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ORIGINAL ARTICLE

Esophageal cancer global burden profiles, trends, and contributors

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ABSTRACT

Objective: This study aimed to provide a comprehensive overview of the global burden of esophageal cancer (EC) and determine the temporal trends and factors influencing changes in the global burden.

Methods: The latest incidence and mortality data for EC worldwide were obtained from GLOBALCAN 2022. The mortality and disability-adjusted life years (DALYs) rates for EC from 1990–2019 were sourced from the 2019 Global Burden of Diseases. Trends in EC mortality and DALYs attributable to 11 risk factors or clusters of risk were analyzed using the joinpoint regression model. The trends in age-related EC burden were assessed using a decomposition approach.

Results: An estimated 511,054 new cases of EC were diagnosed in 2022 with 445,391 deaths worldwide. Approximately 75% of cases and deaths occurred in Asia. Nearly 50% of global EC deaths and DALYs were attributed to tobacco use in men in 2019, while 20% were attributed to high body mass index (BMI) in women. From 1990–2019, EC deaths and DALYs attributable to almost all risk factors had declining trends, while EC deaths and DALYs attributed to high BMI in men had upward trends. The age-related EC burden exhibited an upward trend driven by population growth and aging, which contributed to 307.4 thousand deaths and 7.2 million DALYs due to EC.

Conclusions: The EC burden remains substantial worldwide. Effective tobacco and obesity control measures are critical for addressing the risk-attributable burden of EC. Population growth and aging pose challenges for EC prevention and control efforts.

KEYWORDS Esophageal cancer; incidence; mortality; disability-adjusted life years; risk factors; aging; trends

Introduction

Esophageal cancer (EC) is ranked as the 11th most common cancer and the 7th leading cause of cancer-related deaths worldwide[1]. Contributors to the EC burden include modifiable and non-modifiable risk factors[2,3]. Modifiable risk factors for EC include behavioral factors, such as smoking, alcohol consumption, and dietary habits, as well as metabolic factors, such as obesity[3-7]. EC is also associated with non-modifiable risk factors, such as aging. Trends in the EC burden are influenced by demographic shifts. Population aging contributes, in part, to the age-related burden of EC[2,8]. Monitoring these trends and understanding the contributors to the EC burden on a global scale is essential for the development and adaptation of targeted cancer prevention and control strategies, as well as for the rational allocation of public health resources.

Therefore, this study aimed to provide a comprehensive overview of the global burden of EC based on data from GLOBALCAN 2022[1,9], and to investigate the temporal trends and contributors influencing changes in the EC burden based on the comprehensive data from the 2019 Global Burden of Diseases study[10]. This study sought to offer insights into the adjustment and optimization of EC prevention and control policies.

Materials and methods

Data source

The global incidence and mortality rates for EC in 2022 were extracted from the GLOBOCAN 2022 database[1,9]. Age-standardized incidence rates (ASIRs) and age-standardized

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mortality rates (ASMRs) per 100,000 person-years were calculated based on the 1966 Segi-Doll World standard population[11]. GLOBALCAN 2022 is a project established by the International Agency for Research on Cancer, which enabled a comprehensive assessment of the cancer burden for 2022 in 185 countries or territories across 36 cancer types categorized by gender and age group. This assessment is based on the collection, aggregation, and estimation of national cancer registry data. The methodology adopted for estimating the incidence and mortality at the national level is described in detail elsewhere[9,12]. In brief, incidence and mortality rates were initially obtained from national or sub-national cancer registries for the most recent years and short-term prediction models were used to project the corresponding rates for 2022. In cases for which no reliable cancer registry data were available, incidence or mortality rates from neighboring countries were applied to estimate national incidence or mortality rates within the country.

