exhibited a high burden of CRC due to high BMI (Supplementary Fig. S3 and S4).

Projection of mortality to 2046

Over the next 25 years, the ASMR of CRC due to high FPG is expected to decline slightly from 1.247 in 2021 to 1.241 by 2046 in males, and increase slightly from 0.768 to 0.783 in females. The ASMR of CRC due to high BMI was projected to rise from 1.331 in 2021 to 1.398 by 2046 in males, and from 1.040 to 1.129 in females (Supplementary Tables S5 and S6). Throughout this period, the ASMR of CRC due to high metabolic risks in males will remain higher compared to females, while the deaths of CRC due to high BMI was projected to converge between sexes (Fig. 6).

Discussion

Based on GBD 2021, this study assessed the global burden and time change of CRC due to high metabolic risks by sex, age groups, regions, countries and SDI levels from 1990 to 2021 and predicted the burden from 2022 to 2046. We found that CRC burden due to high metabolic risks has risen steadily from 1990 to 2021. Both

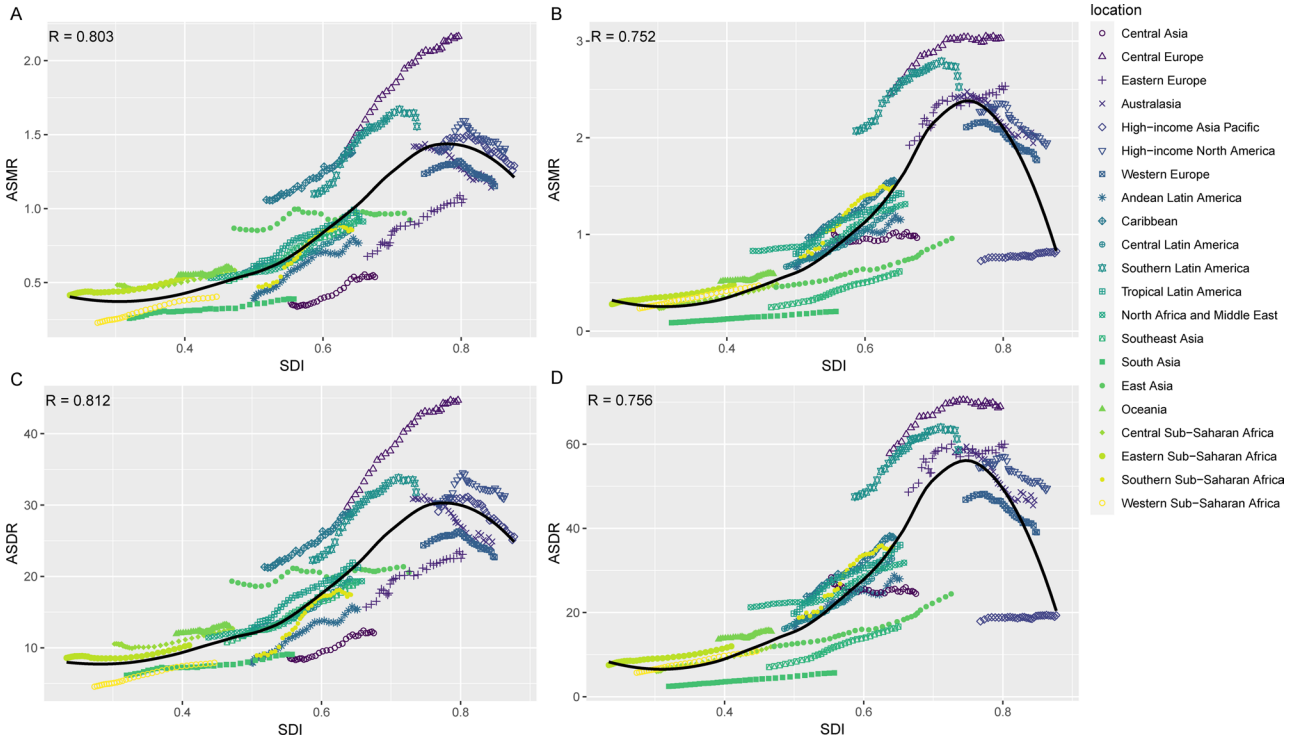

Fig. 5 The relationship between age-standardized rates of CRC attributable to metabolic risks and SDI in 21 GBD regions from 1990 to 2021. (**A**): The relationship between ASMRs attributable to high FPG and SDI and the Pearson correlation coefficient was 0.803 ($P<0.01$). (**B**): The