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Global burden and cross-country health inequalities of early-onset colorectal cancer and its risk factors from 1990 to 2021 and its projection until 2036

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Abstract

Purpose To explore the worldwide, regional, and country-specific burden of early-onset colorectal cancer (EO-CRC) and identify its associated risk factors between 1990 and 2021, and to project its incidence and mortality rates for 2036.

Methods We acquired data on EO-CRC categorized by gender, socio-demographic index (SDI), and risk factors based on the Global Burden of Disease (GBD) Study 2021. Joinpoint regression analysis was utilized to explore the variation in disease burden. The autoregressive integrated moving average (ARIMA) model was performed to forecast the disease burden up to 2036.

Results Globally, the incidence rate, prevalence rate, mortality rate, and disability-adjusted life years (DALYs) rate of EO-CRC were estimated at 5.37 (95%UI: 4.91 to 5.86)/100,000, 34 (95%UI: 30.96 to 37.35)/100,000, 2.01 (95%UI: 1.84 to 2.19)/100,000, and 101.37 (95%: 92.85 to 110.18)/100,000 in 2021. The prevalence and incidence rates of EO-CRC showed an ascending trajectory, whilst the DALYs and mortality rates demonstrated a downward trajectory between 1990 to 2021. The high-middle SDI regions and East Asia exhibited the highest EO-CRC burden among the five SDI regions and 21 GBD regions respectively. A low-whole-grains diet was the chief risk factor contributing to EO-CRC. It was predicted that the age-standardized rate (ASR) of EO-CRC incidence would increase by 5.56%, while the ASR of mortality would decrease by 13.9% globally until 2036.

Conclusion The current and future global burden of EO-CRC is heavy and varies significantly across different regions and countries.

Keywords Early-onset colorectal cancer, Global burden of disease, Disability-adjusted life years

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Introduction

Gastrointestinal cancers is a collective term for common malignant tumors of the digestive system, including esophageal cancer, gastric cancer, liver cancer, colorectal cancer (CRC), pancreatic cancer, and gallbladder cancer. These cancers account for one-fourth of all global cancer cases and one-third of cancer-related deaths, making them one of the major global health issues [1]. It is well known that gastrointestinal cancers primarily affect the elderly population aged 65 and above. However, recent data show a significant increase in the incidence of gastrointestinal cancers among individuals under 50 years old, including esophageal, gastric, colorectal, pancreatic, and biliary tract cancers, collectively referred to as early-onset gastrointestinal cancers (EO-GICs) [2–4]. EO-GICs often exhibit poorer pathological features and prognosis compared to those occurring in older age groups. Moreover, they are more likely to be overlooked in early screening [3]. The rising incidence of these EO-GICs has emerged as a significant public health challenge.

Early-onset colorectal cancer (EO-CRC) is one of the EO-GICs that exhibiting the most significant increase in the incidences and mortality rates in the past three decades [4]. The incidence of EO-CRC is steadily rising in Europe and the United States, with projections indicating an approximate doubling by 2030 [5]. Australia has also observed a significant increase in colon cancer cases among individuals under 50 years old [6]. Furthermore, in the Caribbean and Latin American regions, CRC incidence among individuals aged 15–49 has doubled from 1990 to 2019 [7]. The Asia–Pacific region has experienced substantial growth in EO-CRC rates as well, particularly in Southeast Asia and the Western Pacific, which showed age-standardized incidence rate increases of 16.9% and 26.2%, respectively, between 2010 and 2019 [8]. East Asia had the highest incidence rate, mortality rate, and the fastest increase in EO-CRC among all GBD regions in 2019 [7].

Compared to CRC occurring in older individuals, EO-CRC is more likely to exhibit aggressive pathological features such as poorly differentiated adenocarcinoma, signet ring cell carcinoma, as well as lymphovascular and perineural invasion [9]. These characteristics pose greater challenges for treatment and result in worse treatment outcomes. The majority of young patients with CRC are diagnosed with metastasis at the time of initial diagnosis [10]. Despite receiving intensive treatment, these patients exhibited a higher recurrence rate and a lower 5-year survival rate [11]. Most EO-CRC cases are sporadic and lack a genetic or familial background, indicating that acquired factors such as diet, lifestyle, and environment may contribute significantly. It is imperative to conduct further epidemiological studies and research into risk factors in order to gain a better understanding of the underlying mechanisms and develop effective prevention strategies [4].

Although some previous studies have examined the global burden of EO-CRC, the data they used was obtained from the GBD Study 2019, which was published two years ago. Previous studies often focused on a specific population in certain regions or within a certain age range [12–15]. The new data from the GBD Study 2021 was released recently, and there is currently no comprehensive report on the global disease burden of EO-CRC based on this data. Consequently, we conducted this analysis of the global EO-CRC burden, including its distribution across various countries and regions, between 1990 and 2021 [16]. Moreover, we investigated potential risk factors associated with EO-CRC. Additionally, an autoregressive integrated moving average (ARIMA) model was employed to forecast the burden over the next fifteen years. The findings of our analysis will play a crucial role in informing decision-makers and the public, helping formulate evidence-based public policies, efficiently allocate resources for cancer prevention, and reduce exposure to EO-CRC risk factors.

Methods

Date source

A comprehensive evaluation of the negative health impacts associated with 371 diseases, injuries, and disabilities, as well as 88 risk factors, was presented in the GBD Study 2021. The study covers 204 nations and territories, utilizing up-to-date epidemiological data and improved standardized methodologies [16, 17]. The data for this investigation were drawn from the GBD Study 2021 (https://vizhub.healthdata.org/gbd-results/).

Disease burden of EO-CRC

In this research, we acquired and examined GBD 2021 data regarding the prevalence, incidence, DALYs, and mortality of EO-CRC (age 15–49 years) on a global scale as well as at regional and national levels. The 95% uncertainty intervals (UIs) of all the estimates were presented. Moreover, the prevalence, incidence, disability-adjusted life years (DALYs), and mortality rates were all reported per 100,000 persons per year. Comprehensive explanations regarding the methodologies employed in the GBD Study 2021 have been provided by previous research [16–18].

Socio-demographic index (SDI)

Furthermore, the investigation utilized the SDI, which assesses socio-demographic development by considering factors such as income, educational attainment, and fertility patterns in a specific region or country. Based on the calculated SDI score, regions and countries are classified into five distinct quintiles: high SDI, high-middle SDI, middle SDI, low-middle SDI, and low SDI. The SDI quintile categories of 204 countries and territories are shown in Table S1 [18].

Joinpoint regression analysis

We utilized Joinpoint Version 5.1.0, software provided by the National Cancer Institute of the United States, to conduct joinpoint regression analysis in order to evaluate trends in the disease burden of EO-CRC. This software analyzes data trends over time by fitting multiple line segments using a logarithmic scale. Average Annual Percentage Changes (AAPCs) and Annual Percentage Change (APC) were used to evaluate the trends in variation [19]. The 95% confidence interval (CI) was determined using a linear regression model. An increase in age-standardized rate (ASR) is associated with a positive AAPC value and its corresponding 95% CI above zero. Conversely, a decrease in ASR is associated with a negative AAPC value and its corresponding 95% CI below zero [20].

Risk factors

The GBD Study 2021 provides access to 11 risk factors associated with EO-CRC, which are broadly classified into three primary categories: dietary-related factors, metabolic factors, and behavioral factors. Dietary-related factors included a low-calcium diet, low-fiber diet, low-milk diet, low-whole-grain diet, high-processed-meat diet, and high-red-meat diet. Metabolic factors included high fasting plasma glucose and high body mass index (BMI). Behavioral factors included low physical activity, high alcohol use, and smoking [17, 21]. Explanations and methods for estimating the contribution of these risk factors to the EO-CRC burden have been extensively discussed in prior scholarly works [17, 22]. In summary, the GBD Study 2021 utilized an established risk assessment framework to calculate the proportion of the EO-CRC burden associated with each individual risk factor.

Prediction

The ARIMA model is composed of the autoregressive model and the moving average model, which are combined to form the ARIMA model. The fundamental presumption is that data sequences are stochastic variables dependent on time, with their autocorrelation describable through the ARIMA model, enabling the prediction of future values based on preceding ones. The expression of the equation is as follows: $Y_t = \phi_1 Y_{t-1} + \phi_2 Y_{t-2} + \ldots + \phi_p Y_{t-p} + e_t - \theta_1 e_{t-1} - \ldots - \theta_q e_{t-q}$. In this equation, $(\phi_1 Y_{t-1} + \phi_2 Y_{t-2} + \ldots + \phi_p Y_{t-p} + e_t)$ is the component of the autoregressive model, while $(e_t - \theta_1 e_{t-1} - \ldots - \theta_q e_{t-q})$ represents the moving average part. The value observed during period (*t-p*) is represented by (Y_{t-p}), and p and q represent the model orders of the autoregressive and moving average components, with e_t representing the unpredictable deviation occurring during time period t [23]. The ARIMA model necessitates that the time series be a stochastic sequence with a mean of zero and demonstrate stationarity. We employed R version 4.3.2 for all statistical analyses and graphical representations.

Results

Global burden of EO-CRC

Worldwide, from 1990 to 2021, the EO-CRC incidence shows a marked upward trajectory (Fig. 1a, Table 1). The incidence cases increased from 107,310 (95% UI: 99,971 to 114,185) in 1990 to 211,890 (95% UI: 193,832 to 231,272) in 2021; the rate of incidence grew from 3.96 (95% UI: 3.69 to 4.21)/100,000 in 1990 to 5.37 (95% UI: 4.91 to 5.86)/100,000 in 2021, with an AAPC of 0.99% (95% CI: 0.9% to 1.07%), while the APC from 2019 to 2021 was -0.5%. From the perspective of sex, in 2021, the incidence cases and incidence rate for males were 126,666 (110,037 to 144,645) and 6.33 (5.5 to 7.23)/100,000, respectively, which were higher than those for females, 85,224 (77,873 to 93,407) and 4.37 (4 to 4.79)/100,000, respectively. The AAPCs for males were 1.31% (95% CI: 1.18% to 1.45%), which was greater than that for females, 0.57% (95% CI: 0.42% to 0.72%).

The EO-CRC prevalence cases increased from 585,832 (95% UI: 551,999 to 618,952) in 1990 to 1,342,468 (95% UI: 1,222,335 to 1,474,707) in 2021, with the prevalence rate increasing from 21.61 (95% UI: 20.34 to 22.84)/100,000 in 1990 to 34 (95% UI: 30.96 to 37.35)/100,000 in 2021. The AAPC was 1.47% (95% CI: 1.33% to 1.61%) during 1990 to 2021, while the APC was -0.54% during 2019 to 2021. By sex, in 2021, the prevalence cases and prevalence rate for males were 803,681 (95% UI: 698,587 to 923,434) and 40.19 (95% UI: 34.93 to 46.18)/100,000, respectively, which were higher than those for females, 538,787 (95% UI: 492,036 to 591,352) and 27.65 (95% UI: 25.25 to 30.34)/100,000. The AAPC of the prevalence rate for males was 1.82% (95% CI: 1.6% to 2.04%) during 1990 to 2021, which was higher than that for females, 1.02% (95% CI: 0.9% to 1.15%) (Fig. 1b and Table 2).

As illustrated in Fig. 1c and Table 3, the number of deaths due to EO-CRC increased from 59,232 (95% UI: 54,391 to 63,963) in 1990 to 79,504 (95% UI: 72,699 to 86,539) in 2021; nevertheless, the mortality rate declined from 2.19 (95% UI: 2.01 to 2.36)/100,000 in 1990 to 2.01 (95% UI: 1.84 to 2.19)/100,000 in 2021, with an AAPC of -0.23% (95% CI: -0.34% to -0.12%). Additionally, the number of deaths and the mortality rate for males were 47,359 (95% UI: 41,411 to 53,364) and 2.37 (95% UI: 2.07 to 2.67)/100,000, respectively, which were higher than those for females, 32,145 (95% UI: 29,391 to 35,098) and 1.65 (95% UI: 1.51 to 1.8)/100,000. It is worth noting that the AAPC for males was significantly larger than that for females, with an opposite trend (males' AAPC: 0.06%,

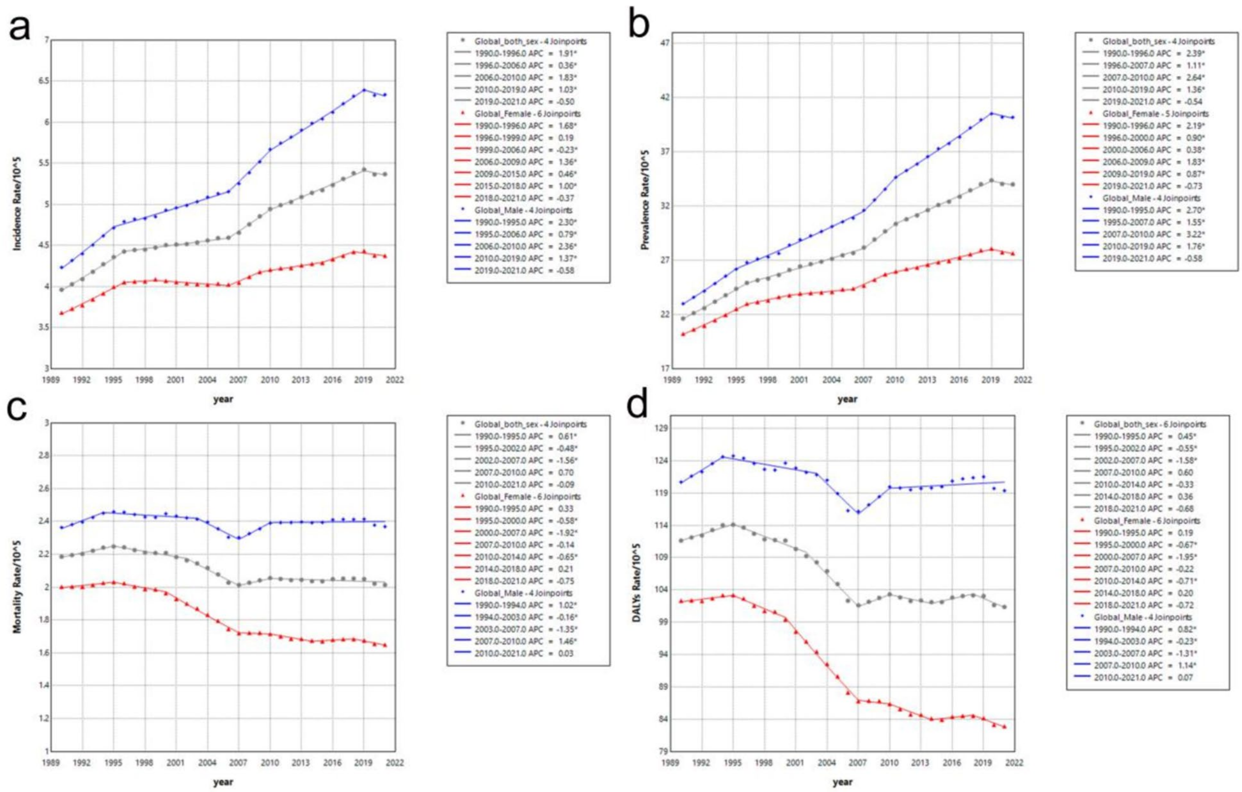

Fig. 1 Trends in global incidence, prevalence, mortality, and DALY rates of early-onset colorectal cancer by sex, from 1990 to 2021. Incidence rate (**a**) Prevalence rate (**b**) Mortality rate (**c**) DALYs rate (**d**). *DALYs* disability-adjusted life years

95% CI: -0.08% to 0.19%; the females' AAPC: -0.62%, 95% CI: -0.78% to -0.46%).