The mortality and disability-adjusted life years (DALYs) rates for EC with population data from 1990–2019 were obtained from the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2019[10]. The corresponding age-standardized rates were calculated using the GBD world population[10]. The GBD 2019 analysis provided a comprehensive evaluation of the global burden attributed to 369 diseases and injuries across 204 countries and territories. GBD 2019 conducted a systematic and scientifically rigorous assessment utilizing published, publicly accessible, and contributed data on disease and injury incidence, prevalence, and mortality rates. This meticulous analysis encompassed a thorough examination of a mutually exclusive and collectively exhaustive list of diseases and injuries. Access to all data relevant to this study is available to the public through the Global Health Data Exchange website (http://healthdata.org/).

The International Classification of Diseases (ICD-10) system was applied to define EC under the diagnosis codes, C15-C15.9[13].

Statistical analysis

Profiles of EC incidence and mortality in 2022

The number, crude rates, and age-standardized rates of EC incidence and mortality in 2022 were obtained from GLOBALCAN2022 by gender (both genders combined, and male and female separately), world regions, and four-tier human development index (HDI) regions[1]. The ASIR and ASMR were calculated using the 1966 Segi-Doll World Standard population for all ages[11].

Trends in the modifiable risk-attributable EC burden from 1990–2019

The EC burden attributable to modifiable risk factors was assessed in terms of deaths and DALYs. Gender-specific deaths and DALYs rates, along with age-standardized rates for all age groups, were provided by the GBD 2019 dataset[10]. The age-standardized mortality and DALYs rates for all ages of EC attributable risk factors from 1990–2019 were extracted by gender (both genders combined, and male and female separately), GBD regions, and five-tier socio-demographic index regions. The age-standardized mortality and DALYs rates for EC attributable risk factors were calculated using the GBD standard population structure.

The hierarchy of risk factors for EC, according to the GBD comparative risk assessment, is as follows: level 0 includes all risk factors combined; level 1 encompasses behavioral and metabolic risk factors; level 2 includes 4 specific risks or clusters of risks [alcohol use, tobacco use, dietary risks, and high body mass index (BMI)]; and level 3 is comprised of 4 specific risks or clusters of risks (chewing tobacco, smoking, a diet low in fruits, and a diet low in vegetables)[3]. **Table S1** is a comprehensive list of risk factors by hierarchy.

Trends in age-standardized mortality and DALYs rates attributable to these risk factors were assessed using the joinpoint regression model, implemented with joinpoint regression software (version 5.0.2) produced by the US National Cancer Institute[14]. The average annual percentage change (AAPC) from 1990–2019 was estimated to quantify changes in ASMRs and age-standardized DALYs rates (ASDRs) for EC. A $P < 0.05$ was considered statistically significant.

Trends in the non-modifiable age-related EC burden from 1990–2019

EC has been classified as an age-related disease with incidence rates among adults (≥ 25 years of age) exhibiting a quadratic increase with age, as indicated by the GBD study[2]. The number and crude mortality and DALYs rates for EC in 1990 and 2019 were extracted by gender (both genders combined, and male and female separately), age (25–95 years in 5-year increments and 95+ years), GBD regions, and 5-tier socio-demographic index regions. The corresponding age-standardized rates were calculated using the GBD standard population structure[10]. The age-related burden of EC encompasses the sum of all deaths and DALYs among adults (≥ 25 years of age). The

changes in age-related EC deaths and DALYs from 1990–2019 were decomposed into 4 non-modifiable components (size of the adult population, age structure of the adult population, disease incidence or prevalence, and case fatality and disease severity). The deaths and DALYs associated with each of these four components contribute to the total changes in the age-related EC burden between 1990 and 2019. The decomposition of these four components is presented in the equation below:

$$\text{Deaths} = \sum_a \text{pop size}_y * \frac{\text{pop age}_y}{\text{pop size}_y} * \frac{\text{incidence}_{a,y}}{\text{pop age}_y} * \frac{\text{DALY}_{a,y}}{\text{incidence}_{a,y}}$$

$$\text{DALYs} = \sum_a \text{pop size}_y * \frac{\text{pop age}_y}{\text{pop size}_y} * \frac{\text{prevalence}_{a,y}}{\text{pop age}_y} * \frac{\text{DALY}_{a,y}}{\text{prevalence}_{a,y}}$$

In the equation, *a* represents the age group and *y* represents the year. The methodology for this analysis has been detailed elsewhere[2,15-17]. Additionally, we calculated the percentage change in deaths and DALYs attributable to the four components relative to the absolute deaths and DALYs in 1990. The ASMR and ASDR for EC in 1990 and 2019 were calculated using the GBD World Standard population for ages ≥ 25 years[10].

