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Analysis

Assessing cross-country inequalities in global burden of gastrointestinal cancers: slope and concentration index approach

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Abstract

Purpose New cases and deaths of gastrointestinal cancers are predicted to increase significantly by 2040. This study aims to explore cross-country inequalities and trends in global burdens of colon and rectum cancer (CRC), esophageal cancer (EC) and gastric cancer (GC).

Methods Data from the Global Burden of Diseases Study 2019 were analyzed to examine trends in disability-adjusted life-years (DALYs) for three gastrointestinal cancers with estimated annual percentage change (EAPC) and Joinpoint analysis. Inequality in their DALYs rates was assessed with the slope index of inequality and the concentration index, based on the Socio-Demographic Index (SDI).

Results From 1990 to 2019, the age standardized DALYs rate of CRC decreased in these countries from high and high-middle SDI regions, with the EAPC values of – 1.018% and – 0.161%, respectively, but increased among low, low-middle and middle SDI regions (EAPC = 1.035%, 0.926% and 0.406%, respectively). The age standardized DALYs rates of EC and GC decreased in all SDI regions. Moreover, the slope index changed from 358.42 (95% confidence interval 343.28 to 370.49) to 245.13 (217.47 to 271.24) for CRC, from – 63.88 (– 87.48 to – 48.28) to – 1.36 (– 32.44 to 25.87) for EC, and from 126.37 (101.97 to 146.47) to 58.04 (20.54 to 96.12) for GC. The concentration index for CRC moved from 29.56 (28.99 to 29.84) to 23.90 (23.19 to 24.26), from – 9.47 (– 10.30 to – 9.24) to – 14.64 (– 15.35 to – 14.24) for EC, and from 8.44 (7.85 to 8.72) to – 6.42 (– 7.65 to – 6.12) for GC.

Conclusion This study suggests strong heterogeneity in global DALYs for gastrointestinal cancers across different SDI regions. Higher SDI regions faced a greater burden of CRC, while the burdens of EC and GC were more prevalent in lower SDI regions.

Keywords Health inequality · Disability-adjusted life-years (DALYs) · Gastrointestinal cancers · Socio-Demographic Index (SDI)

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Abbreviations

CRC Colon and rectum cancer
EC Esophageal cancer
GC Gastric cancer
EAPC Estimated annual percentage change
DALYs Disability-adjusted life-years
SDI Socio-Demographic Index
CI Confidence interval
WHO World Health Organization
GBD Global Burden of Diseases, Injuries, and Risk Factors
YLDs Years of life lived with disability
YLLs Years of life lost
NCI National Cancer Institute
GDP Gross Domestic Product

1 Introduction

Gastrointestinal cancers are one of the leading causes of death [1]. According to the predictions of global mortality and incidence of cancer [2], new cases and deaths of gastrointestinal cancers are expected to increase significantly by 2040. Colon and rectum cancer (CRC) ranks the third among the most common cancers in the world, gastric cancer (GC) ranks sixth and esophageal cancer (EC) ranks the eighth. According to the report by World Health Organization (WHO) in 2020 [1], there were 1,089,103 new cases and 768,793 deaths from GC worldwide, 604,100 new cases and 544,076 deaths from EC and a total of 1,880,725 new cases and 915,880 deaths from CRC. Gastrointestinal related cancers cause a huge burden of disease [3].

The geographical distribution of different gastrointestinal-related cancers varies greatly [4–7]. The incidence rate of CRC is high in Europe, North America, Australia, New Zealand, East Asia [4]. The incidence rate of GC is high in East Asia, Western Europe, South America [5]. The incidence rate of EC is high in East Asia, South Africa, East Africa and Northern Europe [6, 7]. Gastrointestinal related cancers are an important obstacle to improving life expectancy.

The levels of social and digital development vary in different regions. The Global Burden of Diseases, Injuries, and Risk Factors (GBD) studies have become an important tool for major organizations and countries to provide epidemiological evidence and formulate relevant health policies. It can not only assess the incidence, prevalence, and mortality rate of diseases, but also assess the disease burden index including disability-adjusted life-years (DALYs), years lived with disability (YLDs), and years of life lost (YLLs). The GBD 2019 study covers 204 countries and territories and divides them into five levels based on the Socio-Demographic Index (SDI), including low, low-middle, middle, high-middle, and high SDI, allowing for the comparison of countries based on their social and demographic development levels [8, 9]. The SDI serves as a standardized measure that allows us to examine the relationship between socioeconomic status and cancer burden across diverse national contexts, providing a consistent framework to study disparities in gastrointestinal cancer burden globally [9].