Worldwide, the DALYs attributed to EO-CRC increased from 3,026,077 (95% UI: 2,769,994 to 3,263,327) in 1990 to 4,002,756 (95% UI: 3,666,300 to 4,350,056) in 2021, while the DALYs rate decreased from 111.64 (95% UI: 102.2 to 120.39)/100,000 in 1990 to 101.37 (95% UI: 92.85 to 110.18)/100,000 in 2021. The AAPC was -0.31% (95% CI: -0.46% to -0.16%). From a gender perspective, the DALYs and DALYs rate for males were significantly higher than those for females (Fig. 1d and Table 4).

EO-CRC burden by regions

As exhibited in Tables 1, 2, 3, 4 and Fig. 2, the high-middle SDI region exhibited the heaviest EO-CRC burden among all SDI regions, while the low SDI region showed the lightest burden. Specifically, the high-middle SDI region exhibited the maximal prevalence rate (2.72/100,000, 95% UI: 2.56 to 2.88), mortality rate (3.09/100,000, 95% UI: 2.72 to 3.53), and DALYs rate (155.3/100,000, 95% UI: 136.66 to 177.18); whereas the low SDI region exhibited the minimal incidence rate (1.3/100,000, 95% UI: 1.12 to 1.49), prevalence rate (5.86/100,000, 95% UI: 5.07 to 6.68), mortality rate (0.93/100,000, 95% UI: 0.8 to 1.08), DALYs rate (47.47/100,000, 95% UI: 40.89 to 55.15), AAPC for the incidence rate (-0.02%, 95% CI: -0.16 to 0.12%), and AAPC for the prevalence rate (0.35%, 95% CI: 0.2 to 0.5%). The APCs of incidence and prevalence rates in high SDI regions were -1.74% and -1.68% from 2018 to 2021 respectively.

The detailed data of EO-CRC burden in the 21 GBD regions of the world from 1990 to 2021 are shown in Tables 1, 2, 3, and 4. Notably, in 2021, East Asia exhibited the largest incidence rate (11.86/100,000, 95% UI: 9.56 to 14.45), mortality rate (3.7/100,000, 95% UI: 2.97 to 4.51), and DALYs rate (187.93/100,000, 95% UI: 151.08 to 228.06). In contrast, Western Sub-Saharan Africa showed the smallest incidence rate (0.82/100,000, 95% UI: 0.61 to 1.06), prevalence rate (3.63/100,000, 95% UI: 2.7 to 4.63), mortality rate (0.6/100,000, 95% UI: 0.45 to 0.77), and DALYs rate (30.33/100,000, 95% UI: 22.72 to 38.94). From 1990 to 2021, Central Latin America had the fastest increases in the incidence rate (3.48%, 95% CI: 3.32 to 3.64%), mortality rate (2.18%, 95% CI: 1.76 to 2.59%), prevalence rate (3.97%, 95% CI: 3.8 to 4.13%), and DALYs rate (2.07%, 95% CI: 1.72 to 2.43%) of EO-CRC. Central Asia had the lowest AAPC for the incidence rate

Table 1 Incidence of early-onset colorectal cancer in 1990 and 2021, and the AAPCs from 1990 to 2021

Location	1990		2021		AAPCs % (95%CI) 1990–2021
	Number(95% UI)	Rate per 100,000 population (95% UI)	Number(95% UI)	Rate per 100,000 population (95% UI)	
Global	107,310 (99,971 to 114,185)	3.96 (3.69 to 4.21)	211,890 (193,832 to 231,272)	5.37(4.91 to 5.86)	0.99 (0.9 to 1.07)
Sex					
Female	49,210 (44,835 to 53,755)	3.68(3.35 to 4.02)	85,224 (77,873 to 93,407)	4.37(4 to 4.79)	0.57 (0.42 to 0.72)
Male	58,100 (52,189 to 63,006)	4.23(3.8 to 4.59)	126,666 (110,037 to 144,645)	6.33(5.5 to 7.23)	1.31 (1.18 to 1.45)
SDI					
High SDI	35,483 (34,725 to 36,269)	7.7(7.53 to 7.87)	50,985 (49,341 to 52,745)	10.15(9.82 to 10.5)	0.89 (0.65 to 1.13)
High-middle SDI	31,203 (28,545 to 33,777)	5.53(5.06 to 5.98)	62,134 (54,171 to 72,026)	9.87(8.6 to 11.44)	1.96 (1.76 to 2.16)
Low SDI	2860 (2212 to 3362)	1.29(1 to 1.52)	7037 (6070 to 8090)	1.3(1.12 to 1.49)	-0.02 (-0.16 to 0.12)
Low-middle SDI	8199 (7120 to 9362)	1.49(1.29 to 1.7)	21,402 (18,752 to 24,495)	2.11(1.85 to 2.41)	1.12 (1.03 to 1.21)
Middle SDI	29,452 (25,922 to 32,914)	3.23(2.85 to 3.61)	70,157 (61,014 to 78,922)	5.59(4.86 to 6.29)	1.79 (1.66 to 1.93)
Region					
Andean Latin America	301 (258 to 349)	1.62 (1.39 to 1.87)	1031 (818 to 1283)	2.95 (2.34 to 3.67)	1.95 (1.27 to 2.63)
Australasia	937 (849 to 1032)	8.68 (7.87 to 9.57)	1660 (1419 to 1913)	11.5 (9.83 to 13.25)	0.97 (0.43 to 1.51)
Caribbean	740 (678 to 800)	4.05 (3.71 to 4.38)	1540 (1309 to 1787)	6.43 (5.47 to 7.46)	1.51 (1.2 to 1.81)
Central Asia	1065 (1022 to 1109)	3.19 (3.06 to 3.32)	1350 (1196 to 1506)	2.77 (2.45 to 3.09)	-0.28 (-0.83 to 0.27)
Central Europe	3702 (3533 to 3876)	5.96 (5.69 to 6.24)	4418 (4023 to 4856)	8.38 (7.63 to 9.22)	1.04 (0.53 to 1.54)
Central Latin America	1365 (1316 to 1416)	1.67 (1.61 to 1.74)	6128 (5453 to 6851)	4.6 (4.1 to 5.15)	3.48 (3.32 to 3.64)
Central Sub-Saharan Africa	257 (198 to 327)	1.05 (0.81 to 1.34)	801 (586 to 1116)	1.23 (0.9 to 1.71)	0.53 (0.42 to 0.64)
East Asia	36,382 (30,663 to 42,129)	5.28 (4.45 to 6.12)	81,689 (65,829 to 99,517)	11.86 (9.56 to 14.45)	2.67 (2.51 to 2.83)
Eastern Europe	6415 (6166 to 6668)	5.82 (5.59 to 6.05)	7158 (6545 to 7816)	7.44 (6.8 to 8.12)	0.73 (0.18 to 1.28)
Eastern Sub-Saharan Africa	1335 (1010 to 1554)	1.6 (1.21 to 1.86)	3323 (2795 to 4139)	1.59 (1.33 to 1.98)	-0.02 (-0.15 to 0.11)
High-income Asia Pacific	8246 (7943 to 8557)	8.88 (8.56 to 9.22)	8882 (8204 to 9602)	11.36 (10.49 to 12.28)	0.8 (0.51 to 1.09)
High-income North America	11,839 (11,590 to 12,114)	7.94 (7.78 to 8.13)	19,392 (18,590 to 20,043)	11.5 (11.02 to 11.88)	1.2 (0.67 to 1.74)
North Africa and Middle East	3916 (3089 to 4574)	2.44 (1.93 to 2.85)	13,106 (11,385 to 15,156)	3.92 (3.41 to 4.53)	1.54 (1.37 to 1.71)
Oceania	47 (34 to 58)	1.46 (1.07 to 1.83)	107 (86 to 129)	1.51 (1.22 to 1.83)	0.07 (-0.03 to 0.16)
South Asia	6383 (5572 to 7184)	1.21 (1.05 to 1.36)	15,511 (13,484 to 18,697)	1.54 (1.34 to 1.86)	0.78 (0.49 to 1.08)
Southeast Asia	6262 (5150 to 7252)	2.65 (2.18 to 3.07)	17,969 (15,047 to 20,586)	4.85 (4.06 to 5.55)	2.04 (1.89 to 2.18)
Southern Latin America	957 (858 to 1060)	3.91 (3.5 to 4.33)	2096 (1824 to 2379)	6.04 (5.26 to 6.86)	1.42 (1 to 1.85)
Southern Sub-Saharan Africa	549 (502 to 602)	2.13 (1.95 to 2.34)	1319 (1146 to 1566)	3.05 (2.65 to 3.63)	1.12 (0.5 to 1.74)
Tropical Latin America	1703 (1618 to 1785)	2.17 (2.06 to 2.27)	5938 (5582 to 6312)	4.95 (4.66 to 5.27)	2.58 (2.47 to 2.69)
Western Europe	14,307 (13,675 to 15,000)	7.4 (7.07 to 7.76)	16,581 (15,579 to 17,566)	8.8 (8.26 to 9.32)	0.56 (0.29 to 0.84)
Western Sub-Saharan Africa	603 (498 to 721)	0.7 (0.58 to 0.84)	1892 (1407 to 2436)	0.82 (0.61 to 1.06)	0.51 (0.42 to 0.6)

UI Uncertainty interval, *CI* Confidence interval, *AAPCs* Average annual percent changes, *SDI* Socio-demographic index

(-0.28%, 95% CI: -0.83 to 0.27%) and prevalence rate (0.03%, 95% CI: -0.31 to 0.37%), while Western Europe had the largest decreases in the mortality rate (-1.09%, 95% CI: -1.24 to -0.95%) and DALYs rate (-1.08%, 95% CI: -1.22 to -0.94%).

EO-CRC burden by countries and territories

From the perspective of incidence cases of EO-CRC among 204 countries and territories, China (78,692.27, 95% UI: 62,703.11 to 96,467.59), the USA (17,291.63, 95% UI: 16,665.10 to 17,901.57), and India (12,500.87, 95%

Table 2 Prevalence of early-onset colorectal cancer in 1990 and 2021, and the AAPCs from 1990 to 2021