All other analyses were performed using R (version 4.3.0). This study used only publicly available summary-level statistics and did not involve identifiable individual information.

Results

Profiles of EC incidence and mortality in 2022

Table 1 presents the global and regional incidence and mortality rates of EC for 2022 for both genders combined and separately for men and women. An estimated 511,054 new cases of EC were diagnosed globally with 365,225 in males and 145,829 in females. Additionally, 445,391 deaths from EC were estimated with 318,433 in males and 126,958 in females. Regionally, approximately 75% of both cases and deaths were estimated to occur in Asia, a significantly higher proportion than in any other continent. The ASIR and ASMR for EC were highest in Asia for both genders combined with an ASIR of 6.20/100,000 and an ASMR of 5.30/100,000. The lowest ASIR and ASMR were reported in Latin America and the Caribbean (2.40/100,000 and 2.20/100,000, respectively). The highest ASIR and ASMR for men were also reported in Asia (9.30/100,000 and 7.90/100,000, respectively) and the lowest ASIR and ASMR for men were reported in Latin America and the Caribbean (4.00/100,000 and 3.80/100,000, respectively). Conversely, women had the highest ASMR in Africa (2.90/100,000) and the lowest ASMR in North America (0.86/100,000). In contrast to other regions, the ASIR and ASMR for both genders were higher in Eastern Asia, Eastern Africa, South Africa, South Central Asia, and Northern Europe. The peak ASIR and ASMR were reported in Eastern Asia for males (12.20/100,000 and 9.70/100,000, respectively), while the peak ASIR and ASMR for females occurred in Eastern Africa (6.30/100,000 and 6.00/100,000, respectively).

Figure 1 illustrates the country-level EC incidence and mortality rates by the 4-tier HDI in 2022. EC incidence patterns based on the 4-tier HDI differed between males and females. The ASIR and ASMR increased with decreasing HDI levels for women, ranging from 1.30/100,000 and 0.95/100,000 in countries with a very high HDI to 3.70/100,000 and 3.50/100,000 in countries with a low HDI. However, among men, the highest ASIR and ASMR were both reported in countries with a high HDI (9.70/100,000 and 8.20/100,000, respectively). Countries with a low HDI had the lowest ASIR (4.90/100,000), while countries with a very high HDI had the lowest ASMR (4.30/100,000).

Profile and trends in the risk-attributable EC burden

Figure 2, and **Tables S2** and **S3** illustrate the profiles and trends in risk-attributable deaths and DALYs for EC based on the SDI and GBD regions from 1990–2019. An estimated 339,546 EC deaths (68.2% of EC deaths) and 8,098,678 DALYs (69.4% of EC DALYs) were attributed to all risk factors in 2019. At level 2 of the risk factor hierarchy, nearly 50% of the global EC deaths and DALYs in men were attributed to tobacco use, while 20% were attributed to high BMI in women.

In 2019 the leading level 2 risk factor globally for attributable EC deaths in males was tobacco (smoking and chewing), which accounted for 194.5 thousand deaths (53.2% of male EC deaths), followed by alcohol use, which accounted for 103.8 thousand deaths (28.4% of male EC deaths). The third largest level 2 risk factor for EC attributable deaths among males in 2019 was high BMI, with 65.5 thousand deaths (17.9% of male EC deaths), followed by dietary risks (a diet low in fruits and vegetables), accounting for 45.7 thousand deaths (12.5% of male EC deaths). However, there were significant

Table 1 Age-standardized incidence and mortality rates of esophageal cancer by world regions and four-tier HDI, 2022