In this study, we employ an ecological study design to focus on colorectal cancer (CRC), esophageal cancer (EC), and gastric cancer (GC) due to their significant impact on global health [10]. Ecological studies analyze population-level data to identify broad patterns and trends, making them particularly suitable for examining how socioeconomic development, as represented by the Socio-Demographic Index (SDI), relates to disparities in cancer burden [11]. These cancers contribute substantially to the overall burden of gastrointestinal cancers, with distinct epidemiological patterns and significant variations in prevalence and mortality across regions [4–7]. This variability makes them suitable models for exploring how differences in socioeconomic development, as represented by the SDI, relate to disparities in cancer burden [11].

This study employs the inequality analysis methods recommended by the WHO to investigate whether there are socioeconomic disparities in the DALYs burden of gastrointestinal cancers across countries or regions, and to further determine the extent and trends of these disparities [10]. Our research aims to provide epidemiological evidence to inform public health policymakers in prioritizing resource allocation, thereby helping to address inequalities in cancer burden and contributing to efforts to reduce global health disparities.

2 Methods

2.1 Data source

The GBD 2019 study is a systematic effort to estimate incidence, prevalence, mortality, YLLs, YLDs, and DALYs for 369 causes of death and disability and 87 risk factors and groups of risk factors at the global level, regionally, and for 204 countries and territories. Data for CRC, EC, and GC each year were extracted from the GHDx section of the GBD Results Tool (http://ghdx.healthdata.org/). The original data for CRC, EC, and GC were obtained from vital registrations, vital registration samples, verbal autopsies, hospital and claims data, literature data, and epidemiological survey data [3]. Age standardized rates of DALYs for CRC, EC, and GC were computed based on the global population reported by GBD [3]. This study utilized the SDI to describe DALYs for CRC, EC, and GC across different regions. The SDI is closely related to social development status and population health outcomes according to per-capita income, total fertility rate, and average education level [8].

2.2 Description of the burden of disease and percent changes

This study used linear regression to evaluated annual percentage change (EAPC) of the age standardized DALYs rate of CRC, EC and GC over years. In the linear regression, the natural logarithm of the DALYs rate was used as the dependent variable and the year as the independent variable. A positive EAPC value represented an increase in the DALYs rate from 1990 to 2019, while a negative value indicated a decrease. We computed the EAPC by age and sex using the following general formula:

$$y = \alpha + \beta x + \varepsilon$$

$$y = \ln(\text{rate}),\ x = \text{calendar year}$$

$$\text{EAPC} = 100 \times \left(e^{\beta} - 1\right)$$

The joinpoints of percent changes in DALYs rate of the three cancers from 1990 to 2019 were calculated using the Joinpoint regression model. The annual percent changes and their statistically significant differences for each trend phases were calculated using the National Cancer Institute (NCI) Joinpoint regression program software (version 4.1.0; Statistical Research and Applications Branch, NCI). A positive value of annual percent change represented an increase in the DALYs rate over time, while a negative value indicated a decrease. Each SDI region was set up to three joinpoints to function.

2.3 Cross-country inequality analysis

The inequalities in the distribution of the cancer burden among countries were quantified through absolute inequality and relative inequality. The slope index and concentration index of inequality, as proposed by the WHO [11–13], were used to evaluate absolute and relative inequality. These calculations involved weighting by population size to quantify inequality while accounting for differences in population distribution.

The slope index of inequality was calculated by ranking a weighted sample of the entire population from the lowest SDI subgroup to the highest SDI subgroup. An appropriate model was then used to regress the DALYs rate with the midpoint of the SDI groups, and the predicted values for the two extreme SDI regions were calculated. The difference between these two predicted values generated the slope index of inequality. A positive value represented that the DALYs rate was more common in high SDI regions, while a negative value indicated the opposite.

