

Mortality and years of life lost of colorectal cancer in China, 2005–2020: findings from the national mortality surveillance system

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Abstract

Background: Colorectal cancer (CRC) is the fourth cause of cancer death in China. We aimed to provide national and subnational estimates and changes of CRC premature mortality burden during 2005–2020.

Methods: Data from multi-source on the basis of the national surveillance mortality system were used to estimate mortality and years of life lost (YLL) of CRC in the Chinese population during 2005–2020. Estimates were generated and compared for 31 provincial-level administrative divisions in China.

Results: Estimated CRC deaths increased from 111.41 thousand in 2005 to 178.02 thousand in 2020; age-standardized mortality rate decreased from 10.01 per 100,000 in 2005 to 9.68 per 100,000 in 2020. Substantial reduction in CRC premature mortality burden, as measured by age-standardized YLL rate, was observed with a reduction of 10.20% nationwide. Marked differences were observed in the geographical patterns of provincial units, and they appeared to be obvious in areas with higher economic development. Population aging was the dominant driver which contributed to the increase in CRC deaths, followed by population growth and age-specific mortality change.

Conclusions: Substantial discrepancies were observed in the premature mortality burden of CRC across China. Targeted considerations were needed to promote a healthy lifestyle, expand cost-effective CRC early screening and diagnosis, and improve medical treatment to reduce CRC mortality among high-risk populations and regions with inadequate healthcare resources.

Keywords: China; Colorectal cancer; Mortality; Prevention and control strategy; Years of life lost

Introduction

Colorectal cancer (CRC) is the mainly prevalent malignant gastrointestinal cancer which is a collective term for colon cancer, rectal cancer, and anal cancer.^[1] CRC is the second most common cause of cancer and the fourth cause of cancer death in China, in 2020; it caused 0.55 million new incident cases and 0.29 million death cases, and it accounts for around 8% of all cancer death in 2019.^[2,3] It was reported that the majority of cases of CRC mortality were attributable to modifiable risk factors and thus preventable, such as removal of precancerous lesions could prevent the CRC occurrence, and CRC diagnosis at an early stage could improve the overall survival rate.^[4,5]

Therefore, clarifying the CRC premature mortality burden in different periods, regions, and populations will be of great necessity to facilitate targeted health policies and government-dominant strategies to reduce the risk of CRC

mortality. However, previous epidemiological studies related to CRC mortality over time across China were either of limited scope in premature mortality patterns or failed to provide adequate analysis of drivers of CRC mortality change over time.^[1,6,7] Accordingly, explicit evaluation of data from national mortality surveillance is needed to appropriately guide efforts to potentially fill remaining knowledge gaps.

In this study, by using data from the national mortality surveillance system (NMSS) in China, we aimed to provide national and subnational estimates of premature mortality burden for CRC during 2005–2020, with special attention paid to describe temporal trends and geographical variations of CRC mortality pattern, sex differences, and dominant drivers of its change. It will further facilitate the development of locality responses that could support the healthcare system to improve the CRC health of the Chinese population.

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Methods

Data source

Data for CRC mortality were derived from the NMSS housed in the Chinese Center for Disease Control and Prevention (CDC). NMSS covers more than 300 million individuals from 605 surveillance points in 31 provincial-level administrative divisions (PLADs in the mainland of China) that account for 24% of China's population with both national and provincial representativeness, and NMSS routinely collects individual details of death information in real-time through an internet-based approach. Detailed descriptions of NMSS have been reported elsewhere.^[8] Data for underreporting adjustment were obtained from underreporting field survey for national mortality surveillance, which collected underreporting data during 2006–2017. The under-5 mortality rate (U5MR) at a county level was extracted from a combination estimation of data derived from census, national surveys, Intra-Census Surveys, Maternal and Child Health Surveillance System (MCHS), and Disease Surveillance Point system (DSP).^[9] Data for surveillance population and socioeconomic covariates were all sourced from the National Bureau of Statistics.^[10,11] Data for rate standardization were acquired from the 2010 population census.^[10,11]