Location	1990		2021		AAPCs % (95% CI) 1990–2021
	Number(95% UI)	Rate per 100,000 population (95% UI)	Number(95% UI)	Rate per 100,000 population (95% UI)	
Global	585,832 (551,199 to 618,952)	21.61(20.34 to 22.84)	1,342,468 (1,222,335 to 1,474,707)	34(30.96 to 37.35)	1.47 (1.33 to 1.61)
Sex					
Female	270,245 (249,295 to 291,296)	20.21(18.64 to 21.78)	538,787 (492,036 to 591,352)	27.65(25.25 to 30.34)	1.02 (0.9 to 1.15)
Male	315,588 (285,782 to 338,428)	22.98(20.81 to 24.65)	803,681 (698,587 to 923,434)	40.19(34.93 to 46.18)	1.82 (1.6 to 2.04)
SDI					
High SDI	229,274 (223,561 to 235,118)	49.75(48.51 to 51.02)	361,976 (350,193 to 374,033)	72.07(69.73 to 74.47)	1.2 (1.03 to 1.38)
High-middle SDI	166,716 (153,734 to 179,773)	29.54(27.24 to 31.85)	415,420 (360,559 to 483,495)	65.98(57.27 to 76.8)	2.72 (2.56 to 2.88)
Low SDI	11,559 (9044 to 13,638)	5.23(4.09 to 6.17)	31,778 (27,485 to 36,258)	5.86(5.07 to 6.68)	0.35 (0.2 to 0.5)
Low-middle SDI	35,591 (31,038 to 40,540)	6.46(5.63 to 7.36)	105,351 (92,700 to 119,971)	10.37(9.12 to 11.81)	1.54 (1.44 to 1.64)
Middle SDI	142,104 (125,592 to 158,043)	15.61(13.79 to 17.36)	426,887 (368,909 to 483,710)	34.01(29.39 to 38.54)	2.55 (2.42 to 2.67)
Region					
Andean Latin America	1573 (1354 to 1817)	8.44 (7.26 to 9.75)	6620 (5252 to 8215)	18.92 (15.02 to 23.49)	2.66 (1.85 to 3.47)
Australasia	6159 (5597 to 6800)	57.08 (51.87 to 63.02)	12,135 (10,409 to 13,924)	84.04 (72.09 to 96.42)	1.24 (0.74 to 1.75)
Caribbean	3979 (3651 to 4274)	21.78 (19.99 to 23.4)	9036 (7726 to 10,412)	37.74 (32.27 to 43.48)	1.82 (1.52 to 2.11)
Central Asia	5279 (5057 to 5512)	15.83 (15.17 to 16.53)	7319 (6470 to 8102)	15.01 (13.27 to 16.62)	0.03 (-0.31 to 0.37)
Central Europe	19,202 (18,310 to 20,057)	30.92 (29.49 to 32.3)	27,216 (24,777 to 29,886)	51.65 (47.02 to 56.72)	1.57 (1.2 to 1.94)
Central Latin America	6826 (6569 to 7083)	8.36 (8.05 to 8.68)	35,202 (31,284 to 39,468)	26.44 (23.5 to 29.65)	3.97 (3.8 to 4.13)
Central Sub-Saharan Africa	1039 (809 to 1321)	4.25 (3.31 to 5.41)	3525 (2594 to 4862)	5.41 (3.98 to 7.46)	0.8 (0.69 to 0.9)
East Asia	181,333 (154,184 to 208,439)	26.32 (22.38 to 30.26)	547,652 (440,519 to 664,853)	79.54 (63.98 to 96.57)	3.68 (3.54 to 3.83)
Eastern Europe	34,727 (33,325 to 36,034)	31.49 (30.22 to 32.67)	44,108 (40,426 to 47,703)	45.84 (42.01 to 49.57)	1.23 (0.84 to 1.63)
Eastern Sub-Saharan Africa	5296 (4099 to 6148)	6.35 (4.91 to 7.37)	14,782 (12,412 to 18,374)	7.06 (5.93 to 8.77)	0.34 (0.25 to 0.44)
High-income Asia Pacific	53,689 (51,711 to 55,867)	57.84 (55.71 to 60.19)	64,327 (59,572 to 69,420)	82.24 (76.16 to 88.75)	1.14 (0.93 to 1.35)
High-income North America	80,923 (78,688 to 83,141)	54.3 (52.8 to 55.79)	138,938 (133,599 to 143,698)	82.38 (79.21 to 85.2)	1.37 (0.87 to 1.88)
North Africa and Middle East	20,752 (16,461 to 24,080)	12.95 (10.27 to 15.02)	84,793 (74,134 to 96,858)	25.36 (22.17 to 28.97)	2.2 (2.03 to 2.37)
Oceania	208 (154 to 257)	6.5 (4.81 to 8.05)	495 (407 to 595)	7 (5.75 to 8.4)	0.22 (0.04 to 0.4)
South Asia	26,679 (23,421 to 30,040)	5.04 (4.43 to 5.68)	72,674 (63,855 to 87,344)	7.22 (6.34 to 8.68)	1.16 (0.87 to 1.45)
Southeast Asia	28,426 (23,564 to 32,729)	12.01 (9.96 to 13.83)	94,393 (79,125 to 108,222)	25.46 (21.34 to 29.19)	2.52 (2.39 to 2.65)
Southern Latin America	4873 (4407 to 5371)	19.9 (17.99 to 21.93)	12,444 (10,897 to 13,921)	35.88 (31.42 to 40.13)	1.93 (1.52 to 2.35)
Southern Sub-Saharan Africa	2458 (2249 to 2680)	9.54 (8.73 to 10.4)	6092 (5317 to 7246)	14.11 (12.32 to 16.78)	1.26 (0.66 to 1.86)
Tropical Latin America	8088 (7698 to 8485)	10.3 (9.8 to 10.81)	32,384 (30,409 to 34,452)	27.03 (25.38 to 28.75)	3.08 (2.97 to 3.19)
Western Europe	91,843 (87,819 to 96,149)	47.48 (45.4 to 49.71)	120,015 (112,862 to 127,517)	63.66 (59.87 to 67.64)	0.91 (0.58 to 1.25)
Western Sub-Saharan Africa	2480 (2051 to 2954)	2.9 (2.4 to 3.45)	8318 (6192 to 10,625)	3.63 (2.7 to 4.63)	0.73 (0.66 to 0.8)

UI Uncertainty interval, *CI* Confidence interval, *AAPCs* Average annual percent changes, *SDI* Socio-demographic index

Table 3 Mortality of early-onset colorectal cancer in 1990 and 2021, and the AAPCs from 1990 to 2021

Location	1990		2021		AAPCs % (95% CI) 1990–2021
	Number(95% UI)	Rate per 100,000 population (95% UI)	Number(95% UI)	Rate per 100,000 population (95% UI)	
Global	59,232 (54,391 to 63,963)	2.19(2.01 to 2.36)	79,504 (72,699 to 86,539)	2.01(1.84 to 2.19)	-0.23 (-0.34 to -0.12)
Sex					
Female	26,780 (23,917 to 29,935)	2(1.79 to 2.24)	32,145 (29,391 to 35,098)	1.65(1.51 to 1.8)	-0.62 (-0.78 to -0.46)
Male	32,451 (28,468 to 35,780)	2.36(2.07 to 2.61)	47,359 (41,411 to 53,364)	2.37(2.07 to 2.67)	0.06 (-0.08 to 0.19)
SDI					
High SDI	13,064 (12,770 to 13,393)	2.83(2.77 to 2.91)	12,316 (11,905 to 12,747)	2.45(2.37 to 2.54)	-0.47 (-0.62 to -0.33)
High-middle SDI	17,682 (16,053 to 19,291)	3.13(2.84 to 3.42)	19,428 (17,107 to 22,242)	3.09(2.72 to 3.53)	-0.03 (-0.2 to 0.15)
Low SDI	2335 (1799 to 2744)	1.06(0.81 to 1.24)	5058 (4355 to 5858)	0.93(0.8 to 1.08)	-0.42 (-0.55 to -0.29)
Low-middle SDI	6273 (5427 to 7186)	1.14(0.98 to 1.3)	13,388 (11,782 to 15,442)	1.32(1.16 to 1.52)	0.47 (0.29 to 0.66)
Middle SDI	19,818 (17,431 to 22,197)	2.18(1.91 to 2.44)	29,246 (25,664 to 32,574)	2.33(2.04 to 2.6)	0.22 (0.13 to 0.31)
Region					
Andean Latin America	223 (190 to 259)	1.2 (1.02 to 1.39)	524 (414 to 651)	1.5 (1.18 to 1.86)	0.66 (-0.14 to 1.47)
Australasia	325 (296 to 360)	3.02 (2.74 to 3.34)	335 (293 to 384)	2.32 (2.03 to 2.66)	-0.92 (-1.38 to -0.45)
Caribbean	326 (292 to 358)	1.78 (1.6 to 1.96)	529 (442 to 638)	2.21 (1.85 to 2.67)	0.7 (0.39 to 1.01)
Central Asia	691 (662 to 720)	2.07 (1.99 to 2.16)	745 (657 to 834)	1.53 (1.35 to 1.71)	-0.91 (-1.28 to -0.54)
Central Europe	2090 (2001 to 2183)	3.37 (3.22 to 3.52)	1659 (1519 to 1807)	3.15 (2.88 to 3.43)	-0.23 (-0.64 to 0.17)
Central Latin America	862 (830 to 893)	1.06 (1.02 to 1.09)	2724 (2424 to 3031)	2.05 (1.82 to 2.28)	2.18 (1.76 to 2.59)
Central Sub-Saharan Africa	212 (164 to 270)	0.87 (0.67 to 1.11)	602 (438 to 841)	0.92 (0.67 to 1.29)	0.2 (0.07 to 0.33)
East Asia	23,326 (19,679 to 26,968)	3.39 (2.86 to 3.91)	25,486 (20,478 to 31,043)	3.7 (2.97 to 4.51)	0.28 (0.14 to 0.43)
Eastern Europe	3556 (3414 to 3697)	3.22 (3.1 to 3.35)	2931 (2660 to 3227)	3.05 (2.76 to 3.35)	-0.11 (-0.58 to 0.35)
Eastern Sub-Saharan Africa	1107 (824 to 1295)	1.33 (0.99 to 1.55)	2448 (2072 to 3062)	1.17 (0.99 to 1.46)	-0.41 (-0.55 to -0.27)
High-income Asia Pacific	3012 (2893 to 3125)	3.24 (3.12 to 3.37)	1943 (1834 to 2068)	2.48 (2.35 to 2.64)	-0.87 (-1.15 to -0.6)
High-income North America	3669 (3589 to 3752)	2.46 (2.41 to 2.52)	4499 (4345 to 4646)	2.67 (2.58 to 2.75)	0.29 (-0.35 to 0.93)
North Africa and Middle East	2443 (1917 to 2854)	1.52 (1.2 to 1.78)	5100 (4369 to 5941)	1.53 (1.31 to 1.78)	0.05 (-0.07 to 0.16)
Oceania	34 (24 to 43)	1.05 (0.76 to 1.34)	74 (59 to 90)	1.04 (0.83 to 1.28)	-0.06 (-0.15 to 0.03)
South Asia	5057 (4408 to 5705)	0.96 (0.83 to 1.08)	10,169 (8852 to 12,284)	1.01 (0.88 to 1.22)	0.2 (-0.08 to 0.49)
Southeast Asia	4453 (3652 to 5181)	1.88 (1.54 to 2.19)	9834 (8231 to 11,284)	2.65 (2.22 to 3.04)	1.19 (1.06 to 1.32)
Southern Latin America	594 (534 to 654)	2.42 (2.18 to 2.67)	921 (812 to 1045)	2.66 (2.34 to 3.01)	0.3 (-0.06 to 0.66)
Southern Sub-Saharan Africa	392 (357 to 430)	1.52 (1.39 to 1.67)	862 (744 to 1026)	2 (1.72 to 2.38)	0.83 (0.21 to 1.45)
Tropical Latin America	1163 (1107 to 1218)	1.48 (1.41 to 1.55)	3101 (2922 to 3288)	2.59 (2.44 to 2.74)	1.78 (1.5 to 2.06)
Western Europe	5211 (4977 to 5454)	2.69 (2.57 to 2.82)	3649 (3451 to 3863)	1.94 (1.83 to 2.05)	-1.09 (-1.24 to -0.95)
Western Sub-Saharan Africa	485 (400 to 582)	0.57 (0.47 to 0.68)	1369 (1027 to 1756)	0.6 (0.45 to 0.77)	0.17 (0.07 to 0.28)

UI Uncertainty interval, *CI* Confidence interval, *AAPCs* Average annual percent changes, *SDI* Socio-demographic index

UI: 10,752.57 to 15,048.28) ranked as the top three. The three highest incidence rates were observed in Monaco (19.08/100,000, 95% UI: 12.71 to 26.98/100,000), Taiwan Province of China (18.61/100,000, 95% UI: 16.47 to 20.94/100,000), and Bermuda (18.16/100,000, 95% UI: 13.37 to 23.47/100,000). The three countries/territories with the most DALYs were China (1,243,552.26, 95% UI: 983,058.92 to 1,524,383.13), India (401,362.02, 95% UI: 342,013.10 to 488,763.26), and the USA (205,519.95, 95% UI: 197,696.94 to 213,092.23). The three countries/territories with the highest DALY rates were Taiwan Province of China (239.59/100,000, 95% UI: 214.67 to 264.27/100,000), Thailand (235.78/100,000, 95% UI: 175.47 to 310.31/100,000), and Bulgaria (232.41/100,000, 95% UI: 185.10 to 285.33/100,000). The global distributions of incidence, prevalence, mortality, and DALYs of EO-CRC are illustrated in Figs. 3, 4, 5 and 6 respectively. Detailed data for each indicator can be found in Tables S2-S5.