Region	Incidence									Mortality								
	Both genders			Male			Female			Both genders			Male			Female		
	Case	CIR[a]	ASIR[b]	Case	CIR	ASIR	Case	CIR	ASIR	Case	CMR[c]	ASMR[d]	Case	CMR	ASMR	Case	CMR	ASMR
World	511,054	6.50	5.00	365,225	9.20	7.60	145,829	3.70	2.60	445,391	5.70	4.30	318,433	8.00	6.50	126,958	3.30	2.20
Continent																		
Africa	29,965	2.10	3.60	16,722	2.40	4.30	13,243	1.90	3.00	28,276	2.00	3.50	15,765	2.20	4.20	12,511	1.80	2.90
Latin America and the Caribbean	20,366	3.10	2.40	15,493	4.70	4.00	4,873	1.40	0.98	18,895	2.80	2.20	14,466	4.40	3.80	4,429	1.30	0.88
North America	21,888	5.90	2.90	17,045	9.20	4.80	4,843	2.60	1.20	19,116	5.10	2.40	15,298	8.30	4.20	3,818	2.00	0.86
Asia	382,892	8.20	6.20	273,705	11.50	9.30	109,187	4.80	3.40	329,803	7.10	5.30	235,426	9.90	7.90	94,377	4.20	2.80
Europe	53,513	7.20	3.30	40,516	11.20	5.70	12,997	3.40	1.30	47,212	6.30	2.80	35,963	10.00	4.90	11,249	2.90	1.00
Oceania	2,430	5.60	3.30	1,744	8.00	5.10	686	3.10	1.60	2,089	4.80	2.70	1,515	6.90	4.30	574	2.60	1.30
HDI																		
Very HDI country	107,524	6.60	3.10	81,713	10.10	5.30	25,811	3.10	1.30	88,639	5.40	2.50	68,136	8.40	4.30	20,503	2.50	0.95
High HDI country	261,867	9.50	6.10	194,596	14.00	9.70	67,271	4.90	2.80	222,730	8.10	5.10	165,904	11.90	8.20	56,826	4.20	2.20
Medium HDI country	112,931	5.00	5.30	73,332	6.30	7.00	39,599	3.60	3.60	106,923	4.70	5.00	69,656	6.00	6.70	37,267	3.40	3.40
Low HDI country	28,588	2.40	4.30	15,485	2.50	4.90	13,103	2.20	3.70	26,967	2.20	4.10	14,645	2.40	4.70	12,322	2.10	3.50
Region																		
Eastern Africa	17,936	3.80	7.60	9,817	4.20	9.10	8,119	3.40	6.30	16,933	3.60	7.20	9,255	4.00	8.70	7,678	3.30	6.00
Middle Africa	2,617	1.40	2.90	1,676	1.80	3.90	941	0.99	2.00	2,480	1.30	2.80	1,562	1.60	3.80	918	0.96	2.00
Northern Africa	3,231	1.30	1.40	1,772	1.40	1.60	1,459	1.20	1.20	3,126	1.20	1.40	1,718	1.30	1.60	1,408	1.10	1.20
South Africa	3,621	5.20	6.30	2,098	6.20	8.50	1,523	4.30	4.60	3,321	4.80	5.90	1,947	5.70	8.20	1,374	3.90	4.20
Western Africa	2,560	0.60	1.20	1,359	0.64	1.30	1,201	0.57	1.20	2,416	0.57	1.20	1,283	0.60	1.30	1,133	0.54	1.10
Caribbean	1,758	4.00	2.80	1,319	6.10	4.60	439	2.00	1.30	1,625	3.70	2.60	1,230	5.70	4.20	395	1.80	1.10
Central America	1,959	1.10	0.97	1,427	1.60	1.60	532	0.57	0.46	1,755	0.96	0.86	1,301	1.40	1.40	454	0.48	0.39
South America	16,649	3.80	2.80	12,747	5.90	4.80	3,902	1.80	1.10	15,515	3.50	2.60	11,935	5.50	4.50	3,580	1.60	1.00
North America	21,888	5.90	2.90	17,045	9.20	4.80	4,843	2.60	1.20	19,116	5.10	2.40	15,298	8.30	4.20	3,818	2.00	0.86
Eastern Asia	248,384	15.40	7.60	186,824	22.70	12.20	61,560	7.70	3.40	203,035	12.60	5.90	153,056	18.60	9.70	49,979	6.30	2.50
Southeastern Asia	15,108	2.20	2.00	12,147	3.60	3.40	2,961	0.87	0.70	14,334	2.10	1.90	11,535	3.40	3.20	2,799	0.82	0.66
South Central Asia	114,956	5.60	5.80	72,433	6.80	7.30	42,523	4.30	4.20	108,482	5.30	5.50	68,712	6.50	6.90	39,770	4.00	4.00
Western Asia	4,444	1.50	1.70	2,301	1.50	1.80	2,143	1.60	1.60	3,952	1.40	1.50	2,123	1.40	1.70	1,829	1.30	1.30