The indicator for measuring relative inequality was the concentration index. We used the concentration curve to illustrate the concentration index. The weighted samples of the entire population were sorted based on SDI from the most vulnerable subgroup to the most favorable subgroup (x-axis). The y-axis represented the cumulative fraction corresponding to the DALYs rate of each subgroup. The concentration curve was then drawn by connecting these points. The line connecting the bottom left corner to the top right corner was called the equality line. When the concentration curve was below the equality line, it indicated that the DALYs rate was concentrated in the high SDI subgroup. Conversely, when the concentration curve was above the equality line, it indicated that the DALYs rate was concentrated in the low SDI subgroup.

All statistical analyses were conducted using R software (version 4.2.2), Stata software (version 17.0), and ArcMap (version 10.8). A *p* value of < 0.05 was considered to indicate statistically significant differences.

3 Results

3.1 The distribution and trend in age standardized DALYs rate of gastrointestinal cancers

The age standardized DALYs rate of CRC varied remarkably worldwide in 2019 (Supplementary Fig. 1A). The age standardized DALYs rate of CRC decreased in high and high-middle SDI regions (Supplementary Table 1), with EAPC values of – 1.018% and – 0.161%, respectively, but increased in low, low-middle, and middle SDI regions during the study period of 1990–2019 (EAPC = 1.035%, 0.926%, and 0.406%, respectively). Regionally, high and high-middle SDI regions had much higher DALYs rates due to CRC than other SDI regions (Supplementary Fig. 2A and 2B). The most significant DALYs rate occurred in the 95 + years age group (Supplementary Fig. 3A), and males appeared to demonstrate higher DALYs rates than females in most age groups.

The age standardized DALYs rate of EC varied remarkably worldwide in 2019 (Supplementary Fig. 1B). The global age standardized DALYs rate of EC was 139.793 per 100,000 in 2019. From 1990 to 2019, EAPC values of EC were negative for all SDI regions (Supplementary Table 2). The age standardized DALYs rate in the middle SDI region decreased significantly (Supplementary Fig. 2C). EC had a much higher burden in middle and high-middle SDI regions than in other SDI regions (Supplementary Fig. 2C). The most significant DALYs rate occurred in the 70–74 years age group, and the DALYs rate of EC in males was higher than in females across all age groups (Supplementary Fig. 3B).

The age standardized DALYs rate of GC varied remarkably worldwide in 2019 (Supplementary Fig. 1C). Regionally, the age standardized DALYs rate of GC in the middle SDI region was the highest in 2019, with a value of 323.393 per 100,000. EAPC values of GC were negative for all SDI regions (Supplementary Table 3). The age standardized DALYs rate decreased in all SDI regions (Supplementary Fig. 2E). The crude DALYs rate also showed a general downward trend (Supplementary Fig. 2F). Compared to other SDI regions, the high-middle and middle SDI regions had significantly higher age standardized DALYs rates due to GC (Supplementary Fig. 2E). The most significant DALYs rate occurred in the 70–74 years age group, and in most age groups, the DALYs rate in males was higher than in females (Supplementary Fig. 3C).

3.2 Cross-country inequality of cancers

3.2.1 Colon and rectum cancer

It was observed that countries with higher SDI had a higher burden in absolute and relative inequalities in 1990 and 2019 (Fig. 1A–D). As shown by the slope index of inequality, the difference in DALYs rate between the highest and lowest SDI countries decreased from 358.42 (95% confidence interval [CI] 343.28–370.49) in 1990 to 245.13 (95% CI 217.47–271.24) in 2019. The concentration index was 29.56 (95% CI 28.99–29.84) in 1990 and 23.90 (95% CI 23.19–24.26) in 2019. Furthermore, the slope index and concentration index of inequalities showed a general downward trend from 1990 to 2019.

3.2.2 Esophageal cancer

It was observed that countries with lower SDI had a higher burden in absolute and relative inequalities in 1990 and 2019 (Fig. 2A–D). As shown by the slope index of inequality, the difference in DALYs rate between the highest and lowest SDI countries changed from – 63.88 (95% CI – 87.48 to – 48.28) in 1990 to – 1.36 (95% CI – 32.44 to 25.87) in 2019. The concentration index was – 9.47 (95% CI – 10.30 to – 9.24) in 1990 and – 14.64 (95% CI – 15.35 to – 14.24) in 2019. Moreover, the absolute value of the slope index of inequality showed an upward trend from 1990 to 2005, becoming positive in 2002, decreasing from 2005 to 2019, and becoming negative in 2017. The concentration index of inequality showed a general downward trend from 1990 to 2019.