Proportion of EO-CRC among all CRC cases

Our analysis revealed that in 2021, the proportions of EO-CRC incidence cases, prevalence cases, death cases, and DALYs numbers among all CRC cases worldwide

Table 4 DALYs of early-onset colorectal cancer in 1990 and 2021, and the AAPCs from 1990 to 2021

Location	1990		2021		AAPCs % (95% CI) 1990–2021
	Number(95% UI)	Rate per 100,000 population (95% UI)	Number(95% UI)	Rate per 100,000 population (95% UI)	
Global	3,026,077 (2,769,994 to 3,263,275)	111.64(102.2 to 120.39)	4,002,756 (3,666,300 to 4,350,565)	101.37(92.85 to 110.18)	-0.31 (-0.46 to -0.16)
Sex					
Female	1,368,664 (1,215,858 to 1,533,020)	102.34(90.91 to 114.63)	1,615,410 (1,475,902 to 1,767,273)	82.89(75.73 to 90.68)	-0.68 (-0.83 to -0.52)
Male	1,657,413 (1,446,902 to 1,823,378)	120.7(105.37 to 132.79)	2,387,346 (2,093,226 to 2,687,482)	119.38(104.68 to 134.39)	0 (-0.14 to 0.15)
SDI					
High SDI	652,668 (636,929 to 670,832)	141.62(138.21 to 145.56)	619,204 (597,718 to 644,147)	123.29(119.01 to 128.26)	-0.46 (-0.61 to -0.31)
High-middle SDI	902,454 (816,760 to 984,611)	159.89(144.71 to 174.45)	977,720 (860,369 to 1,115,476)	155.3(136.66 to 177.18)	-0.03 (-0.31 to 0.25)
Low SDI	118,015 (91,167 to 138,716)	53.39(41.24 to 62.76)	257,458 (221,802 to 299,099)	47.47(40.89 to 55.15)	-0.4 (-0.54 to -0.26)
Low-middle SDI	319,483 (276,008 to 366,180)	57.97(50.08 to 66.45)	672,958 (590,065 to 780,314)	66.22(58.06 to 76.78)	0.42 (0.27 to 0.58)
Middle SDI	1,030,478 (903,217 to 1,154,923)	113.16(99.19 to 126.83)	1,471,968 (1,287,755 to 1,632,122)	117.28(102.6 to 130.04)	0.12 (0.01 to 0.23)
Region					
Andean Latin America	11,576 (9865 to 13,369)	62.12 (52.94 to 71.74)	26,709 (21,228 to 32,813)	76.36 (60.69 to 93.81)	0.65 (-0.01 to 1.31)
Australasia	16,152 (14,689 to 17,827)	149.68 (136.12 to 165.2)	17,152 (14,963 to 19,533)	118.78 (103.62 to 135.27)	-0.82 (-1.28 to -0.35)
Caribbean	16,700 (14,979 to 18,358)	91.43 (82 to 100.5)	26,648 (22,293 to 32,219)	111.29 (93.1 to 134.55)	0.69 (0.42 to 0.97)
Central Asia	36,314 (34,762 to 37,782)	108.9 (104.25 to 113.3)	37,954 (33,468 to 42,324)	77.84 (68.64 to 86.8)	-0.96 (-1.17 to -0.74)
Central Europe	102,618 (98,188 to 107,243)	165.25 (158.12 to 172.7)	80,299 (73,370 to 87,340)	152.4 (139.25 to 165.76)	-0.28 (-0.74 to 0.17)
Central Latin America	45,343 (43,735 to 46,907)	55.55 (53.58 to 57.46)	138,467 (123,783 to 154,197)	104.01 (92.98 to 115.83)	2.07 (1.72 to 2.43)
Central Sub-Saharan Africa	10,751 (8370 to 13,674)	44.03 (34.28 to 56)	30,449 (22,301 to 42,392)	46.7 (34.2 to 65.02)	0.18 (0.06 to 0.3)
East Asia	1,214,302 (1,021,110 to 1,402,275)	176.28 (148.23 to 203.57)	1,293,878 (1,040,222 to 1,570,229)	187.93 (151.08 to 228.06)	0.22 (0.07 to 0.38)
Eastern Europe	176,370 (169,296 to 183,154)	159.92 (153.5 to 166.07)	143,824 (130,426 to 158,160)	149.47 (135.54 to 164.36)	-0.33 (-0.67 to 0.01)
Eastern Sub-Saharan Africa	56,321 (42,195 to 65,799)	67.52 (50.59 to 78.88)	125,630 (105,878 to 158,037)	60 (50.56 to 75.47)	-0.38 (-0.51 to -0.26)
High-income Asia Pacific	149,582 (143,870 to 155,753)	161.15 (154.99 to 167.79)	96,791 (91,302 to 103,003)	123.74 (116.73 to 131.68)	-0.86 (-1.14 to -0.58)
High-income North America	185,091 (180,635 to 189,666)	124.2 (121.21 to 127.27)	226,870 (218,583 to 235,859)	134.51 (129.6 to 139.84)	0.28 (-0.31 to 0.88)
North Africa and Middle East	126,263 (99,159 to 147,354)	78.78 (61.87 to 91.94)	259,531 (222,572 to 302,029)	77.63 (66.57 to 90.34)	0 (-0.12 to 0.11)
Oceania	1743 (1239 to 2210)	54.56 (38.77 to 69.16)	3781 (3025 to 4631)	53.44 (42.75 to 65.46)	-0.1 (-0.2 to -0.01)
South Asia	254,463 (222,591 to 286,666)	48.1 (42.07 to 54.19)	505,534 (438,178 to 616,020)	50.22 (43.53 to 61.19)	0.15 (-0.13 to 0.43)
Southeast Asia	230,811 (188,588 to 268,507)	97.55 (79.71 to 113.49)	493,115 (412,834 to 566,189)	132.99 (111.34 to 152.69)	1.06 (0.93 to 1.19)
Southern Latin America	29,481 (26,563 to 32,348)	120.38 (108.46 to 132.08)	46,132 (40,588 to 52,461)	132.99 (117.01 to 151.24)	0.32 (-0.11 to 0.75)
Southern Sub-Saharan Africa	20,264 (18,441 to 22,127)	78.68 (71.6 to 85.91)	43,269 (37,458 to 51,424)	100.23 (86.77 to 119.12)	0.74 (0.11 to 1.37)

Table 4 (continued)

Location	1990		2021		AAPCs % (95% CI) 1990–2021
	Number(95% UI)	Rate per 100,000 population (95% UI)	Number(95% UI)	Rate per 100,000 population (95% UI)	
Tropical Latin America	59,866 (57,072 to 62,855)	76.24 (72.68 to 80.05)	154,279 (145,471 to 163,866)	128.75 (121.4 to 136.75)	1.57 (1.46 to 1.69)
Western Europe	257,612 (245,945 to 269,775)	133.19 (127.16 to 139.48)	182,900 (172,565 to 195,136)	97.02 (91.54 to 103.51)	-1.08 (-1.22 to -0.94)
Western Sub-Saharan Africa	24,454 (20,161 to 29,331)	28.57 (23.55 to 34.26)	69,545 (52,090 to 89,296)	30.33 (22.72 to 38.94)	0.18 (0.02 to 0.34)

DALYs disability-adjusted life years, *UI* Uncertainty interval, *CI* Confidence interval, *AAPCs* Average annual percent changes, *SDI* Socio-demographic index

were 9.66%, 11.49%, 7.61%, and 16.4%, respectively (Fig. 7a-d). From 1990 to 2021, these proportions showed a gradual decline globally. Furthermore, in low-SDI regions, these proportions exhibited a gradual increase during this period, while they demonstrated downward trends in other SDI regions (Fig. 7e-h).

Risk factor

We analyzed the percentage contribution of 11 risk factors to the DALYs of EO-CRC globally from 1990 to 2021. We found that the three major risk factors contributing to DALYs for EO-CRC worldwide in 2021 were a diet low in whole grains (17%), a diet low in milk (15.8%), and a diet high in red meat (13.8%) (Fig. 8a). The percentage contribution of these three risk factors also ranked among the top in most of the five SDI regions and 21

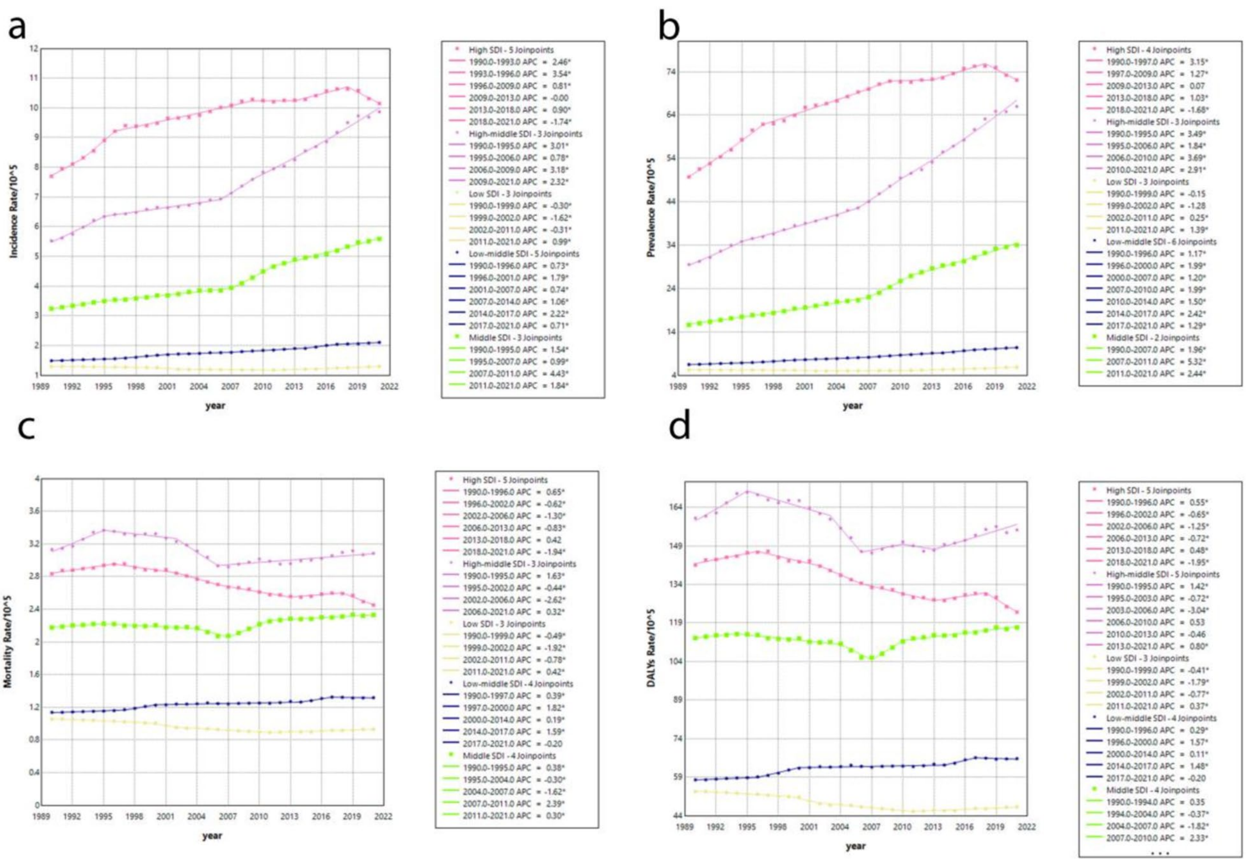

Fig. 2 Trends in global incidence, prevalence, mortality, and DALYs rates of early-onset colorectal cancer, by SDI quintiles, from 1990 to 2021. Incidence rate (**a**) Prevalence rate (**b**) Mortality rate (**c**) DALYs rate (**d**). *DALYs* disability-adjusted life years

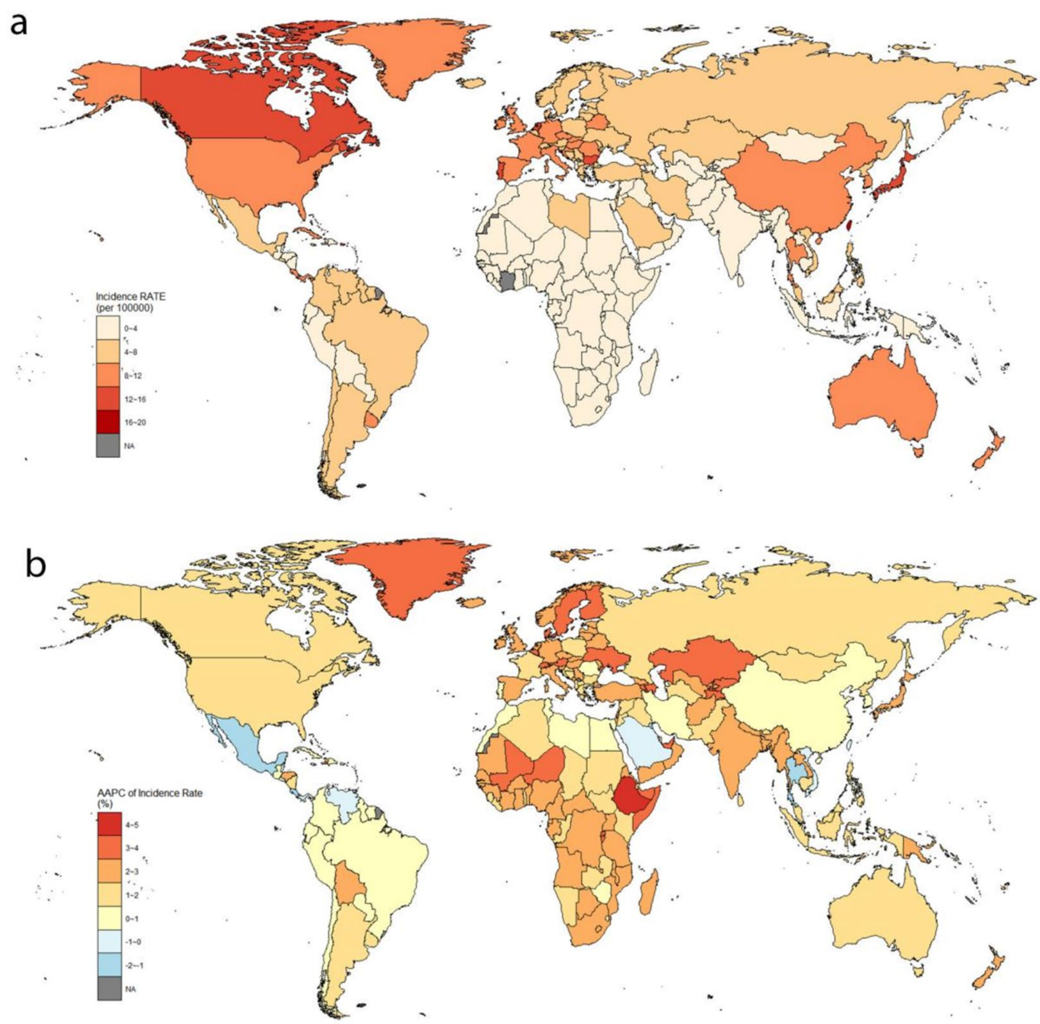

Fig. 3 Incidence rates (**a**) and average annual percent changes (AAPCs) (**b**) of early-onset colorectal cancer in 204 countries and territories

GBD regions. Additionally, a diet low in calcium was significantly higher than other risk factors in middle-low and low SDI regions, as well as in most African regions (Fig. 8a and Fig. S1). After analyzing the changes in each risk factor from 1990 to 2021, we found that two metabolic factors, high BMI and high fasting plasma glucose, showed the fastest growth globally, particularly in middle, low-middle, and low SDI regions such as East Asia, Southeast Asia, and some African regions. Meanwhile, these regions experienced a substantial rise in high alcohol use (Figs. 8b and 9). Stratified analysis by age and gender indicated that smoking and high alcohol use had a much higher impact on males with EO-CRC compared to females; the smoking factor was significantly higher among individuals aged 40–49 compared to those aged 15–39 (Fig. S2).