Table 1 Continued

Region	Incidence									Mortality								
	Both genders			Male			Female			Both genders			Male			Female		
	Case	CIR[a]	ASIR[b]	Case	CIR	ASIR	Case	CIR	ASIR	Case	CMR[c]	ASMR[d]	Case	CMR	ASMR	Case	CMR	ASMR
Eastern Europe	17,102	5.90	3.20	13,690	10.00	6.10	3,412	2.20	0.95	15,551	5.30	2.80	12,590	9.20	5.60	2,961	1.90	0.79
Western Europe	17,325	8.80	3.80	13,101	13.50	6.10	4,224	4.20	1.70	14,801	7.50	2.90	11,198	11.60	4.90	3,603	3.60	1.20
Southern Europe	6,440	4.30	1.80	4,995	6.70	3.10	1,445	1.90	0.66	5,605	3.70	1.50	4,356	5.90	2.50	1,249	1.60	0.50
Northern Europe	12,646	11.80	5.00	8,730	16.50	7.60	3,916	7.20	2.60	11,255	10.50	4.10	7,819	14.80	6.40	3,436	6.30	2.10
Australia-New Zealand	2,151	7.00	3.30	1,554	10.10	5.10	597	3.80	1.60	1,828	5.90	2.70	1,341	8.70	4.30	487	3.10	1.10
Melanesia	249	2.20	3.30	161	2.70	4.30	88	1.60	2.30	233	2.00	3.10	147	2.50	4.10	86	1.50	2.30
Polynesia	21	3.00	2.70	20	5.70	5.20	1	0.29	0.27	19	2.70	2.40	18	5.10	4.70	1	0.29	0.27
Micronesia	9	1.60	1.50	9	3.20	3.00	0	0.00	0.00	9	1.60	1.50	9	3.20	3.00	0	0.00	0.00

HDI, human development index. [a]CIR, crude rate of incidence (per 100,000); [b]ASIR, age-standardized incidence rate (per 100,000) was calculated using the Segi world standard population; [c]CMR, crude rate of mortality (per 100,000); [d]ASMR, age-standardized mortality rate (per 100,000) was calculated using the Segi world standard population.

differences between attributable deaths in males and females. In women, the level 2 risk factor ranking was high BMI, tobacco, dietary risks, and alcohol use, accounting for 18.4%, 16.3%, 15.2%, and 7.3% of female EC deaths in 2019, respectively. When considering DALYs, the ranking and proportion of DALYs attributed to each risk factor were similar to deaths. Tobacco ranked first for males and a high BMI was the leading cause for females with respect to attributable DALYs, accounting for 4.6 million and 0.5 million DALYs, respectively.