relationship between ASMRs attributable to high BMI and SDI and the Pearson correlation coefficient was 0.752 ($P<0.01$). (**C**): The relationship between ASDRs attributable to high FPG and SDI and the Pearson correlation coefficient was 0.812 ($P<0.01$). (**D**): The relationship between ASDRs attributable to high BMI and SDI and the Pearson correlation coefficient was 0.756 ($P<0.01$). The solid line shows the expected value between the entire SDI between ASMR and ASDR. For each region, points from left to right depict estimates from each year from 1990 to 2021. Abbreviations: ASMR, age-standardized mortality rate; ASDR, age-standardized DALY rate; DALY, disability-adjusted life year; CRC, colorectal cancer; SDI, socio-demographic index; GBD, the Global Burden of Disease; FPG, fasting plasma glucose; BMI, body-mass index

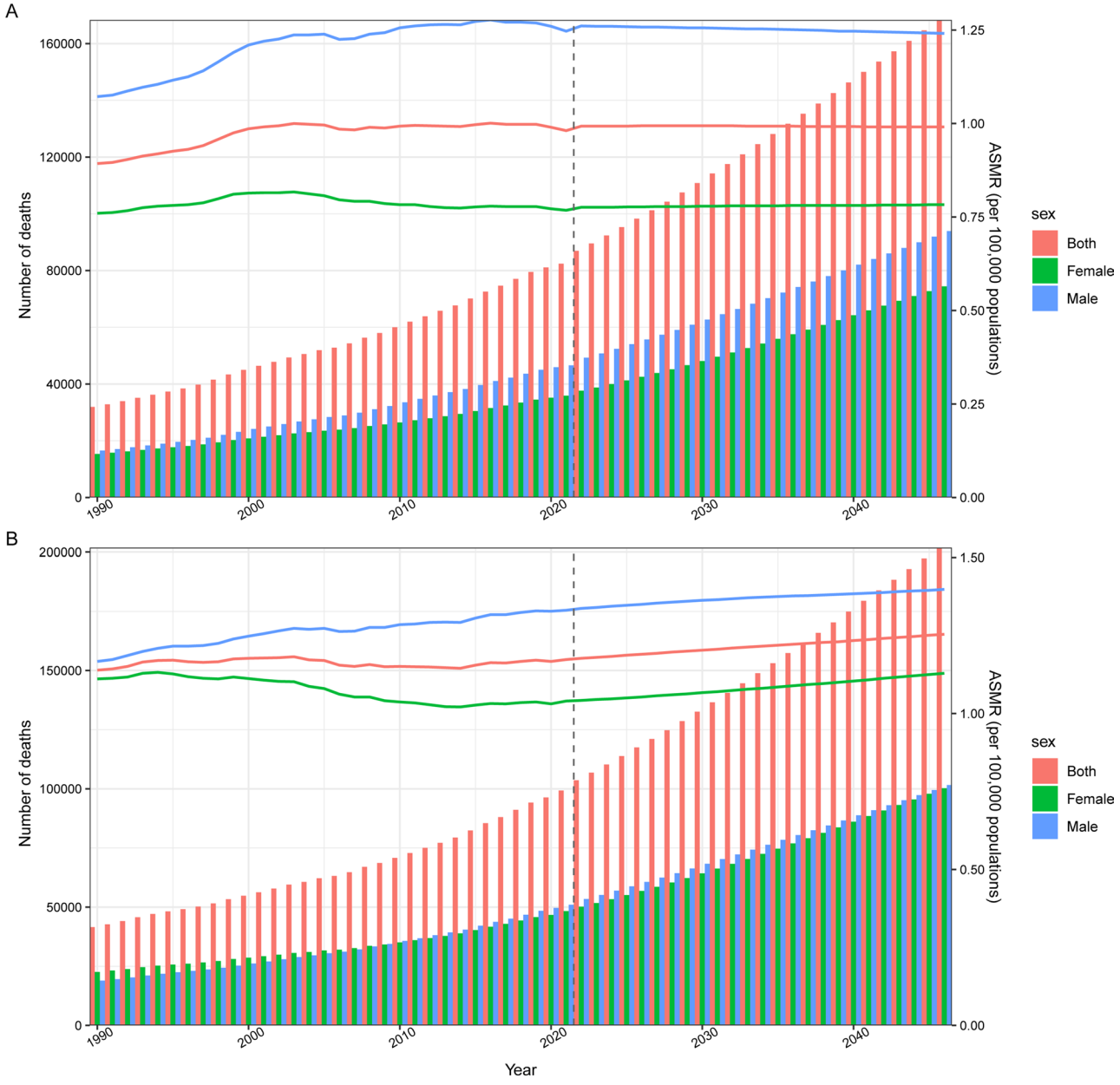

Fig. 6 The observed and predicted global burden of colorectal cancer attributable to metabolic risk factors by sex from 1990 to 2046. (**A**): The observed and predicted deaths and ASMR of colorectal cancer attributable to high FPG. (**B**): The observed and predicted deaths and ASMR of colorectal cancer attributable to high FPG. Abbreviations: ASMR, age-standardized mortality rate; FPG, fasting plasma glucose; BMI, body-mass index