Prediction

The estimated worldwide incidence ASR of EO-CRC is projected to be 5.42 /100,000 in 2036, reflecting a growth rate of 5.56% from 2021 (Fig. 10a). The projected mortality ASR of EO-CRC for 2036 is estimated to be 1.66/100,000, reflecting a decline of 13.85% compared to 2021 (Fig. 10b). From 2021 to 2036, the incidence ASR among males is predicted to be greater than that among females. In males, the projected incidence ASR in 2036 is estimated to be 6.72/100,000, reflecting a growth of 10.3%. Conversely, the incidence ASR in females is expected to remain consistent with that observed in 2021 at 4.16/100,000. From 1990 to 2015, the mortality ASR of EO-CRC in males exhibited a decrease compared to that observed among females. However, the ASR of mortality in males became higher than that in females after 2016. The projected ASR of mortality in 2036 for males is expected to decline by 5.7%, standing at 1.52/100,000.

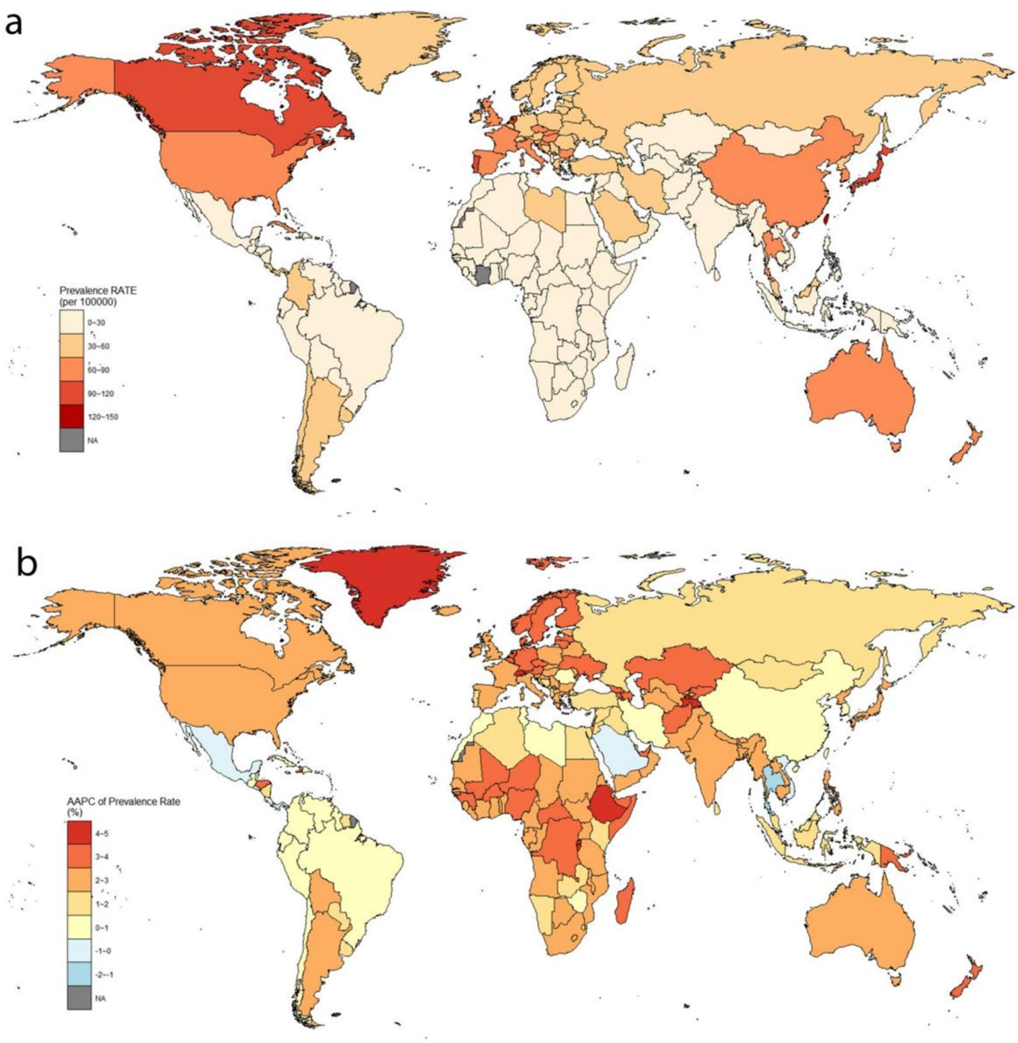

Fig. 4 Prevalence rates (**a**) and average annual percent changes (AAPCs) (**b**) of early-onset colorectal cancer in 204 countries and territories

Similarly, the mortality ASR of females is projected to decrease significantly by 10.4% to 1.41/100,000 in 2036.

Discussion

EO-CRC has attracted significant concern in recent years, driven not only by its rapidly increasing incidence but also by several other critical factors. First, EO-CRC predominantly affects individuals under the age of 50, who often serve as primary breadwinners and essential contributors to society. Their illness impacts not only their health but also the well-being of their families and the broader community [24, 25]. Second, patients with EO-CRC are more susceptible to psychological issues, sexual dysfunction, and fertility challenges compared to those with traditional colorectal cancer, leading to a diminished overall quality of life [26]. Third, clinical studies indicate that EO-CRC patients present with more adverse pathological features, higher rates of chemotherapy resistance, increased recurrence rates, and poorer prognoses than their traditional colorectal cancer counterparts [9, 27–29]. Finally, emerging research reveals that EO-CRC involves distinct mechanisms of development, risk factors, pathophysiology, and genomic characteristics compared to traditional colorectal cancer. This highlights the urgent need for targeted research focused specifically on early-onset colorectal cancer [9–11].

As shown in our study, the global incidence and prevalence of EO-CRC have exhibited a rapid increasing trend from 1990 to 2021, which is consistent with previous research [30, 31]. However, we further observed that the trend shifted to a decline from 2019 to 2021, as indicated by corresponding APC values of less than zero. Further analysis shows that this declining trend occurred only in high SDI regions, while the incidence and prevalence

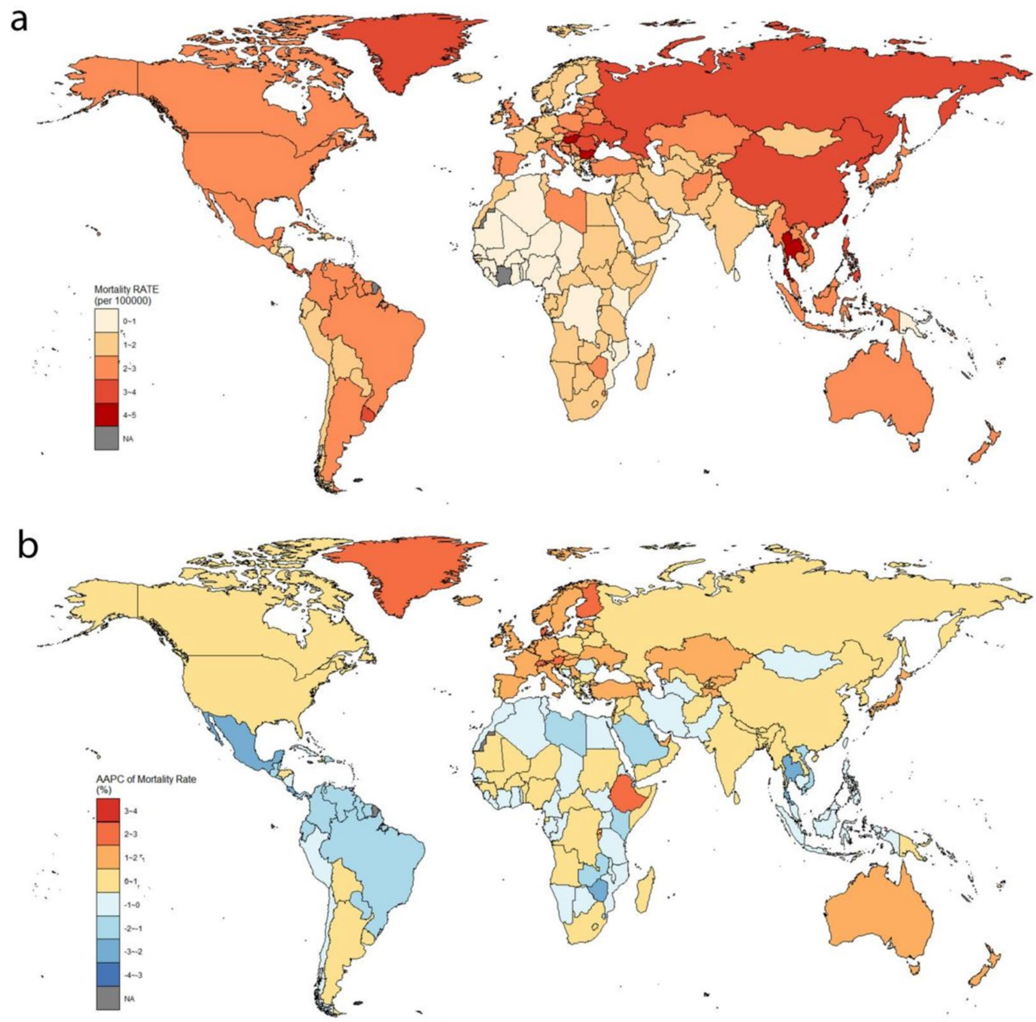

Fig. 5 Mortality rates (**a**) and average annual percent changes (AAPCs) (**b**) of early-onset colorectal cancer in 204 countries and territories

in the other four SDI regions continued to increase rapidly during the same period. This suggests that healthcare measures in high SDI regions have yielded effective results in recent years, which may serve as a reference for research and practice in other regions. Over the past three decades, EO-CRC has shown the most rapid increase in high-middle SDI regions, while demonstrating the slowest growth rate in low SDI regions. This may be attributed to the rapid industrialization in high-middle SDI regions, leading to lifestyle changes such as increased consumption of red meat, alcohol, processed food, and cigarettes, alongside a decrease in physical activity and an increase in obesity rates. These factors potentially contribute to an elevated risk of EO-CRC [32, 33]. Furthermore, advancements in medical screening technologies may also result in a higher number of EO-CRC cases being diagnosed in high-middle SDI regions [7]. Conversely, due to limited healthcare resources and lower levels of medical expertise, many cases of early-onset CRC remain undiagnosed or unregistered in low SDI areas [34, 35]. While the burden of EO-CRC in lower SDI regions is currently lower, it is essential to consider the rising trends in alcohol consumption and metabolic risk factors. Recent studies indicate significant increases in metabolic disorders and alcohol-related complications in these regions [36–38], which may contribute to a future rise in EO-CRC cases. Therefore, caution is warranted against overly optimistic conclusions regarding the current burden. Proactive public health strategies and continued monitoring are crucial to address these emerging risks in vulnerable populations.

There are notable differences in the disease burden of EO-CRC across different continents and countries, even among regions with similar SDI levels. This disparity may stem from variations in population size, lifestyle patterns, racial genetics, and healthcare conditions. Prior research

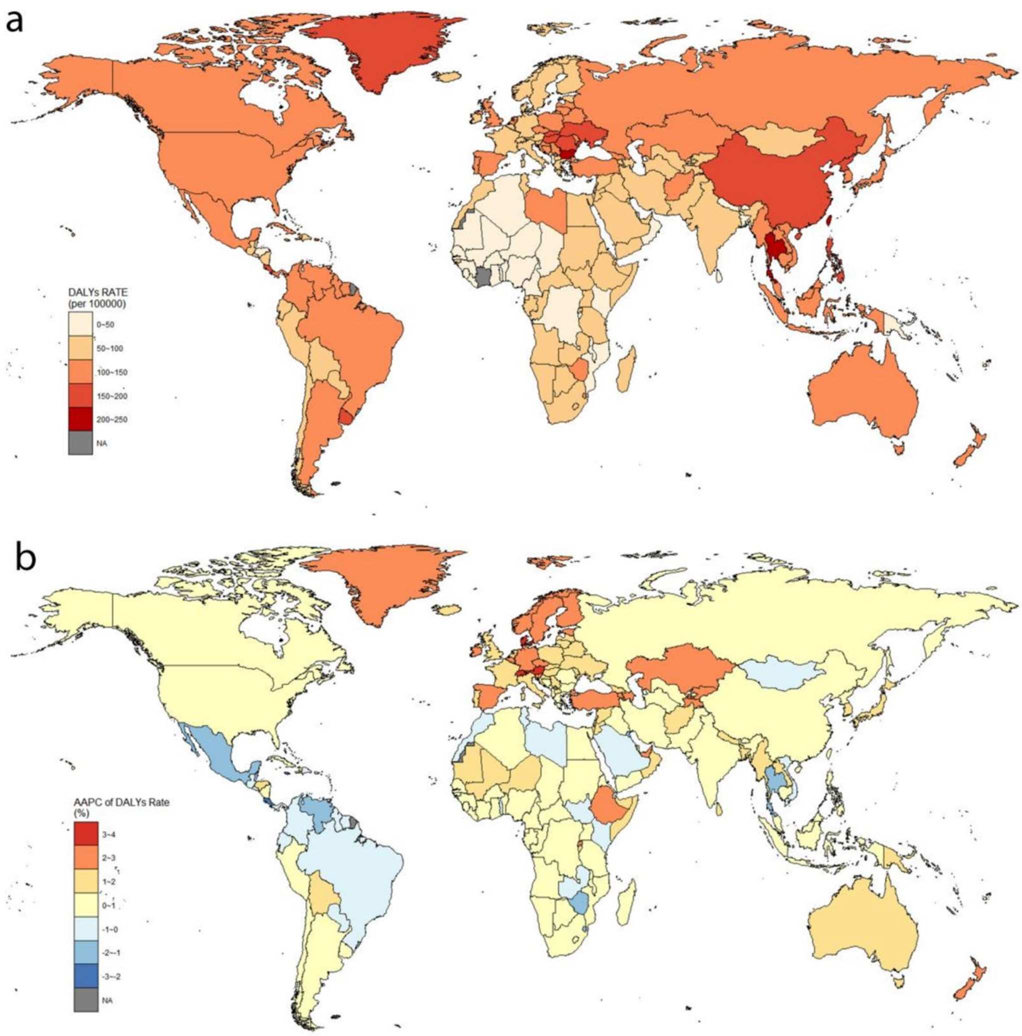

Fig. 6 DALYs rates (**a**) and average annual percent changes (AAPCs) (**b**) of early-onset colorectal cancer in 204 countries and territories. *DALYs* disability-adjusted life years