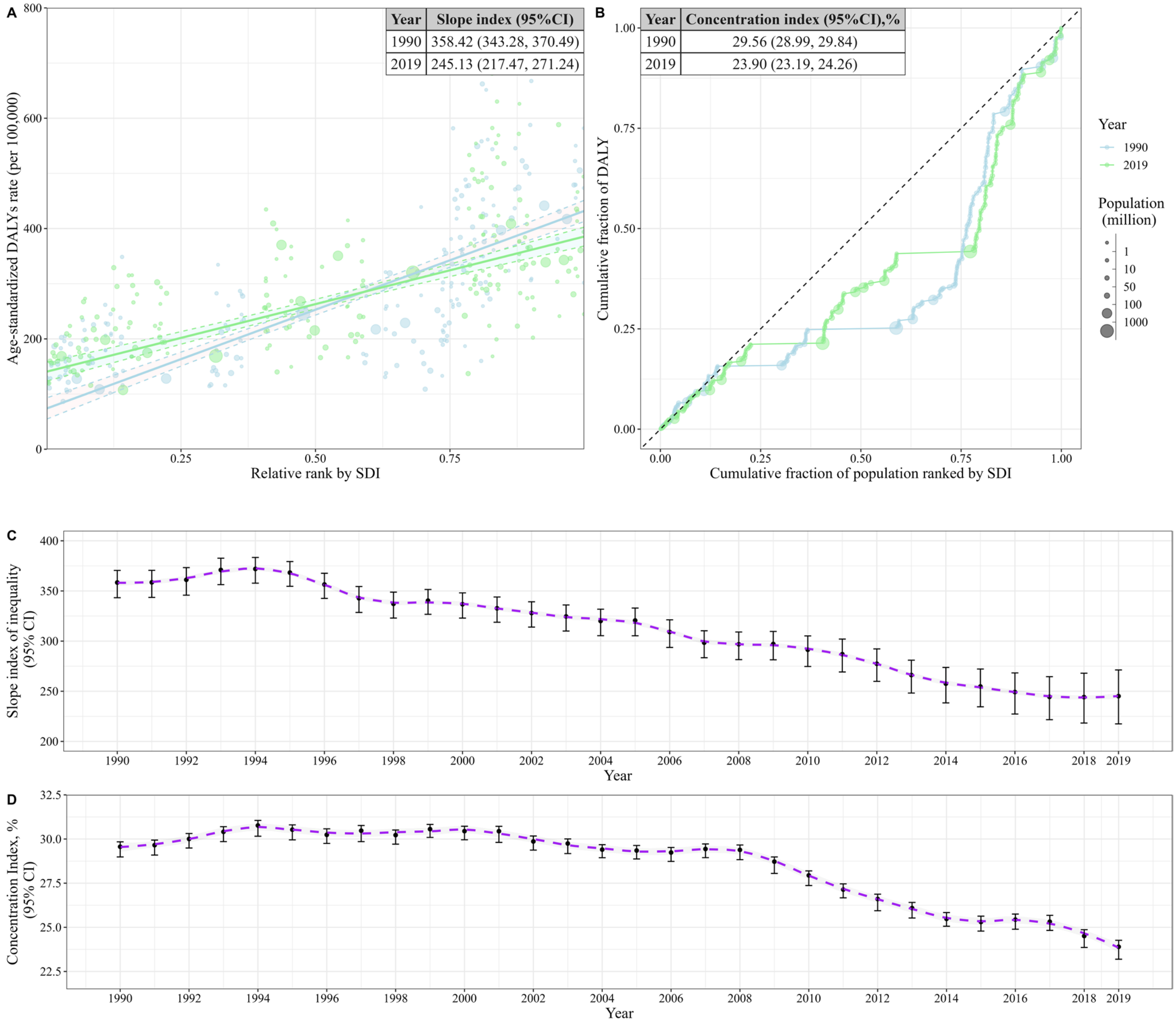

Fig. 1 Health inequality regression curves and concentration curves for the DALYs of CRC. *DALYs* disability-adjusted life-years, *CI* confidence interval, *CRC* colon and rectum cancer