the number of deaths and DALYs increased and were expected to continue increasing globally through 2046. We speculate that this increase is partly attributable to population growth, aging [23], and improvements in screening methods which have enhanced detection rates [24]. Metabolic factors remain a major contributor to the high global burden of CRC. To reduce CRC related to metabolic risks, greater efforts are needed to control metabolic disorders such as obesity and diabetes [25, 26].

Our study revealed a higher burden of CRC attributed to high metabolic risks in males than in females, with significant upward trends observed in males compared to females. Research indicates that BMI has a stronger correlation with CRC risk in males [27]. From 2000 to 2019, there was an annual increase of 0.48% in ASDR related to obesity, with a more pronounced rise observed in males (0.74%) compared to females (0.25%) [28]. In addition, the global age-standardized prevalence of diabetes rose by 90.5% from 1990 to 2021. This prevalence was notably higher in males than in females (6.5%vs 5.8%), resulting in a male-to-female ratio of 1.14 [29]. Therefore, diabetes

and high BMI will further increase the burden of CRC, especially in males.

The burden of CRC attributed to high metabolic risks increased with age, reaching its peak among individuals aged 90 years and older. CRC is primarily a disease affecting older individuals, with increasing age being one of the non-modifiable risk factors. According to a study, individuals over the age of 50 face an elevated risk of CRC progression attributed to age-related cholesterol accumulation within tissue and the subsequent decline in squalene epoxidase levels [30]. Additionally, aging in adults leads to alterations in fat distribution, which may further contribute to the increased risk of type 2 diabetes [31].

We found that High-income North America and North Africa and Middle East (NAME) exhibit the highest proportion of CRC burden. The increased burden of CRC in high-income countries may be due to an increased metabolic risks related lifestyle, which are more prevalent in developed countries [32]. Unlike the global level [16], most high-income countries in NAME region were unable to control the burden of CRC, which seems to be caused by unfavorable behavioral changes in lifestyle resulting from industrialization and urbanization [33]. Currently, the region with the highest burden of CRC attributed to high metabolic risks is Central Europe, mainly in Hungary, which may be related to economic level and lifestyle [34]. Barbados has the heaviest burden of high FPG, which may be associated with higher consumption of sugar-sweetened beverages and diabetes. And sugar-sweetened beverages (SSB) were associated to the increasing risk of diabetes [35].

Moreover, Andean Latin America and Southern Sub-Saharan Africa exhibited the most significant rise in the burden of CRC attributable to high FPG. A study indicated that Latin American countries exhibit high consumption rates of both total and added sugars [36]. A report on CRC survival in sub-Saharan Africa shows that 5-year survival rate of CRC patients was poor and the mortality rates were 3 times higher than in developed countries [37]. Countries experiencing the highest increases are Cabo Verde, Egypt, and Lesotho. Therefore, the lifestyle choices of residents, the differences in the level of economic development in different regions, urbanization and industrialization may all have an impact on the CRC attributed to high metabolic risks. It is crucial to allocate resources judiciously, enhance the quality of medical care, reduce healthcare costs, and strive for equitable healthcare access in the future.

Southeast Asia and South Asia showed the most significant increase in CRC burden attributable to high BMI. That aligns with a previous study: The increase in BMI has accelerated in East and South Asia among both sexes, and in Southeast Asia particularly among boys [38]. And the countries experiencing the highest increases are Cabo Verde, Viet Nam, and Lesotho.

Varied trends in ASRs across regions and countries with differing SDI levels reflect geographic disparities and variations in the development of CRC burden. And a positive correlation was identified between SDI and ASRs. The ASMR and ASDR of CRC due to high metabolic risks were consistently highest in high-SDI regions. The prevalence of obesity and diabetes is reported to be higher in high-income countries than in low-income countries [39, 40]. Despite the abundant medical resources in high SDI regions, the CRC burden remains relatively high, which may be related to the high prevalence of lifestyle and metabolic risk factors [41]. Urbanization brings about changes in lifestyle, such as high-calorie diets, lack of exercise, and excessive consumption of sugary drinks, all of which are associated with an increase in metabolic risk factors. In high SDI regions, where urbanization levels are higher, the prevalence of metabolic risk factors is also higher, which may be one of the reasons for the higher CRC burden in these areas.