has suggested that in East Asia, race plays an important role in the development of CRC. Certain ethnic groups, such as Chinese, Koreans, and Japanese, have higher incidence rates of CRC. Even in countries like Singapore and Malaysia, where diverse racial populations live in similar environments and dietary habits, the risk of CRC is significantly increased among Chinese compared to Malays and Indians. Furthermore, within the same ethnic group in China, individuals residing in coastal areas exhibit higher incidence and mortality rates than those living inland [39, 40]. The screening guidelines for CRC of different countries may impact the burden of EO-CRC. Most countries recommend CRC screening for the general risk population starting at age 50 [41]. With increasing focus on EO-CRC, the Chinese CRC Screening Guidelines lowered the starting age for screening in the general risk population to 40 in 2020 [42]. The US Preventive Services Task Force (USPSTF) recommendation also reduced the initial screening age from 50 to 45 for CRC in 2021 [43, 44]. Adults aged 40 and above were required to undergo routine screenings for CRC in Japan since 1992 [41]. We found that the ranks of EO-CRC mortality in Japan, China, and the USA were much lower than those of their corresponding incidence rates. Research by indicated that Japan had the lowest mortality-to-incidence ratio of EO-CRC in Asia from 1990 to 2019 [45]. This suggests that while early screening might not reduce the incidence of EO-CRC, it can lower the risk of fatal outcomes from CRC. However, further research is needed to confirm these findings in the future.

Our study found that although the incidence, prevalence, mortality, and DALYs of EO-CRC have shown a rapid increase over the past 30 years, these indicators are declining relative to the proportions of overall CRC. This

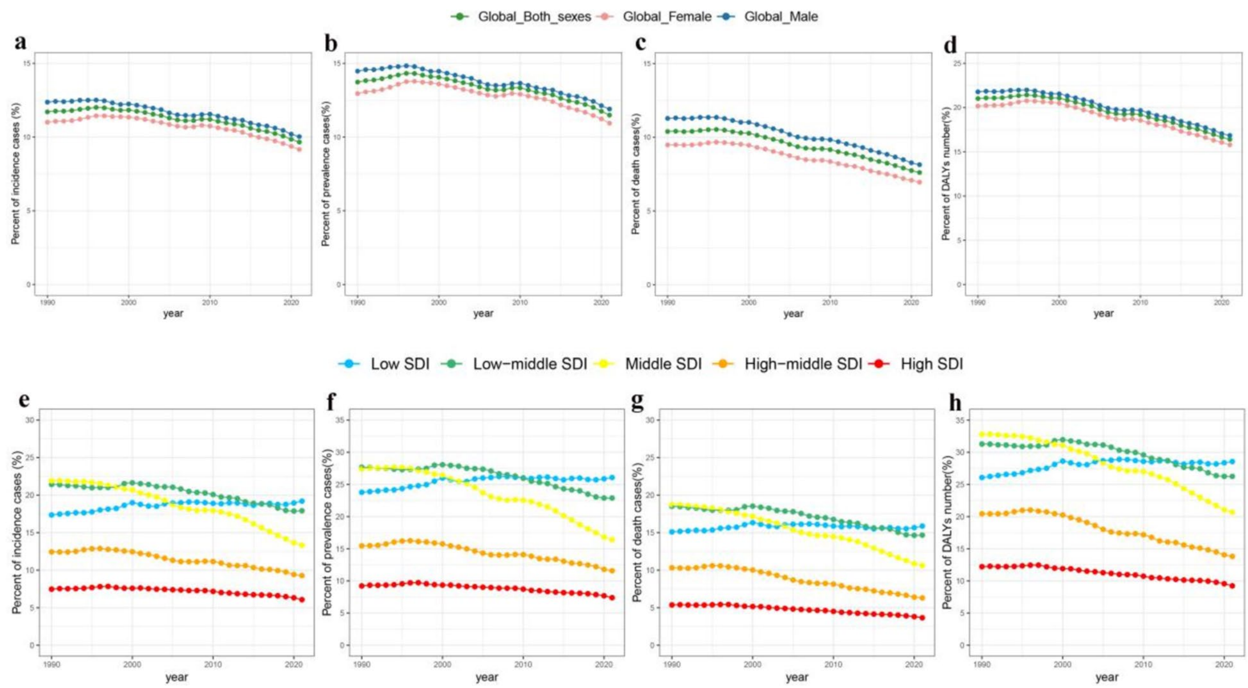

Fig. 7 Trends in proportion of early-onset colorectal cancer (EO-CRC) disease burden Among All colorectal cancer (CRC) Cases from 1990 to 2021. Trends in proportion of EO-CRC incidence cases (**a**) prevalence cases (**b**) death cases (**c**) DALYs number (**d**) globally by sex; trends in proportion of EO-CRC incidence cases (**e**) prevalence cases (**f**) death cases (**g**) DALYs number (**h**) by SDI quintiles

result reflects that the growth rate of the disease burden associated with EO-CRC is relatively slower compared to that of all CRC cases. Similar findings have been reported in other studies [13, 34]. This may be due to age being one of the risk factors for CRC, combined with the increase in life span and the effects of population aging [31]. Consequently, CRC in older populations is also a significant public health concern that requires focused attention.

Through our analysis of risk factors, we found that a diet low in whole grains, a diet low in milk, and a diet high in red meat have consistently been the major risk factors for DALYs in EO-CRC patients worldwide, regardless of whether in developed or low-income regions from 1990 to 2021. Similar results have also been reported in previous literature [7, 35]. According to another study [46], 21.5% of global gastrointestinal cancer cases in 2018 were attributable to poor dietary habits, with excessive processed meat consumption and insufficient fruit and whole grain intake being major risk factors. Therefore, encouraging people to increase their consumption of whole grains and milk while reducing their intake of red meat can help lower the global disease burden of EO-CRC. It is also worth noting that from 1990 to 2021, the two metabolic factors, high BMI and high fasting plasma glucose, were the fastest-growing risk factors for DALYs in EO-CRC patients globally, especially in economically underdeveloped middle, low-middle, and low SDI regions such as East Asia, South Asia, Southeast Asia, and Central and Eastern sub-Saharan Africa. We also observed a significant increase in high alcohol use in these regions. This indicates that the disease burden of early-onset colorectal cancer caused by high BMI and high fasting plasma glucose has increased significantly over the past 30 years. This also corroborates the earlier findings by Tan et al. regarding GBD2019 [47], which reported a substantial rise in the global cancer-related mortality burden attributable to high BMI from 2010 to 2019, including cancers of the liver, colorectal, esophagus, and breast. In recent years, the incidence of early-onset colorectal cancer has significantly increased, closely associated with changes in various risk factors. Notably, the rising trends in alcohol consumption and inflammatory bowel disease (IBD) may play critical roles in this phenomenon [48, 49]. Research indicates that the increase in alcohol consumption among younger populations is significantly linked to the rising rates of early-onset colorectal cancer. Metabolites of alcohol can cause DNA damage in intestinal cells, thereby increasing the risk of malignant transformation.

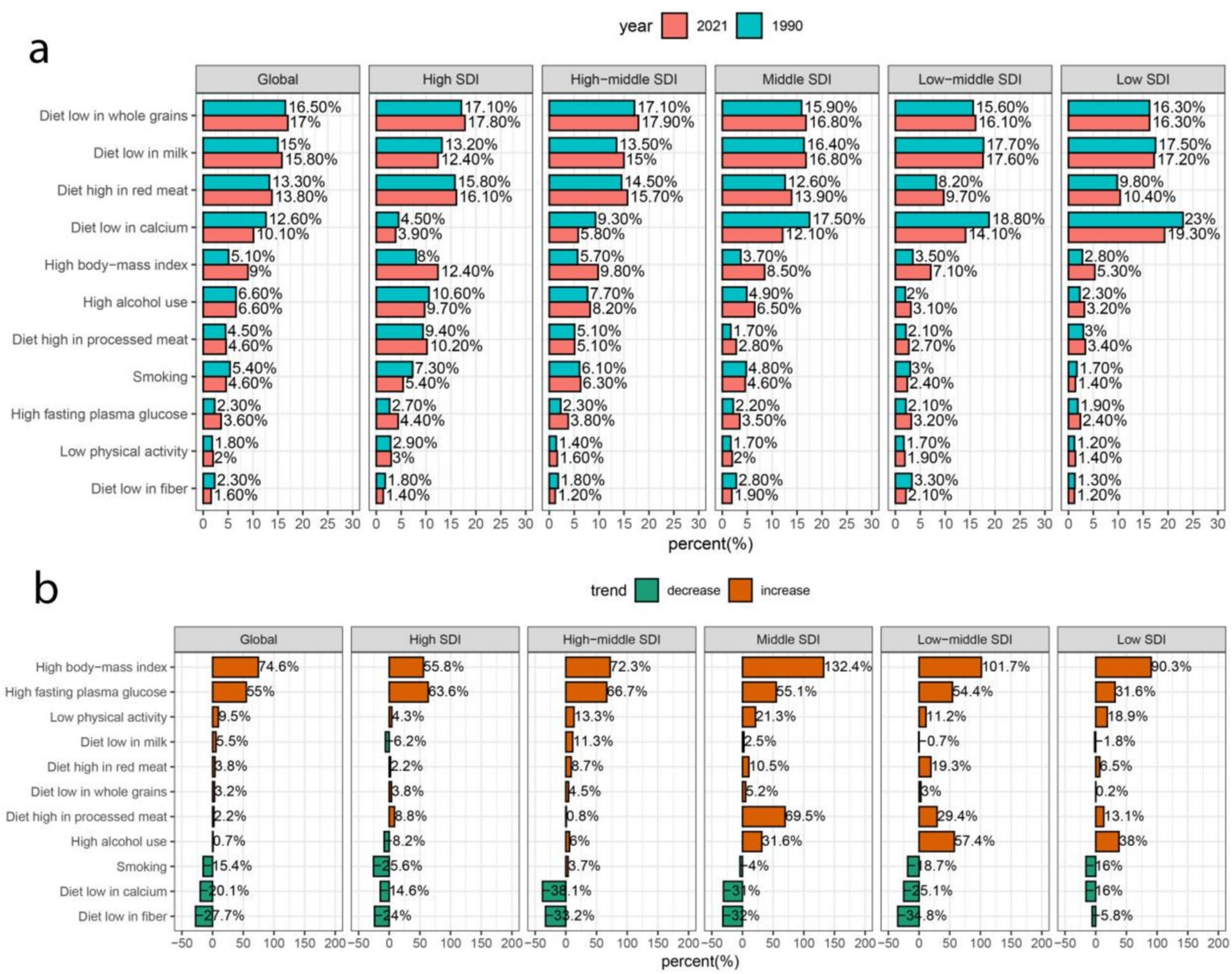

Fig. 8 Percentage contribution of 11 risk factors to the DALYs of EO-CRC globally, by SDI quintiles, in 1990 and 2021 (**a**), and the trends from 1990 to 2021 (**b**). *DALYs* disability-adjusted life years, *EO-CRC* early-onset colorectal cancer, *SDI* Socio-demographic index

Moreover, alcohol consumption may alter the gut microbiome and promote inflammatory responses, further compromising gut health [48, 50]. Concurrently, the prevalence of IBD continues to rise among young individuals. Chronic intestinal inflammation is recognized as a major contributing factor to colorectal cancer development. Studies have shown that individuals with IBD have a significantly higher risk of developing colorectal cancer compared to the general population, particularly with prolonged disease duration. Therefore, early identification and management of IBD might be crucial in reducing the risk of early-onset colorectal cancer [49, 51]. Furthermore, high alcohol consumption can also increase the risk of obesity [24], which further raises the risks of diabetes, hyperlipidemia, and other metabolic factors [52]. Reports show that obesity, diabetes, and hyperlipidemia are independent risk factors for EO-CRC [53–55]. Thus, urgent measures are needed to reduce obesity and alcohol consumption, particularly among teenagers. Low and middle-low SDI regions, such as East Asia, South Asia, Southeast Asia, and Central and Eastern sub-Saharan Africa, should pay more attention to this issue and implement effective measures. Moreover, the conclusions of our study still need further research to be substantiated.