3.2.3 Gastric cancer

It was observed that countries with higher SDI had a higher burden in absolute inequality in 1990 and 2019 (Fig. 3A–D). The countries with higher SDI had a higher burden in relative inequality in 1990, but in 2019, the countries with higher SDI had a lower burden in relative inequality. As shown by the slope index of inequality, the difference in DALYs rate between the highest and lowest SDI countries decreased from 126.37 (95% CI 101.97 to 146.47) in 1990 to 58.04 (95% CI 20.54 to 96.12) in 2019. The concentration index was 8.44 (95% CI 7.85 to 8.72) in 1990 and − 6.42 (95% CI − 7.65 to − 6.12) in 2019. In addition, the slope index of inequality showed a trend of first decreasing, then increasing, and finally decreasing, while the absolute value of the concentration index of inequality showed a trend of first decreasing and then increasing.

Overall, in 2019, from the perspective of the slope index of inequality, high SDI countries bore relatively more of the burden caused by CRC and GC, while low SDI countries bore more of the burden caused by EC. From the perspective of the concentration index, high SDI countries bore relatively more of the burden caused by CRC, while low SDI countries bore more of the burden caused by EC and GC.

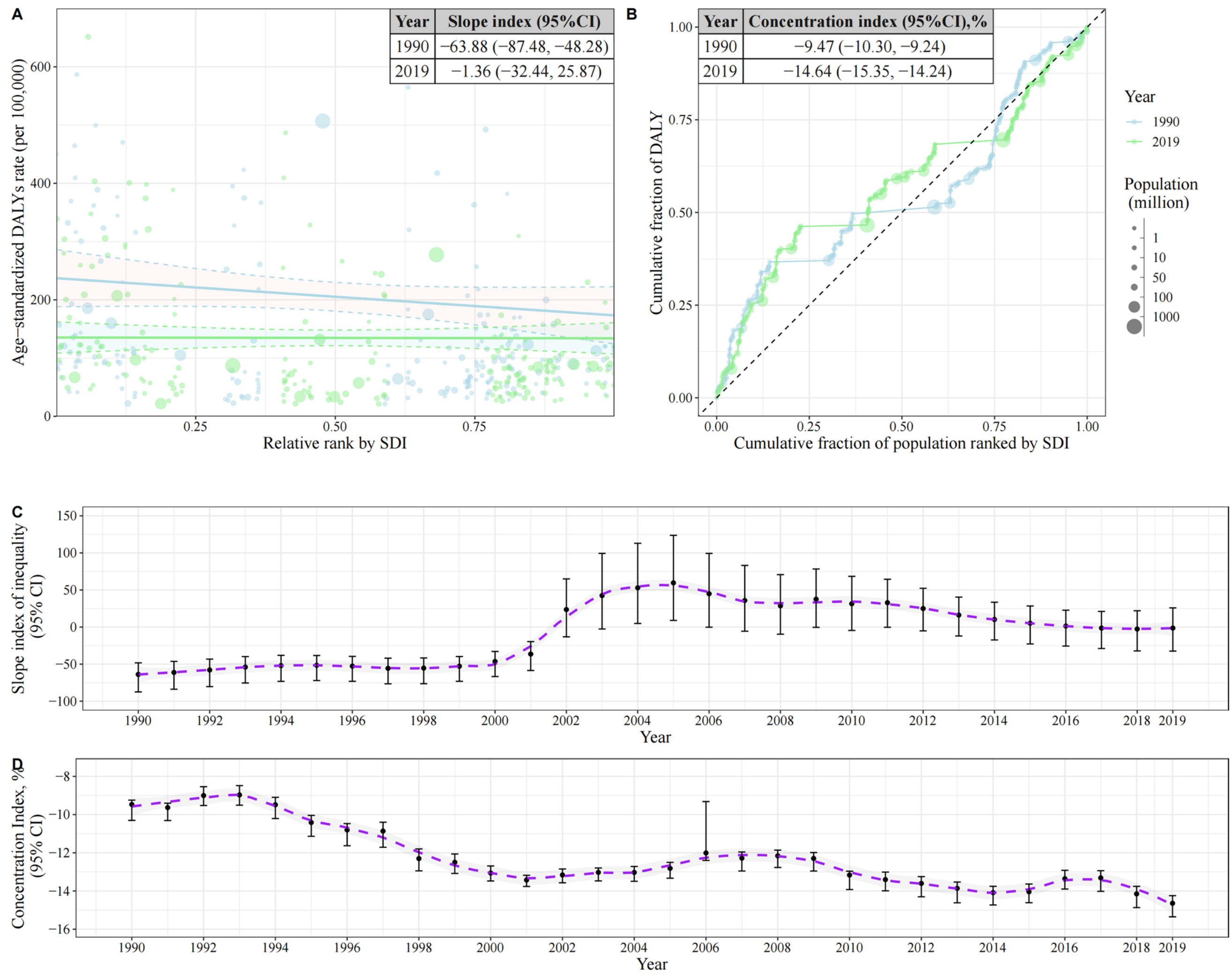

Fig. 2 Health inequality regression curves and concentration curves for the DALYs of EC. *DALYs* disability-adjusted life-years, *CI* confidence interval, *EC* esophageal cancer

4 Discussion