Additionally, we observed a rapid increase in the burden of CRC in low-SDI, low-middle-SDI, and middle-SDI regions. This rise may be linked to the absence of well-established prevention and treatment systems in these regions [42]. The disparities in disease burden reveal deep-rooted factors related to gender, regional differences, and socioeconomic status, with obesity-related mortality rates rising with the level of social development [43]. Studies have shown that a healthy diet and regular exercise can significantly reduce the incidence of obesity and diabetes, thereby reducing the burden of CRC. Therefore, conducting educational activities targeting diet and exercise is an important strategy for reducing the global burden of CRC.

Furthermore, with the accelerating pace of our lives and the increasing social pressures, excessive food consumption and sedentary behaviors are more frequent. The proportion of males and females with high BMI exceeded 30% from 1980 to 2013 [39]. Early-onset type 2 diabetes is also emerging as a significant global health issue for adolescents and young adults [44]. Therefore, more effective strategies and interventions are urgently needed in the future to reduce cancer burden caused by metabolic disorders.

This study has several limitations. Firstly, because of the modeling of unavailable data using the GBD data inevitably introduced bias, cohort studies are needed to use multivariate regression models to more accurately assess the relationship between metabolic factors and CRC. Secondly, due to a lack of data, we were unable to determine the burden of CRC subtypes based on tumor location (proximal colon, distal colon, and rectum). Thirdly, the data in our study came from different regions and

countries, which varied in quality and may introduce bias in the collection and data processing. By improving data quality, controlling for confounding factors, adjusting model assumptions, and implementing targeted interventions, biases can be effectively reduced, and the reliability of disease burden estimates can be enhanced. Fourthly, the Pearson's correlation coefficient has inability to infer causality and control the interference of confounding factors. Finally, the lack of adequate health services and incomplete statistics in countries with low SDI may lead to the underestimation of the cancer burden.

Conclusion

Globally, CRC burden attributable to high metabolic risk factors increased annually, and was predicted to continue to increase slightly by 2046. The burden of males was higher, with increasing trends. High-SDI regions had the largest proportion of burden, but it was increasing in low and low-middle SDI regions. The CRC was expected to place a heavier burden on global health in the future due to population growth and aging and an increase in metabolic related diseases. It is necessary to develop strategies to reduce the prevalence of high BMI and diabetes to decrease the burden of CRC caused by metabolic factors.

Abbreviations

CRC	Colorectal cancer
DALY	Disability-adjusted life year
SDI	Sociodemographic index
FPG	Fasting plasma glucose
BMI	Body mass index
ASMR	Age-standardized mortality rate
ASDR	Age-standardized rate of DALY
AAPC	Average annual percent changes
GBD	Global Burden of Disease
ICD	International Classification of Diseases
UI	Uncertainty interval
CI	Confidence Interval
LOESS	Locally weighted regression
NAME	North America and North Africa and Middle East

Supplementary Information

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Supplementary Material 1

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Author contributions

PW and JZ provided the design of the study and manuscript review. XZ conducted the interpretation, statistical analysis and manuscript preparation. ZX, LS and QY conducted study concepts, quality control of data. XZ and HY conducted data analysis and interpretation. HL, YZ, YL, ZZ, and ML conducted data acquisition and manuscript editing. All authors read and approved the final manuscript.

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Data availability

Data is provided within the manuscript or supplementary information files. The data that support the findings of this study are openly available at 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.

Author details

[1]Department of Pharmacy, the First Affiliated Hospital of Zhengzhou University, Zhengzhou, Henan Province 450052, China
[2]College of Public Health, Zhengzhou University, Zhengzhou, Henan Province 450001, China
[3]Henan Key Laboratory of Tumor Epidemiology and State Key Laboratory of Esophageal Cancer Prevention & Treatment, Zhengzhou University, Zhengzhou, Henan Province 450052, China
[4]Department of Science and Technology of Henan Province, Zhengzhou, Henan Province 450008, China
[5]Prenatal Diagnosis Center, The Third Affiliated Hospital of Zhengzhou University/Maternal and Child Health Hospital of Henan Province, Zhengzhou, Henan Province 450052, China

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