CRC mortality estimation

All-cause mortality estimation

(1) Underreporting rate (URR) calculation: We calculated the URR annually for each age-sex stratum among all surveillance points during 2006–2017, in which the proportion of missed deaths among the total number of deaths identified in underreporting surveys was determined for every 5-year-old group from 5 years to 9 years as the first age group till 80 years and older as the last. We used spline regression to predict the URR in each stratum in 2005 and 2018. (2) Adjusted all-cause mortality rate calculation: We derived underreporting-adjusted all-cause mortality rate by age and sex for all points by dividing the reported number of deaths by (1-URR). We used log-linear model to predict U5MR between 2013 and 2018 by fitting a time-varying trend using 1996–2012 results. Afterward, we used locally weighted regression by time and space to handle the discontinuity for each surveillance point after data quality control. (3) Probability of death for children aged younger than 5 years ($5q_0$) and probability of death for adults aged 15–60 years ($45q_{15}$) estimation: We produced age-sex all-cause mortality rate at a provincial level by weighting population counts in each point during 2005–2018 and subsequently generate $5q_0$ and $45q_{15}$. We adopted univariate analysis and collinearity diagnostics to examine significant socioeconomic covariates at a provincial level in relation to $45q_{15}$, including urbanization rate (%), average years of educational attainment (unit), beds of medical institutions per 10,000, non-agricultural population per 10,000, and per capita gross regional product (yuan/person). We used a non-linear mixed-effect model to acquire sex-specific $45q_{15}$ estimation at a provincial level during 2005–2018. (4) Age-specific

mortality rate estimation: We used a new relational model life table system with flexible standard (MLTFS) based on two parameters, $5q_0$ and $45q_{15}$, to generate a full set of age-sex-specific mortality rates for 31 provinces during 2005–2018.^[12,13] (5) Age-standardized mortality rate (ASMR) calculation: ASMR was calculated by age-specific mortality rate multiplied by 2010 population census, which we used as a standard population structure.

Cause of death (COD) mortality estimation, cause aggregation, and central rescale

(1) COD identification: In this study, the International Classification of Disease 10th Edition (ICD-10) code for CRC was C18-C21.8. (2) Garbage code redistribution: Methods used for this redistribution as developed by Naghavi *et al*^[14] were reported elsewhere. (3) Proportion of COD calculation: We calculated the COD proportion for all reported cases followed by reweighting the proportion of each cause based on the fraction of in-hospital or non-hospital death and urban/rural death from NMSS by each location, age, and sex to reduce the potential bias caused by unequal distribution of in-hospital/non-hospital and urban/rural deaths.^[15] (4) COD mortality estimation: COD mortality rate of CRC by location, sex, and age was calculated by multiplying the all-cause mortality rate generated in the first step and the proportion of COD calculated previously. To attenuate fluctuations in location-, year-, sex-, and age-specific mortality, where small numbers of deaths resulted in high variability of mortality between patterns across each stratum, we used spline regression to adapt its trend over time and across space to fit COD mortality rate within the same rubric after data quality control. (5) Cause aggregation and central rescale: We used a top-down hierarchical format containing five levels for all-cause and cause-specific number of deaths in cause aggregation and central rescale for the period 2005–2018. Details of methods were reported previously.^[16] (6) For each location, sex, and age group stratum of CRC mortality from 2005 to 2018, we used a generalized linear model to project the result for 2019 and 2020 by using 2005–2018 results under the same rubric.

Years of life lost computation

Years of life lost (YLLs) is a metric of premature mortality calculated as the sum of each death multiplied by the standard life expectancy at each age. The metric therefore highlights premature mortality by applying a larger weight to deaths that occur in younger age groups.^[16] We used a theoretical minimum risk reference life table as standard life expectancy in YLL computation for CRC and its subcategories during 2005–2020^[16] [Supplementary Digital Content, Table 1, <http://links.lww.com/CM9/A665>].

Statistical analysis

Annual rate of change calculation

To describe the CRC premature mortality burden over time in China and its provinces, we calculated the annual rate of change (ARC) developed by Preston *et al*^[17,18] by

using the logarithm of time period difference for CRC age-standardized YLL rate between 2005 and 2020 divided by the duration of study period of 15 years and then depicted the result by adding an ARC heatmap.