In this study, we described the disease burden and age, gender, and geographical distribution of CRC, EC, and GC, and analyzed the cross-country inequalities in the disease burden of these three cancers. The great advantage of our research is that it shows the cross-country inequalities in different SDI levels related to CRC, EC, and GC. Our article could provide epidemiological evidence for the global inequalities of gastrointestinal related cancers.

Our research showed that 2004 was a significant joint point for the three types of cancer, with the age standardized DALYs rates of these diseases showing a downward trend. We speculated that this might be related to the improved medical standards. As reported, some molecular targeted therapies can focus on specific molecules in gastrointestinal cancer cells [14, 15]. For example, Bevacizumab was approved in February 2004 for the treatment of CRC [16, 17].

The results of this study showed that compared to low SDI countries, high SDI countries bore a greater burden of disease related to CRC. The burden of CRC varied greatly, depending on geographical region, gender, age and socio-economic status [18]. Common sense believed that compared to high SDI countries, low SDI countries would suffer a greater burden of CRC. However, the results of our study indicate that countries with high SDI actually had disproportionately a higher disease burden. This might be because the lifestyle of people in countries with high SDI increased the incidence rate of cancer. Related studies have shown that individual factors such as overweight or obesity, other disease burdens, and lifestyle habits such as consuming processed meat and alcohol could increase the risk of CRC