From 1990–2019, EC deaths and DALYs attributable to all risk factors exhibited a declining trend globally, except for deaths and DALYs attributed to a high BMI in men, which demonstrated an AAPC of 0.99% and 0.84% for ASMR and ASDR, respectively. For both men and women, esophageal cancer deaths and DALYs attributable to tobacco, alcohol, and dietary factors decreased in most regions. In contrast, deaths and DALYs attributable to a high BMI increased, especially in low-middle SDI regions. Notably, EC deaths and DALYs attributable to each risk factor increased among men in Western sub-Saharan Africa, and deaths and DALYs attributable to alcohol use also increased in South and Southeast Asia.

Profile and trends in the age-related EC burden

Figure 3, and **Tables S4** and **S5** depict the profile and trends in age-related deaths and DALYs for EC based on the SDI and GBD regions from 1990–2019. There were an estimated 497.7 thousand age-related EC deaths in 2019, which was defined as deaths occurring in adults ≥ 25 years of age, with 365.4 thousand deaths in males and 132.3 thousand deaths in females. Additionally, there were 11.6 million age-related EC DALYs with 8.8 million DALYs in males and 2.8 million DALYs in females.

The change in global age-related deaths and DALYs for EC were 56.1% and 42.3% of the absolute level in 1990, respectively. Decomposition analysis revealed that the contributors to the increased age-related EC burden during this time period were the adult population growth and population aging. Conversely, the decrease in case fatality rate and disease severity, as well as the incidence and prevalence of age-related EC, led to a decrease in age-related EC deaths and DALYs globally. The magnitude of change in age-related EC deaths in men across the SDI associated with population growth showed a decline ranging from 117.8% in countries with a low SDI to 47.9% in countries with a high SDI, while the magnitude of the change associated with the case fatality rate increased, ranging from −1.2% to −18.5%. The