Decomposition of changes for CRC deaths

To explore the drivers of change in CRC deaths in China and its provinces, by using methods developed in demographic research from Das Gupta, we decomposed change from 2005 to 2020 into three explanatory components: as growths of the total population; as shifts in population structure by age or sex; or as changes for age-specific mortality rate.^[13,16,19] In contrast to simple comparisons between mortality rates as usual, Das Gupta's method of standardization and decomposition integrates interactions between component effects, including population growth, population aging, and mortality patterns transition, into the additive main effects.^[20] Methods of decomposition of changes for CRC deaths have been reported elsewhere.^[16,19]

In this study, all analysis was performed in SAS, version 9.4 (SAS Institute Inc., Cary, NC, USA), Stata/MP (Stata Corporation College Station, TX, USA), version 14.1 and R, version 4.0.4 (The R foundation for Statistical Computing, Vienna, Austria).

Results

Nationwide, it was estimated that the number of CRC deaths increased from 111.41 thousand in 2005 to 178.02 thousand in 2020. The ASMR of CRC decreased from 10.01 per 100,000 in 2005 to 9.68 per 100,000 in 2020 by 3.30%. The age-standardized YLL rate of CRC fell by 10.20% between 2005 and 2020. Overall, higher CRC mortality among men than women was observed [Table 1]. For the geographical variations of ASMR for CRC at the subnational level, in 2020, the top three provinces with the highest ASMR were Fujian (15.50 per 100 000), Zhejiang (14.07 per 100 000), and Guangdong (13.05 per 100 000), and the last three provinces were Tibet (3.93 per 100 000), Hebei (5.61 per 100 000), and Henan (5.90 per 100 000). And, during 2005–2020, change of ASMR for CRC varied substantially among regions; 18 of 31 provinces decreased, whereas the rest of 13 units increased, with Hebei (–37.90%) and Tibet (56.30%) the most. Nationally, the number of CRC deaths and age-specific mortality rate increased with age, reaching its peak among the population

aged 80 years and older. Men showed comparatively higher CRC deaths and mortality rates than women except for the mortality rate of the last age group [Figure 1]. As shown in Figure 2, in 2020, more than half of CRC premature mortality burden occurred among the elderly aged 60 years and older (70.73% at the national level). Compared with men, women were inclined to experience CRC death at an older age. Shanghai (90.47%), Beijing (79.74%), and Zhejiang (71.25%) were the top three provinces holding the highest proportion of YLLs among people aged 60 years and older, whereas Tibet (48.86%) showed a substantial difference for its mortality pattern as nearly 40% of CRC premature mortality occurred among population younger than 40 years, and men at an older age showed much more CRC deaths compared with women. During 2005–2020, the ARC heatmap demonstrated that a relative reduction of CRC premature mortality burden among the population aged 0 to 29 years was higher than the other age groups, varying from 18.51% in Shanxi to 0.29% in Guangdong with a national level of 2.14%, whereas the elderly aged 75 years and older with an increased ARC of 0.94% on a national average. Besides, it was estimated that the CRC premature mortality burden intensified perceptibly in Tibet among the population aged 30 to 44 years (19.45%) and 75 years and older (16.47%) [Figure 3].

During 2005–2020, there was a 59.79% increase in CRC deaths in China with 61.21% in men and 57.98% in women [Figure 4]. Population aging contributed the largest fraction to increase CRC deaths across the country, accounting for 55.84% of total change, followed by 8.48% for population growth and 4.53% for age-specific CRC mortality rate reduction. Nationwide, population aging was the dominant driver in the increase of CRC deaths, and shifts in age-specific CRC mortality rate contributed to the decrease of CRC deaths substantially; and population growth exerted both positive and negative effects on CRC deaths change. Referring to different regions, the top three provinces holding the largest contributions of population growth increasing CRC deaths were Beijing (44.24%), Tianjin (42.52%), and Shanghai (39.39%), whereas the smallest ones were Guizhou (–7.20%), Sichuan (–4.01%), and Heilongjiang (–1.72%). Besides, the top three provinces holding the largest contributions of population aging-related CRC death increase were Ningxia (87.28%), Heilongjiang (86.65%), and Jilin (83.40%), whereas the smallest ones were Guangxi (27.97%), Hainan (34.93%), and Henan

Table 1: Estimated deaths and ASMR, estimated YLLs, and age-standardized YLL rate of CRC in China, 2005, 2010, 2015, and 2020.