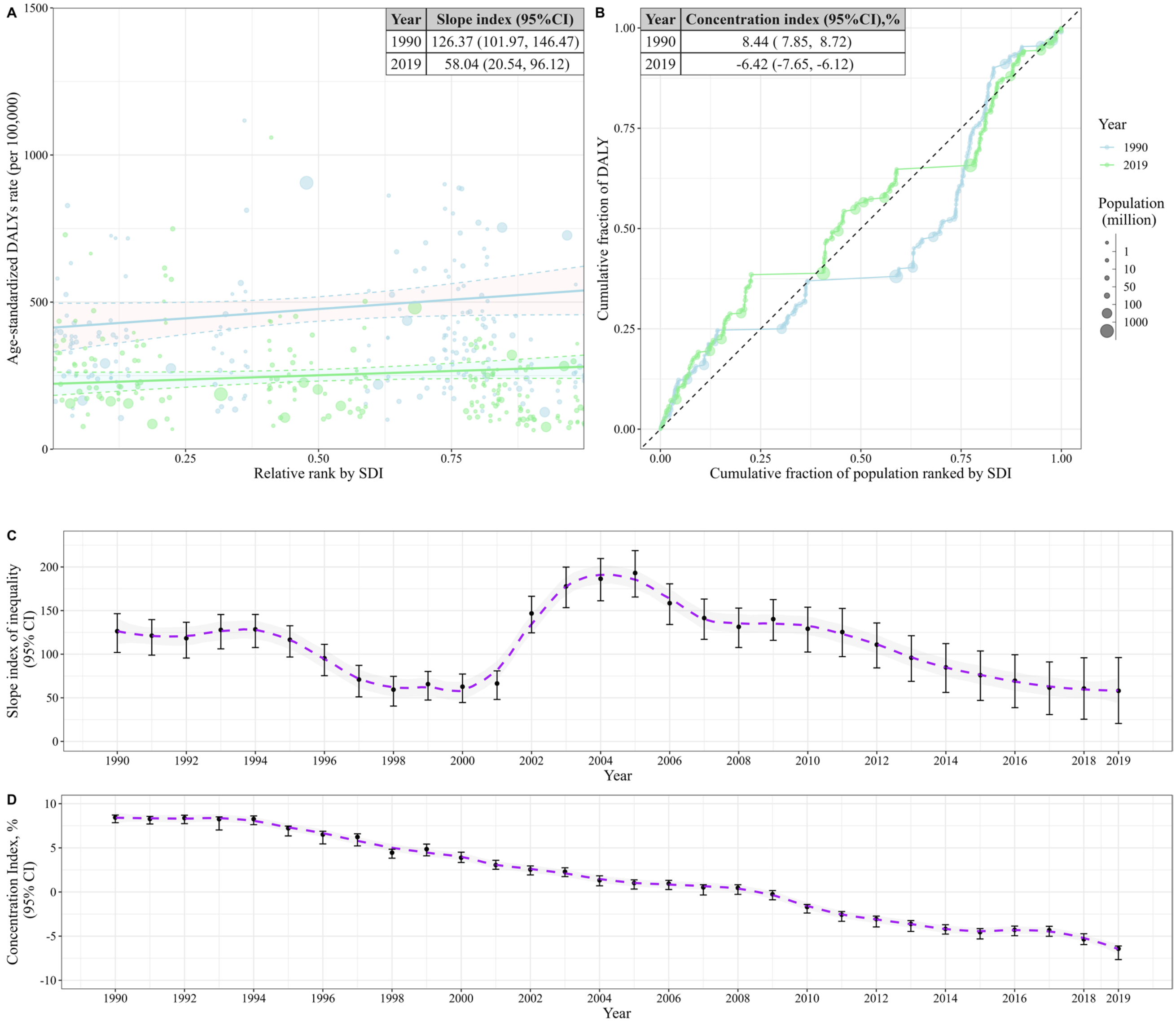

Fig. 3 Health inequality regression curves and concentration curves for the DALYs of GC. *DALYs* disability-adjusted life-years, *CI* confidence interval, *GC* gastric cancer

[19–21]. Many risk factors for CRC, such as sedentary lifestyle and dietary patterns in developed Western countries, are common behaviors among people in high SDI countries [22]. The study by Hongmeizhu et al. suggested that areas with high SDI should pay more attention to CRC [23]. A Chinese study also showed that the age standardized incidence rate of CRC was positively correlated with Gross Domestic Product (GDP) per capita. GDP measures the total value of goods and services produced in a country and is often used as an indicator of economic performance and living standards [24]. In our study, GDP is relevant because it is used to calculate per capita income, which is one of the important indicators for estimating SDI [3]. A study on the global disease burden of CRC had concluded that the incidence rate of CRC in more developed regions was 2.5 times that in less developed regions, and the mortality rate was twice that in less developed regions [25, 26].

Our study concluded that in low SDI regions, there is a relatively greater burden of disease caused by EC. This is similar to the research results of Yang Zhixun et al., who found that the incidence rate and mortality of EC were higher in middle and low GDP regions than in high GDP regions [25].

Due to the lack of specific symptoms of early EC, most tumors are diagnosed in the late stage and rapidly progressed to the late stage when treatment options are limited and cure is impossible. In high-income environments, only about a quarter of EC patients survive within 5 years after diagnosis [27]. Therefore, disease prevention is particularly important.

Risk factors for developing EC included smoking and alcohol abuse [28–31], drinking hot tea [32, 33], poor oral health [34], and low intake of fresh fruits and vegetables [35, 36]. Relevant departments or governments can develop prevention strategies to reduce the risk of disease occurrence, such as discouraging smoking and alcohol consumption, promoting dental care, encouraging the consumption of fruits and vegetables, and incorporating foods with high antioxidant properties into local diets.