We projected the global burden of EO-CRC beyond 2021, covering a period of 15 years. Our concern lies in the predicted 5.56% increase in the ASR of EO-CRC incidence after this timeframe. Notably, the ASR of EO-CRC incidence among males is expected to rise by 10.3%, surpassing the corresponding change observed in females. This finding aligns with previous relevant studies and underscores the urgent need to enhance colonoscopy screening and early detection measures for CRC, while

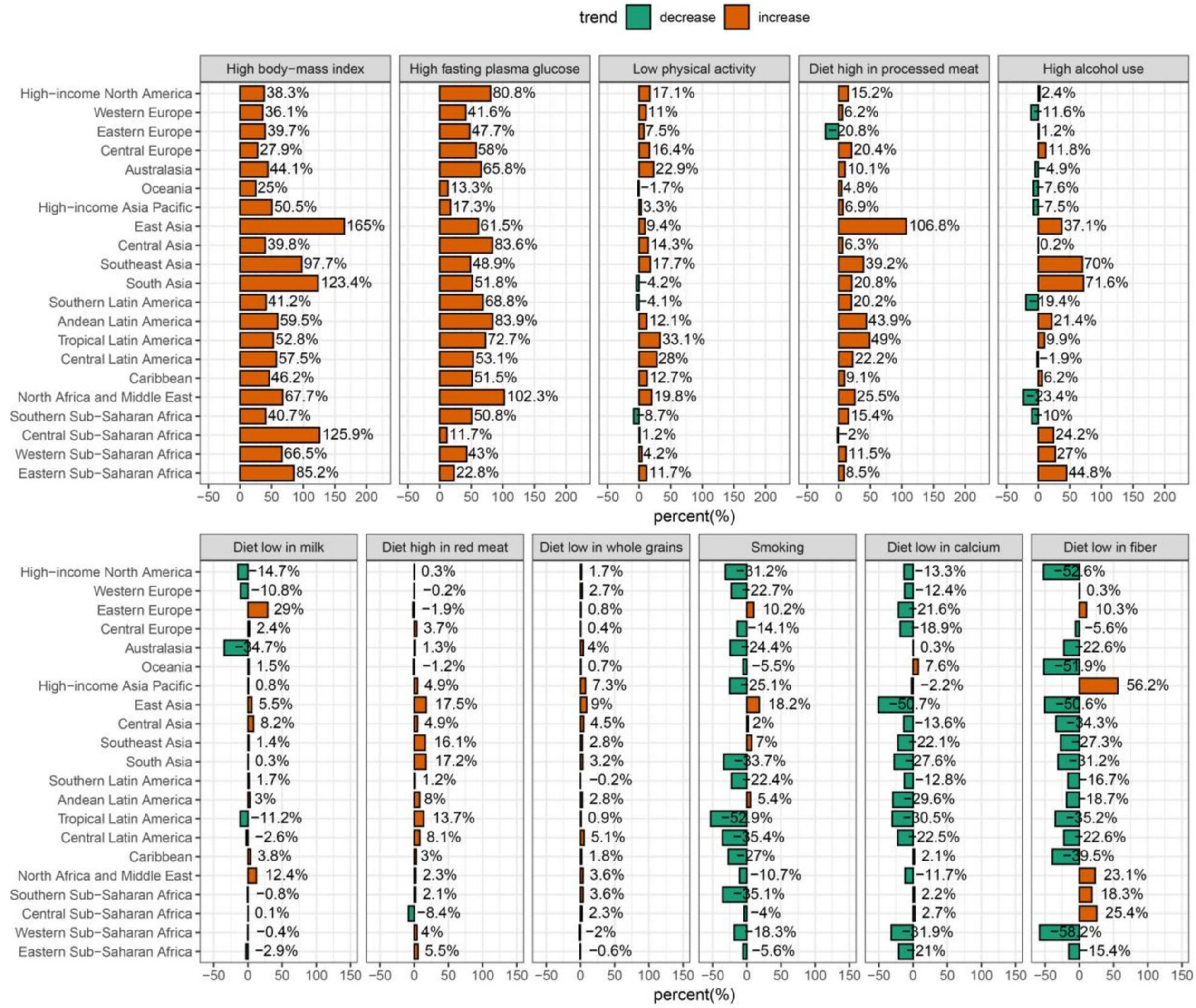

Fig. 9 Trends of percentage contribution of 11 risk factors to the DALYs of EO-CRC in 21 GBD regions from 1990 to 2021. *DALYs* disability-adjusted life years, *EO-CRC* early-onset colorectal cancer, *GBD* global burden of disease

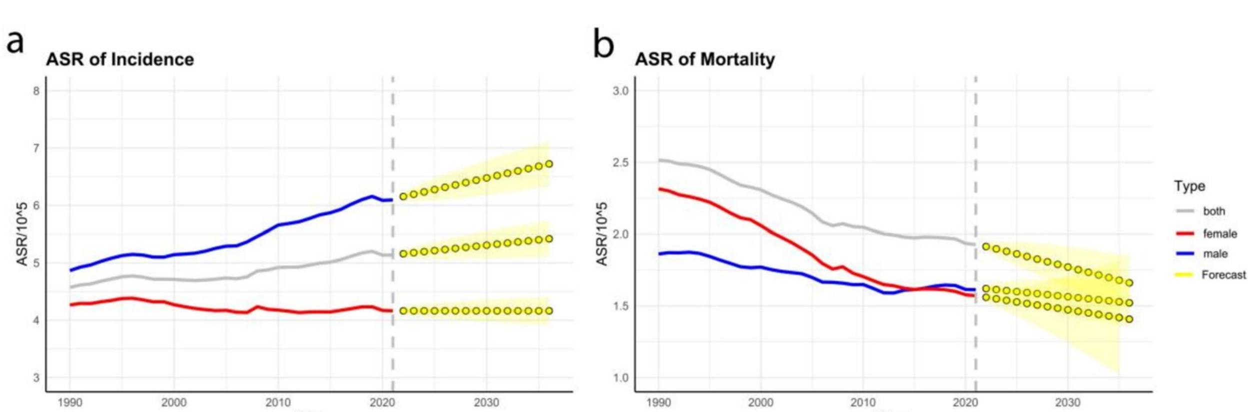

Fig. 10 Forecasts of age-standardized rates (ASR) for incidence (**a**) and Mortality (**b**) of early-onset colorectal cancer (EO-CRC), stratified by sex, over the next 15 years using the ARIMA model. *ARIMA* autoregressive integrated moving average

intensifying health education about the associated risk factors to effectively prevent CRC occurrence, particularly among males [14]. Fortunately, there is an estimated reduction of 13.9% in the ASR of EO-CRC mortality in 2036. Notably, this decline is more significant among females than among males. These results are aligned with the findings noted in previous pertinent research and can be attributed to advancements in the treatment of CRC as well as an increased focus on promoting a healthy diet among women [56].

The innovations of this study are as follows: this is the first study analyzing the global burden and cross-country health inequalities of EO-CRC from 1990 to 2021 utilizing newly published data derived from the GBD Study 2021. Moreover, we conducted in-depth analyses of the percentage contribution and trends of risk factors for EO-CRC, stratified by sex and age. Admittedly, there are several limitations in this study. Firstly, the GBD data we used has a wide range of time spans and spatial spans, inevitably leading to variations in measurement standards. In addition, the rigor and completeness of data registration may vary across different regions, which can potentially interfere with the analysis results [16, 35]. Secondly, The GBD database is unable to evaluate demographic factors such as age, sex, and ethnicity, as well as comorbidities like diabetes and cardiovascular diseases. These factors are crucial in understanding the epidemiology of EO-CRC, as they may influence risk factors and disease outcomes. Future research should aim to incorporate demographic factors and comorbidities to enhance our understanding of the disease and inform prevention and treatment strategies more effectively [57, 58]. Thirdly, when conducting the analysis of risk factors, using age-standardized rates may lead to an underestimation of the true risk for certain factors highly correlated with specific age groups. Finally, it is important to acknowledge that the GBD database exhibits significant differences in data quality and collection methods compared to other databases, such as SEER (Surveillance, Epidemiology, and End Results) and GLOBOCAN (Cancer's Global Cancer Observatory). The GBD database integrates various data sources, including hospital records, death certificates, and survey data, aiming to estimate the global burden of disease through modeling. However, this reliance on models may lead to inaccuracies in the estimation of specific diseases [1, 16]. Moreover, the SEER database is primarily based on cancer registries in the United States, providing detailed epidemiological data for American cancer patients, but it has a relatively smaller sample size, covering only about 34% of the population [59]. In contrast, GLOBOCAN relies on reports from national cancer registries, with a lower frequency of data updates, potentially impacting the timeliness and accuracy of global cancer burden assessments [50]. Consequently, the results derived from the GBD database may be influenced by data quality considerations stemming from these differences in sample size and data update frequency. According to previous studies, the incidence for most digestive cancers, including CRC, in GBD 2019 were lower than those in GLOBOCAN 2020 in Asia [60]. Therefore, these limitations may influence our assessment of the burden of EO-CRC. At last, given the variations in data sources and analytical methods among these databases, future research should approach the interpretation and comparison of results from different datasets with caution.

Conclusion

In brief, our findings indicated that the incidence and prevalence rates of EO-CRC exhibited an upward trend, while the mortality and DALYs rates demonstrated a downward trajectory from 1990 to 2021 globally. The highest EO-CRC disease burden among the five SDI regions occurred in the high-middle SDI region in 2021, while East Asia demonstrated the highest mortality rate, incidence rate, and DALYs rate among the 21 GBD regions. Dietary risk factors, such as a diet low in whole grains, a diet low in milk, and a diet high in red meat, were primary factors contributing to the DALYs of EO-CRC. The two metabolic factors, high BMI and high fasting plasma glucose, were the fastest-growing risk factors contributing to DALYs in EO-CRC patients globally from 1990 to 2021. In the next 15 years, the ASR of incidence is projected to increase by 5.56%, while the ASR of mortality is expected to decrease by 13.9%. The current and future burdens of EO-CRC remain substantial at the global, regional, and national levels, displaying significant variation across different regions and nations.

Countries should promptly develop strategies to allocate healthcare resources based on their disease burden and implement effective prevention and early screening measures.

Abbreviations

AAPCs	Average annual percentage changes
ARIMA	Autoregressive integrated moving average
ASR	Age-standardized rate
BMI	Body mass index
CI	Confidence interval
CRC	Colorectal cancer
DALYs	Disability-adjusted life years
EO-CRC	Early-onset colorectal cancer
EO-GICs	Early-onset gastrointestinal cancers
GBD	Global burden of disease
GLOBOCAN	Cancer's Global Cancer Observatory
IBD	Inflammatory bowel disease
NHANES	National Health and Nutrition Examination Survey
SEER	Surveillance, Epidemiology, and End Results

SDI Socio-demographic index
UIs Uncertainty intervals
USPSTF US Preventive Services Task Force

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12889-024-20624-4.

Supplementary Material 1: Table S1. Distribution of 204 Countries and Territories by Socio-Demographic Index (SDI) Quintile Categories.

Supplementary Material 2: Table S2. Early-onset colorectal cancer incidence in 1990 and 2021 with AAPCs from 1990 to 2021 by country/territory, for both sexes.

Supplementary Material 3: Table S3. Early-onset colorectal cancer prevalence in 1990 and 2021 with AAPCs from 1990 to 2021 by country/territory, for both sexes.

Supplementary Material 4: Table S4. Early-onset colorectal cancer mortality in 1990 and 2021 with AAPCs from 1990 to 2021 by country/territory, for both sexes.

Supplementary Material 5: Table S5. Early-onset colorectal cancer DALYs in 1990 and 2021 with AAPCs from 1990 to 2021 by country/territory, for both sexes.

Supplementary Material 6: Fig. S1. Percentage contribution of 11 risk factors to the DALYs of EO-CRC in 21 GBD regions for the years 1990 and 2021. *DALYs* disability-adjusted life years, *EO-CRC* early-onset colorectal cancer, *SDI* Socio-demographic index; Fig. S2 Percentage contribution of 11 risk factors to the DALYs of EO-CRC stratified by age and gender, globally in 2021. *DALYs* disability-adjusted life years, *EO-CRC*early-onset colorectal.

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Authors' contributions
Jinhai Zhang, Dehua Ou, Aosi Xie, Diqun Chen and Xinxin Li contributed to the study conception and design. The first draft of the manuscript was written by Jinhai Zhang, Dehua Ou, Aosi Xie, Diqun Chen and Xinxin Li. Data collection and analysis were performed by Jinhai Zhang, Aosi Xie and Diqun Chen. Jinhai Zhang and Xinxin Li performed the visualization. Diqun Chen provided the language help. All authors read and approved the final manuscript.

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Data availability
No datasets were generated or analysed during the current study.