Items	2005			2010			2015			2020		
	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female
Estimated deaths (10,000)	11.14	6.25	4.89	12.69	7.14	5.55	14.37	8.16	6.21	17.80	10.07	7.73
Age-standardized mortality rate (per 100,000)	10.01	11.87	8.31	9.93	11.80	8.20	9.84	11.81	8.03	9.68	11.78	7.83
Estimated YLLs (10,000)	271.31	157.40	113.90	293.73	169.90	123.84	318.53	184.69	133.84	377.57	218.18	159.39
Age-standardized YLL rate (per 100,000)	236.66	280.51	194.22	228.27	270.51	187.61	220.78	262.69	180.65	212.53	255.23	173.21

ASMR: Age-standardized mortality rate; CRC: Colorectal cancer; YLLs: Years of life lost.

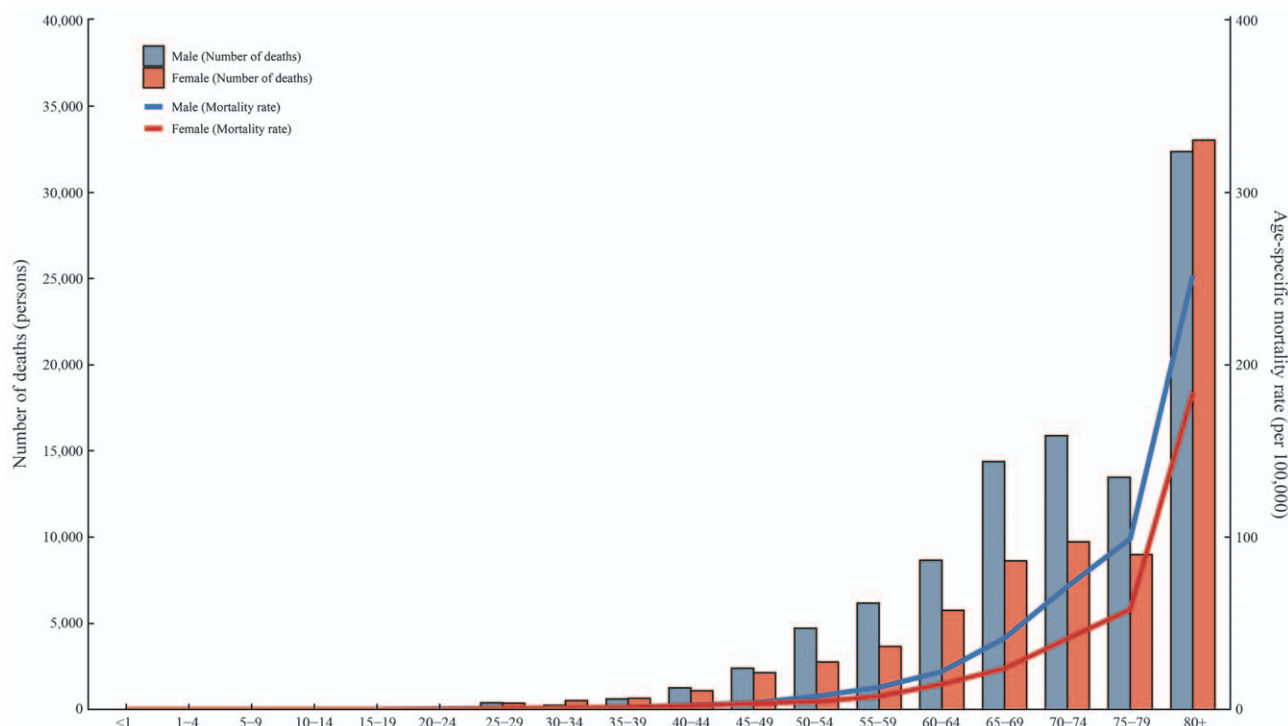


Figure 1: Age-specific deaths and mortality rate of CRC in China, by sex, 2020. CRC: Colorectal cancer.