The results of our study indicated that the slope of inequality related to GC was positive, suggesting that high SDI countries bore more of the burden caused by GC. However, from the perspective of the concentration index, starting from 2009, the concentration index became negative, indicating that low SDI countries bore more of the burden caused by GC. This finding was inconsistent with the results of absolute inequality. The reason for this discrepancy is that the slope index evaluating absolute inequality only represents the difference in predicted values between the highest and lowest SDI levels, while the concentration index evaluating relative inequality considers all SDI subgroups. Relevant explanations can be found in this book published by the WHO [11].

For GC, low SDI regions have borne a greater burden of disease since 2009. On a global scale, many studies have also reached similar conclusions [23, 25, 27]. The diagnosis and treatment costs of GC are high, and we should adhere to the principle of prevention first. Research has shown that taking vitamin D supplements was an effective way to reduce cancer risk [37]. Studies in high-risk areas such as Japan and Korea found that screening also leads to a significant reduction in GC related mortality [38–40].

Several limitations should be noted in our study. First, the timeframe of 1990 to 2019 covers a period with significant changes in diagnostic and treatment methods, which may affect the comparability of cancer burden over time. Second, distinguishing between esophageal and gastric cancers, particularly at the gastroesophageal junction, remains challenging, potentially impacting the accuracy of classification. Third, variations in data quality and completeness, especially in low-SDI areas, may introduce biases despite the use of statistical modeling by the GBD study. Additionally, this study focuses exclusively on CRC, EC, and GC, and does not include other gastrointestinal cancers. This may limit the generalizability of our findings to the broader spectrum of gastrointestinal malignancies and may not capture the full extent of disparities in cancer burden across all types of gastrointestinal cancers. Fourth, while SDI helps standardize socioeconomic differences, it does not fully account for variations in healthcare access, cultural factors, and cancer screening practices across countries. Fifth, this study employs an ecological design, analyzing aggregated population-level data rather than individual-level data. This approach is subject to ecological fallacy, where associations observed at the group level may not hold true at the individual level, potentially limiting the ability to draw causal inferences. Therefore, our study is intended to highlight broad, cross-country trends in cancer burden rather than individual-level causal inferences. Lastly, reliance on GBD data means that the findings are subject to the limitations of its data collection and estimation methods. Future research could explore the factors driving cancer burden inequalities, such as differences in risk factors, healthcare infrastructure, and cultural attitudes in countries with varying SDI levels. Additionally, incorporating high-quality local data and studying cross-national collaborations may enhance understanding and inform strategies to address global health inequalities in cancer.

5 Conclusion

This study provides a comprehensive analysis of cross-country inequalities in the burden of colorectal, esophageal, and gastric cancers, highlighting the influence of socioeconomic disparities as measured by the SDI. Countries with higher levels of social and demographic development bore a higher burden of CRC. EC and GC now pose a greater disease burden in low SDI areas than in high SDI areas. These variations underscore the need for targeted public health interventions that consider socioeconomic contexts to address cancer-related health disparities. By providing epidemiological evidence on global inequalities in gastrointestinal cancer burden, our study offers insights that can inform resource allocation and policy decisions. Policymakers should prioritize healthcare resources for regions with high disease burdens relative to their SDI levels, as this approach could help mitigate cancer disparities and promote more equitable health outcomes on a global scale.

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Author contributions X.L. conceived of the study and participated in its design and coordination. H.Z. and Y.W. led the data collection and analysis, wrote the original draft and oversaw the editing of the final manuscript. F.W., R.M., Y.Y., S.U., Y.Z. and Y.W. contributed to the drafting and revision of the article and read and approved the final manuscript.

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Data availability The datasets analyzed in the current study are available in the GBD repository, https://vizhub.healthdata.org/gbd-results.

Declarations

Ethics approval and consent to participate The datasets analyzed during the current study are published and available in the [Global Burden of Disease Database] repository. Thus, ethics approval and patient consent to participate were not applicable in this study.

Consent for publication Figure, table and other information are confirmed and approved for publication.

Competing interests The authors declare no competing interests.

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