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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References

1. Wang S, Zheng R, Li J, et al. Global, regional, and national lifetime risks of developing and dying from gastrointestinal cancers in 185 countries: a population-based systematic analysis of GLOBOCAN. Lancet Gastroenterol Hepatol. 2024;9(3):229–37. https://doi.org/10.1016/s2468-1253(23)00366-7.
2. Koh B, Tan DJH, Ng CH, et al. Patterns in cancer incidence among people younger than 50 years in the US, 2010 to 2019. JAMA Netw Open. 2023;6(8):e2328171. https://doi.org/10.1001/jamanetworkopen.2023.28171.
3. Danpanichkul P, Auttapracha T, Kongarin S, et al. Global epidemiology of early-onset upper gastrointestinal cancer: trend from the global burden of disease study 2019. J Gastroenterol Hepatol. 2024;39(9):1856–68. https://doi.org/10.1111/jgh.16620.
4. Ben-Aharon I, van Laarhoven HWM, Fontana E, et al. Early-onset cancer in the gastrointestinal tract is on the rise-evidence and implications. Cancer Discov. 2023;13(3):538–51. https://doi.org/10.1158/2159-8290.Cd-22-1038.
5. Wei T, Luo P, Zhang X, et al. Comparison of the incidence of colorectal cancer in young adults between the USA and Europe. Gut. 2020;69(8):1540–2. https://doi.org/10.1136/gutjnl-2019-319391.
6. Jalali A, Smith S, Kim G, et al. Early onset metastatic colorectal cancer in Australia. Cancer Treat Res Commun. 2024;40:100827. https://doi.org/10.1016/j.ctarc.2024.100827.
7. Pan H, Zhao Z, Deng Y, et al. The global, regional, and national early-onset colorectal cancer burden and trends from 1990 to 2019: results from the global burden of disease study 2019. BMC Public Health. 2022;22(1):1896. https://doi.org/10.1186/s12889-022-14274-7.
8. Danpanichkul P, Moolkaew P, Kanjanakot Y, et al. Rising incidence and impact of early-onset colorectal cancer in the Asia-Pacific with higher mortality in females from Southeast Asia: a global burden analysis from 2010 to 2019. J Gastroenterol Hepatol. 2023;38(12):2053–60. https://doi.org/10.1111/jgh.16331.
9. Ugai T, Sasamoto N, Lee HY, et al. Is early-onset cancer an emerging global epidemic? Current evidence and future implications. Nat Rev Clin Oncol. 2022;19(10):656–73. https://doi.org/10.1038/s41571-022-00672-8.
10. Stoffel EM, Murphy CC. Epidemiology and mechanisms of the increasing incidence of colon and rectal cancers in young adults. Gastroenterology. 2020;158(2):341–53. https://doi.org/10.1053/j.gastro.2019.07.055.
11. Fontana E, Meyers J, Sobrero A, et al. Early-onset colorectal adenocarcinoma in the IDEA database: treatment adherence, toxicities, and outcomes with 3 and 6 months of adjuvant fluoropyrimidine and oxaliplatin. J Clin Oncol. 2021;39(36):4009–19. https://doi.org/10.1200/jco.21.02008.
12. Li Q, Yu M, Lv H, et al. Burden of early-onset colorectal cancer along with attributable risk factors from 1990 to 2019: a comparative study between China and other G20 countries. BMC Public Health. 2023;23(1):1463. https://doi.org/10.1186/s12889-023-16407-y.
13. Shao B, Zhu M, Shen K, et al. Disease burden of total and early-onset colorectal cancer in china from 1990 to 2019 and predictions of cancer incidence and mortality. Clin Epidemiol. 2023;15:151–63. https://doi.org/10.2147/clep.S391058.
14. Tang X, Peng J, Huang S, et al. Global burden of early-onset colorectal cancer among people aged 40–49 years from 1990 to 2019 and predictions to 2030. J Cancer Res Clin Oncol. 2023;149(18):16537–50. https://doi.org/10.1007/s00432-023-05395-6.
15. Wang Z, Yao W, Wu W, et al. Global incidence trends of early-onset colorectal cancer and related exposures in early-life: an ecological analysis based on the GBD 2019. Front Public Health. 2024;12:1367818. https://doi.org/10.3389/fpubh.2024.1367818.
16. Global incidence, prevalence, years lived with disability (YLDs), disability-adjusted life-years (DALYs), and healthy life expectancy (HALE) for 371 diseases and injuries in 204 countries and territories and 811 subnational locations, 1990–2021: a systematic analysis for the Global Burden of Disease Study 2021. Lancet, 2024. 403(10440): p. 2133–2161.https://doi.org/10.1016/s0140-6736(24)00757-8.
17. Global burden and strength of evidence for 88 risk factors in 204 countries and 811 subnational locations, 1990–2021: a systematic analysis for the Global Burden of Disease Study 2021. Lancet, 2024. 403(10440): p. 2162–2203.https://doi.org/10.1016/s0140-6736(24)00933-4.
18. Global Burden of Disease Study 2021 (GBD 2021) Socio-Demographic Index (SDI) 1950–2021. Available from: https://ghdx.healthdata.org/

record/global-burden-disease-study-2021-gbd-2021-socio-demographic-index-sdi-1950%E2%80%932021.
19. Kim HJ, Fay MP, Feuer EJ, et al. Permutation tests for joinpoint regression with applications to cancer rates. Stat Med. 2000;19(3):335–51. https://doi.org/10.1002/(sici)1097-0258(20000215)19:3<335::aid-sim336>3.0.co;2-z.
20. Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet, 2020. 396(10258): p. 1204–1222.https://doi.org/10.1016/s0140-6736(20)30925-9.
21. Gu, W.J., J.P. Pei, J. Lyu, et al., The Burden of Early-Onset Colorectal Cancer and Its Risk Factors from 1990 to 2019: A Systematic Analysis for the Global Burden of Disease Study 2019. Cancers (Basel), 2022. 14(14).https://doi.org/10.3390/cancers14143502
22. Su J, Liang Y, He X. The global burden and trends analysis of early-onset colorectal cancer attributable to dietary risk factors in 204 countries and territories, 1990–2019: a secondary analysis for the global burden of disease study 2019. Front Nutr. 2024;11:1384352. https://doi.org/10.3389/fnut.2024.1384352.
23. Schaffer AL, Dobbins TA, Pearson SA. Interrupted time series analysis using autoregressive integrated moving average (ARIMA) models: a guide for evaluating large-scale health interventions. BMC Med Res Methodol. 2021;21(1):58. https://doi.org/10.1186/s12874-021-01235-8.
24. AlKalbani SR, Murrin C. The association between alcohol intake and obesity in a sample of the Irish adult population, a cross-sectional study. BMC Public Health. 2023;23(1):2075. https://doi.org/10.1186/s12889-023-16946-4.
25. Waddell, O., J. McLauchlan, A. McCombie, et al., Quality of life in early-onset colorectal cancer patients: systematic review. BJS Open, 2023. 7(3).https://doi.org/10.1093/bjsopen/zrad030.
26. Garrett C, Koh CE, Solomon MJ, et al. The health-related quality of life of early-onset colorectal cancer patients: an Australian cross-sectional study. Colorectal Dis. 2024;26(6):1166–74. https://doi.org/10.1111/codi.16998.
27. Vuik FER, Nieuwenburg SAV, Nagtegaal ID, et al. Clinicopathological characteristics of early onset colorectal cancer. Aliment Pharmacol Ther. 2021;54(11–12):1463–71. https://doi.org/10.1111/apt.16638.
28. McClelland PH, Liu T, Ozuner G. Early-onset colorectal cancer in patients under 50 years of age: demographics, disease characteristics, and survival. Clin Colorectal Cancer. 2022;21(2):e135–44. https://doi.org/10.1016/j.clcc.2021.11.003.
29. O'Sullivan DE, Cheung WY, Boyne DJ, et al. Treatment patterns and survival outcomes of early-onset colorectal cancer patients in Alberta, Canada: a population-based study. Cancer Treat Res Commun. 2022;32:100585. https://doi.org/10.1016/j.ctarc.2022.100585.
30. Vuik FE, Nieuwenburg SA, Bardou M, et al. Increasing incidence of colorectal cancer in young adults in Europe over the last 25 years. Gut. 2019;68(10):1820–6. https://doi.org/10.1136/gutjnl-2018-317592.
31. Sinicrope FA. Increasing incidence of early-onset colorectal cancer. N Engl J Med. 2022;386(16):1547–58. https://doi.org/10.1056/NEJMra2200869.
32. Siegel RL, Torre LA, Soerjomataram I, et al. Global patterns and trends in colorectal cancer incidence in young adults. Gut. 2019;68(12):2179–85. https://doi.org/10.1136/gutjnl-2019-319511.
33. Keum N, Giovannucci E. Global burden of colorectal cancer: emerging trends, risk factors and prevention strategies. Nat Rev Gastroenterol Hepatol. 2019;16(12):713–32. https://doi.org/10.1038/s41575-019-0189-8.
34. Global, regional, and national burden of colorectal cancer and its risk factors, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet Gastroenterol Hepatol, 2022. 7(7): p. 627–647.https://doi.org/10.1016/s2468-1253(22)00044-9
35. Wang Y, Huang X, Cheryala M, et al. Global increase of colorectal cancer in young adults over the last 30 years: an analysis of the global burden of disease study 2019. J Gastroenterol Hepatol. 2023;38(9):1552–8. https://doi.org/10.1111/jgh.16220.
36. Danpanichkul P, Suparan K, Dutta P, et al. Disparities in metabolic dysfunction-associated steatotic liver disease and cardiometabolic conditions in low and lower middle-income countries: a systematic analysis from the global burden of disease study 2019. Metabolism. 2024;158:155958. https://doi.org/10.1016/j.metabol.2024.155958.
37. Danpanichkul P, Chen VL, Chaiyakunapruk N, et al. Socio-economic association of alcohol use disorder and cardiovascular and alcohol-associated liver disease from 2010 to 2019. Aliment Pharmacol Ther. 2024;60(3):340–9. https://doi.org/10.1111/apt.18095.
38. Templin T, Cravo Oliveira Hashiguchi T, Thomson B, et al. The overweight and obesity transition from the wealthy to the poor in low- and middle-income countries: a survey of household data from 103 countries. PLoS Med. 2019;16(11):e1002968. https://doi.org/10.1371/journal.pmed.1002968.
39. Onyoh EF, Hsu WF, Chang LC, et al. The rise of colorectal cancer in asia: epidemiology, screening, and management. Curr Gastroenterol Rep. 2019;21(8):36. https://doi.org/10.1007/s11894-019-0703-8.
40. Chiu HM, Hsu WF, Chang LC, et al. Colorectal cancer screening in Asia. Curr Gastroenterol Rep. 2017;19(10):47. https://doi.org/10.1007/s11894-017-0587-4.
41. Lui RN, Wong SH, Ding NS, et al. Is this the end of colonoscopy screening for colorectal cancer? An Asia-Pacific perspective J Gastroenterol Hepatol. 2023;38(5):671–7. https://doi.org/10.1111/jgh.16182.
42. China guideline for the screening, early detection and early treatment of colorectal cancer (2020, Beijing). Zhonghua Zhong Liu Za Zhi, 2021. 43(1): p. 16–38.https://doi.org/10.3760/cma.j.cn112152-20210105-00010.
43. Davidson KW, Barry MJ, Mangione CM, et al. Screening for colorectal cancer: US preventive services task force recommendation statement. Jama. 2021;325(19):1965–77. https://doi.org/10.1001/jama.2021.6238.
44. Lin JS, Perdue LA, Henrikson NB, et al. Screening for colorectal cancer: updated evidence report and systematic review for the US preventive services task force. Jama. 2021;325(19):1978–98. https://doi.org/10.1001/jama.2021.4417.
45. Ramadan M, Alsiary RA, Aboalola DA. Mortality-to-incidence ratio of early-onset colorectal cancer in high-income Asian and Middle Eastern countries: a systemic analysis of the global burden of diseases study 2019. Cancer Med. 2023;12(21):20604–16. https://doi.org/10.1002/cam4.6631.
46. Li Y, Jia X, Li C, et al. The global incident gastrointestinal cancers attributable to suboptimal diets from 1990 to 2018. Gastroenterology. 2024;167(6):1141–51. https://doi.org/10.1053/j.gastro.2024.07.009.
47. Tan DJH, Ng CH, Muthiah M, et al. Rising global burden of cancer attributable to high BMI from 2010 to 2019. Metabolism. 2024;152:155744. https://doi.org/10.1016/j.metabol.2023.155744.
48. Siegel RL, Miller KD, Goding Sauer A, et al. Colorectal cancer statistics, 2020. CA Cancer J Clin. 2020;70(3):145–64. https://doi.org/10.3322/caac.21601.
49. Hindson J. Fungi in Crohn's disease and mucosal healing. Nat Rev Gastroenterol Hepatol. 2021;18(5):285. https://doi.org/10.1038/s41575-021-00451-3.
50. Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021;71(3):209–49. https://doi.org/10.3322/caac.21660.
51. Danpanichkul, P., K. Duangsonk, A.H. Ho, et al., Disproportionately Increasing Incidence of Inflammatory Bowel Disease in Females and the Elderly: An Update Analysis from the Global Burden of Disease Study 2021. Am J Gastroenterol, 2024.https://doi.org/10.14309/ajg.0000000000003143.
52. Kansra AR, Lakkunarajah S, Jay MS. Childhood and adolescent obesity: a review. Front Pediatr. 2020;8:581461. https://doi.org/10.3389/fped.2020.581461.
53. Danpanichkul P, Auttapracha T, Sukphutanan B, et al. The burden of overweight and obesity-associated gastrointestinal cancers in low and lower-middle-income countries: a global burden of disease 2019 analysis. Am J Gastroenterol. 2024;119(6):1177–80. https://doi.org/10.14309/ajg.0000000000002819.
54. Danpanichkul P, Ng CH, Tan DJH, et al. The global burden of alcohol-associated cirrhosis and cancer in young and middle-aged adults. Clin Gastroenterol Hepatol. 2024;22(9):1947-1949.e3. https://doi.org/10.1016/j.cgh.2024.02.011.
55. Hillerson D, Li S, Misumida N, et al. Characteristics, process metrics, and outcomes among patients with ST-elevation myocardial infarction in rural vs urban areas in the US: a report from the US National Cardiovascular Data Registry. JAMA Cardiol. 2022;7(10):1016–24. https://doi.org/10.1001/jamacardio.2022.2774.
56. Aldhaleei, W.A., M.B. Wallace, and A.S. Bhagavathula, Trends and Age-Period-Cohort Effect on the Incidence of Early-Onset Colorectal Cancer

(20–44 Years) from 1990 to 2021 in the United States. Cancers (Basel), 2024. 16(16).https://doi.org/10.3390/cancers16162883.
57. Ullah, F., A.B. Pillai, N. Omar, et al., Early-Onset Colorectal Cancer: Current Insights. Cancers (Basel), 2023. 15(12).https://doi.org/10.3390/cancers15123202.
58. Suenghataiphorn T, Danpanichkul P, Kulthamrongsri N, et al. Disparity in trends and characteristics of early onset colorectal cancer: analysis from the National Inpatient Sample, 2016 to 2021. Proc (Bayl Univ Med Cent). 2024;37(6):928–33. https://doi.org/10.1080/08998280.2024.2401757.
59. Che WQ, Li YJ, Tsang CK, et al. How to use the Surveillance, Epidemiology, and End Results (SEER) data: research design and methodology. Mil Med Res. 2023;10(1):50. https://doi.org/10.1186/s40779-023-00488-2.
60. Yu Z, Bai X, Zhou R, et al. Differences in the incidence and mortality of digestive cancer between Global Cancer Observatory 2020 and Global Burden of Disease 2019. Int J Cancer. 2024;154(4):615–25. https://doi.org/10.1002/ijc.34740.

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