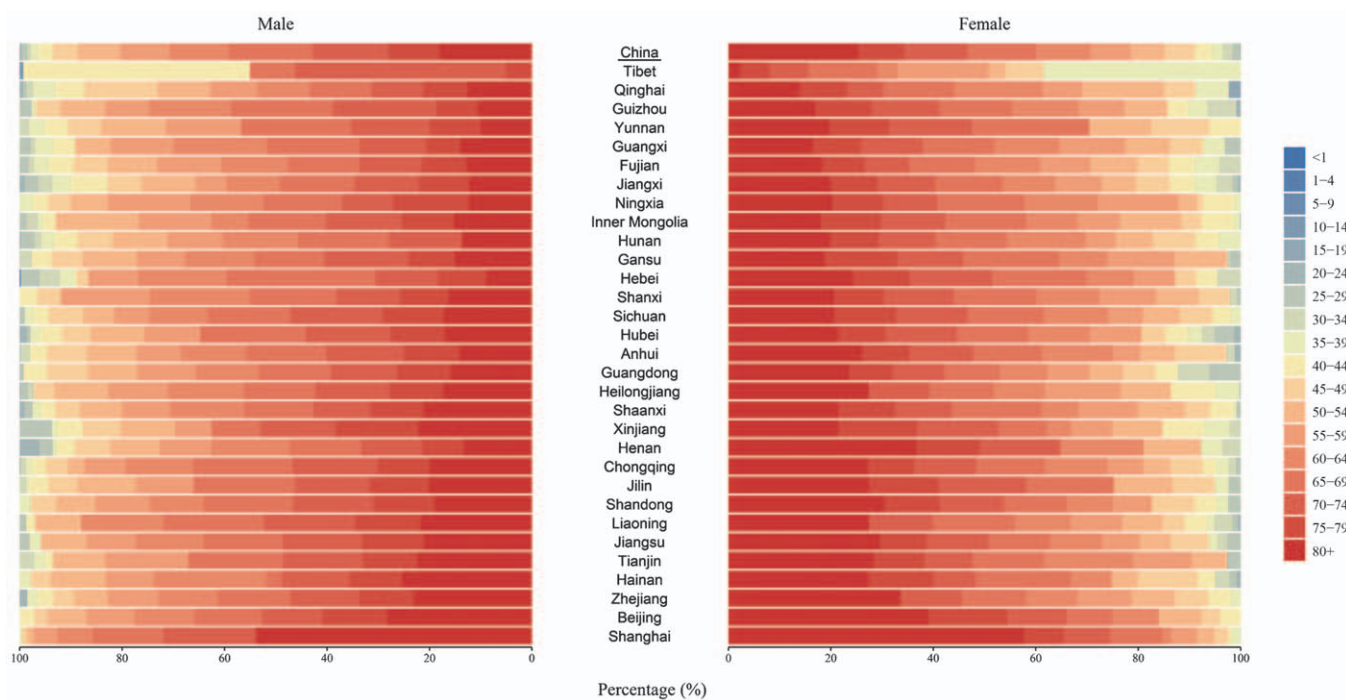


Figure 2: Percentage of YLLs for CRC in China and its provinces, by sex and age, 2020. CRC: Colorectal cancer; YLLs: Years of life lost.

(35.26%). In addition, the top three provinces holding the largest contributions of age- and sex-specific CRC mortality rate decreasing CRC deaths were Hebei (64.86%), Jiangxi (43.43%), and Shanxi (37.71%), whereas the smallest ones were Gansu (0.97%), Chongqing (3.31%), and Qinghai (4.53%).

Discussion

By using data from multi-source on the basis of NMSS, we described temporal trends and geographical variations of premature mortality burden for CRC during 2005–2020 in China and its provinces, with special attention being paid to depict CRC mortality pattern,



Figure 3: ARC heatmap of age-specific YLL rate for total CRC in China and its provinces, between 2005 and 2020. ARC: Annual rate of change; CRC: Colorectal cancer; YLL: Years of life lost.

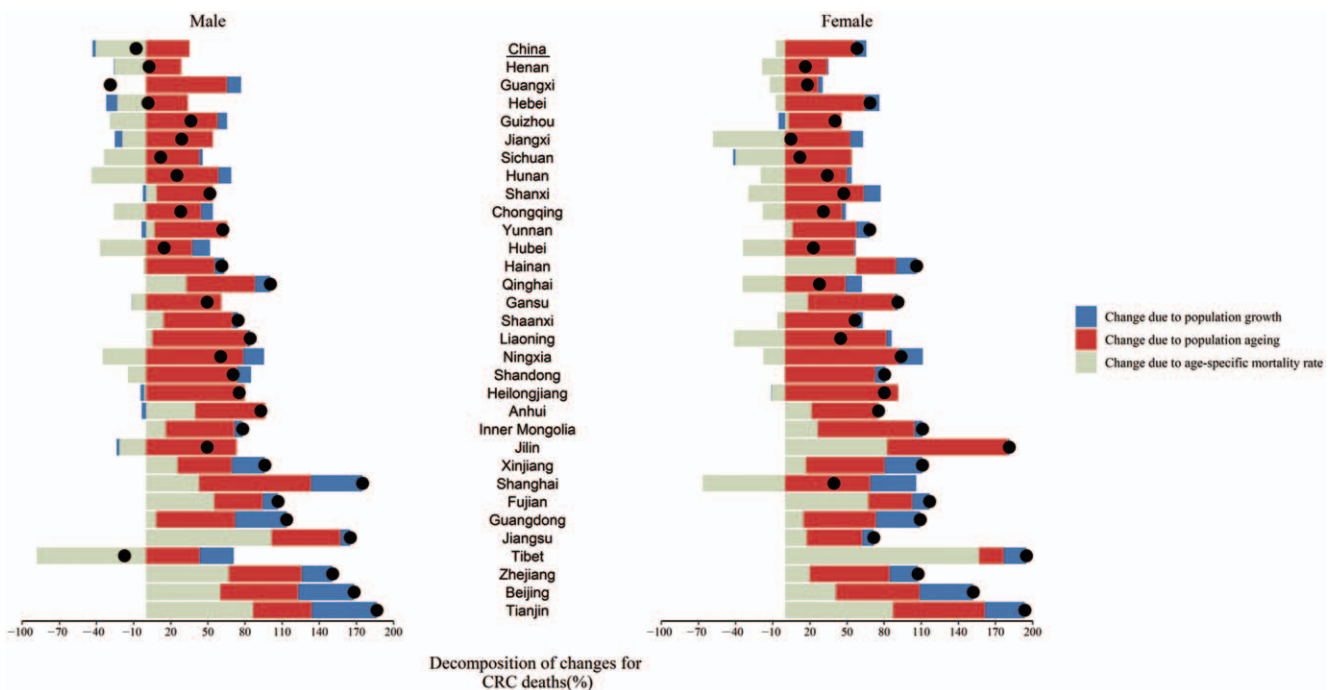


Figure 4: Decomposition of changes for CRC deaths in China and its provinces, by sex, between 2005 and 2020. CRC: Colorectal cancer.

sex differences, and dominant drivers of its change. Comparatively, although there was a decline in CRC mortality, the absolute increase of CRC deaths owing to population aging could not be ignored. The elderly was a high-risk population, and substantial geographical

variations of CRC mortality were observed across the country.

During 2005–2020, the level of CRC ASMR nationwide was lower than the result estimated by the Global Burden

of Disease Study (GBD) (13.69 per 100,000 in 2019),^[20,21] it was also lower than GLOBOCAN 2020 (12.0 per 100,000 in 2020).^[22] Internationally, according to GLOBOCAN 2020, CRC mortality in this study remained at the same level with certain upper-income and upper-middle-income countries, but largely lower than the majority of G20 countries based on GBD2019. Those disparities might be explained by different data sources and methodology used during the estimation process.^[11,23] Previous studies reported that CRC is commonly considered as one of the clearest markers of cancer transition, whereby countries undergoing rapid social and economic changes show rapid increases in cancers that are already more frequent in high-income countries.^[5,24] Thus, three patterns of CRC incidence and mortality trends were identified and ascertained by using the Social Development Index (SDI) and Human Development Index (HDI) as indicators; CRC incidence and mortality rates are still increasing rapidly in many low-income and middle-income countries such as South Africa, Latin America, and South Asia, and these increases are linked to ongoing societal and economic development in countries with low SDI quantile; increasing incidence and decreasing mortality rates are observed in high- to middle-income and middle-income countries with both high SDI and HDI, such as Canada and some European countries; stabilizing or decreasing CRC incidence and mortality trend tend to be seen only in highly developed countries such as North America, Japan, and Australia, where rates remain among the highest in the world.^[1,5,24] As a stable and even subtle downward trend of CRC, mortality was observed in this study during 2005–2020 in China, and this could be related to enhanced availability of healthcare resources, which favor the dissemination of best practices in cancer treatment and management, the early screening, and diagnosis services.^[5,24-26]

Sex- and age-specific disparities of CRC premature mortality were presented substantially. Compared with men, women experienced a less severe burden of CRC premature mortality, and it is more likely to occur in CRC death at an older age, which could be explained by disparities of attributable risk factors among men and women. Alcohol use, smoking, and diets low in calcium, milk, and fiber had considerable attributable CRC burden in men. By contrast, dietary risks, but not alcohol use or smoking, were found to have a considerable attributable burden in women.^[4] Additionally, the elderly aged 60 years and older who contributed more than 70% of the premature mortality burden should be closely focused to consolidate CRC mortality prevention. In most cases, population aging was seldom reported since it is regarded as an unmodifiable attribute of increase for CRC deaths. Except for merely exerted challenges of producing a large number of older patients, most of them had multimorbidity. Since inadequate guidelines have clear recommendations for CRC aging group, understanding the effects of aging on CRC mortality in China was imperative to identify major issues that require to be addressed in further research. During 2005–2020, CRC premature mortality burden among younger age groups reduced significantly, whereas that corresponding to the older age group remained stable or even increased, which similarly

can be attributed to the timely screening and accessible cancer treatment and management.^[5,24,27] Especially for surges of CRC premature mortality burden in Tibet during 2005–2020, the explanation might be attributed to labor force emigrations among people age 30–44 years and increased risk factors prevalent among 75 years and older. Targeted strategies should be thus delivered towards those high risk population, especially among males at older age.

The distribution of CRC mortality and its change over time demonstrated substantial geographical variations across the country. CRC mortality of southeast coastal provinces, such as Zhejiang, Fujian, Guangdong, and Southwest parts of China, such as Sichuan and Chongqing, had largely exceeded the national level, while most of the inland regions, such as middle and north provinces, remained at a lower level. Despite a high CRC mortality at baseline in 2005, Jiangsu, Anhui, Zhejiang, Fujian, Beijing, and Tianjin still got their CRC mortality uncontrolled for a substantial increase by more than 20% during the past 16 years. The shifts and geographical variations at a provincial level might be largely associated with unequal distribution of CRC mortality risk factors, such as unhealthy lifestyles (including dietary patterns, physical inactivity, smoking, and excessive drinking), inadequate medical treatment, metabolic factors, and genetic susceptibility.^[4,5] The marked differences in dietary factors were regarded as the largest contributor. In countries or regions with high SDI and HDI, a dietary pattern characterized by a high intake of red or processed meat, sugar-sweetened beverages, refined grains, desserts, and potatoes was associated with a higher risk of CRC.^[5] As coastal provinces and areas of Beijing, Tianjin, Shanghai far exceed national average economic conditions, local residents have adopted westernized dietary patterns, thus increasing the risk of CRC mortality.^[5] Additionally, as reported by a previous study, there was a positive association between provincial-level population attributable fraction (PAF) of CRC and related risk factors, such as low dietary calcium consumption, low dietary fiber consumption, alcohol drinking, excess body weight, smoking, diabetes, physical inactivity, and consumption of red meat and processed meat. For example, Heilongjiang showed the highest PAF of low dietary calcium consumption and low dietary fiber consumption, along with the highest CRC disease burden, and Tibet showed the lowest PAF of the abovementioned risk factors and corresponding CRC burden.^[28]

Available evidence and inspiring population prevention and treatment practice have proved that CRC is largely preventable.^[5,6] For example, the contribution of lifestyle-related risk factor modifications to reduce the CRC burden is about 40%, and CRC screening with stool-based tests for occult blood or with endoscopic methods is associated with a reduction in CRC incidence and mortality.^[5,29,30] Therefore, lifestyle intervention, especially healthy dietary pattern promotion such as discouraging the consumption of high-energy, obesogenic foods, are commonly regarded as the most important in primary prevention.^[5] For secondary prevention, despite early CRC screening being available in many Chinese cities, initial screening uptake rates remained low. According to data published by the

National Cancer Center of China in 2019, the Chinese Urban Cancer Screening Program conducted in 2012–2015 yielded only a 14% participation rate of colonoscopy screening combined with risk scores.^[30,31] Therefore, CRC screening compliance needs to be improved urgently, including elements such as colonoscopy, flexible sigmoidoscopy, fecal occult blood testing (FOBT), and fecal immunochemical testing (FIT).^[6,29] In practice, CRC screening in China is conducted through using two-step approaches similar to most of the other countries. In the first step, the high-risk groups are identified through CRC screening scores, questionnaires, or common initial screening tests. Afterward, those individuals with high scores or positive results in fecal immunochemical tests and stool DNA tests are considered high risk and undergo colonoscopy.^[30,32] Additionally, in turn, regular screening could offer opportunities toward the public to convey health education messages and subsequently to change health attitudes and thus modify health behaviors.^[5] Additionally, the progress of CRC diagnosis and treatment technology also needed to be substantially advanced, especially for imageological examination, radical surgery, targeted therapy, management of CRC metastasis, and palliative care.^[4,33,34] Other than specific prevention approaches, the suitability of CRC prevention and control measures should also be considered, as unequal distribution of CRC mortality burden and limited healthcare resources were provided in the country, such as maximizing the health benefits of risk factor control, the rationale of choosing targeted regions and population of early screening in CRC, and the feasibility of expanding CRC health-care service coverage.^[26]

To our knowledge, this study was one of the limited research studies that provided comprehensive and explicit estimates of the premature mortality burden caused by CRC in China. By using high-quality data from NMSS, we demonstrated comparable results by selected characteristics over time across the country. However, this study is limited to several limitations. First, ascertainment bias caused by reporting accuracy of COD may attenuate the quantity and quality of CRC mortality estimation, but we worked to through garbage code redistribution for implausible diagnostic. Second, we failed to present the result based on a scientifically defined urban/rural stratification, since we roughly defined counties as rural areas and districts as urban areas; this vague classification may improperly interpret urban/rural disparities in guiding policies. Third, since the CRC mortality result for 2019–2020 was projected by using the existing 2005–2018 data, the accuracy and validity should be used and interpreted as evidence with caution.

China has the world's largest number of CRC deaths, representing a threat to the health of individuals and a heavy socioeconomic burden. Currently, prevention is the priority to reduce CRC premature mortality burden, and it is suggested to be achieved through promoting a healthy lifestyle, especially the optimization of the dietary patterns, optimizing cost-effective early screening and diagnosis strategies for high-risk individuals, implementing strict guidelines for proper oncological treatment, and broadening the accessibility and coverage of CRC health-care services.^[35] Moreover, as the CRC mortality burden is

closely related to socio-economic development, tailored initiatives that vary according to regional and population characteristics are essential.^[1,4-6,26]

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Conflicts of interest

None.

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