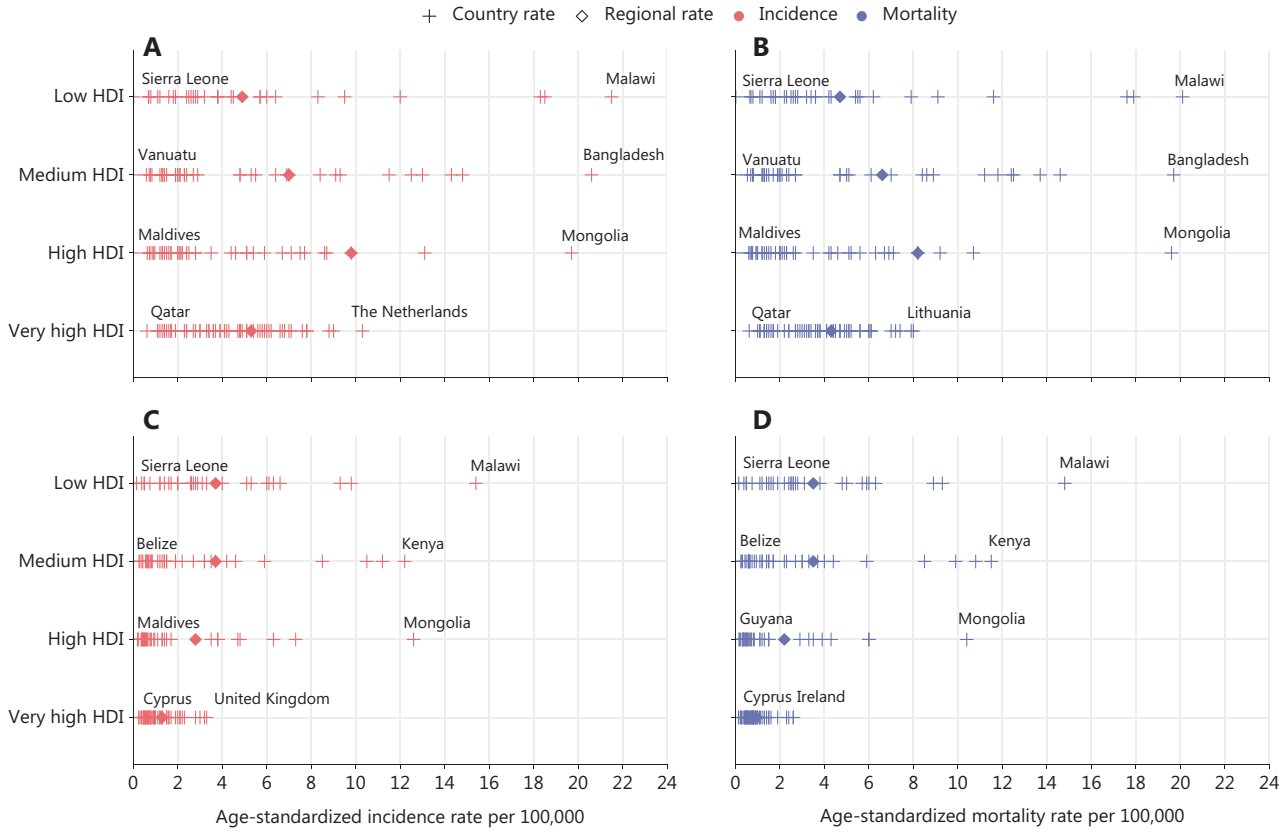

Figure 1 Country-level esophageal cancer incidence and mortality rates by four-tier HDI, 2022. (A) Country-level esophageal cancer incidence rates for males. (B) Country-level esophageal cancer mortality rates for males. (C) Country-level esophageal cancer incidence rates for females. (D) Country-level esophageal cancer mortality rates for females. HDI, human development index.

change in age-related EC DALYs associated with population growth and population aging showed similar trends to deaths. In regions with a low SDI, population aging contributed to a decline in age-related EC deaths and DALYs in males with a −8.8% and −9.0% change, respectively. Age-related EC deaths in women showed almost no growth (3.6%) and DALYs decreased (−8.6%) in regions with a middle SDI, which were largely attributable to decreased incidence and prevalence. In regions with a high-middle SDI, age-related EC deaths and DALYs increased slightly in females (17.5% and 1.2%, respectively).

Discussion

This study presents the 2022 global incidence and mortality rates for EC by world region and HDI, and provides a comprehensive analysis of trends in risk-attributable and age-related EC deaths and DALYs by SDI and GBD regions from 1990–2019. The findings of this study provide an overview of the global epidemiology of EC and the changing patterns of attributable burden. These updated estimates of the global burden of EC provide crucial evidence for prioritizing policy-making and the development and acceleration of cancer control initiatives aimed at reducing the current and future burden of EC.

Approximately 511,100 new EC cases and 445,400 deaths occurred in 2022 with considerable variation across countries and regions. Approximately 75% of cases and deaths occurred in Asia, where 59.2% of the world's population resides. The EC burden in the Asian regions is disproportionately greater than the corresponding population. EC primarily consists of two epidemiologically and pathologically distinct subtypes that share the same anatomic location [esophageal squamous cell carcinoma (ESCC) and esophageal adenocarcinoma (EAC)][18]. High ASIRs and ASMRs were reported in Eastern Asia and Eastern Africa, which could be related to the predominant distribution of ESCC in Asia and Africa, with ESCC being the most prevalent histologic type of EC[19]. While ESCC was predominantly observed in Asian and African countries, EAC


A
B
C
D
Global
Low SDI
Low-middle SDI
Middle SDI
High-middle SDI
High SDI
Central Europe
Eastern Europe
Western Europe
Central Asia
East Asia
South Asia
Southeast Asia
High-income Asia Pacific
Oceania
Australasia
High-income North America
Caribbean
Andean Latin America
Central Latin America
Tropical Latin America
Southern Latin America
North Africa and Middle East
Central Sub-Saharan Africa
Eastern Sub-Saharan Africa
Southern Sub-Saharan Africa
Western Sub-Saharan Africa
All risk factors
Behavioral risks
Alcohol use
Tobacco
Chewing tobacco
Smoking
Dietary risks
Diet low in fruits
Diet low in vegetables
Metabolic risks
High body mass index
AAPC (%)
3
0
−3
−6
−9
−12

Figure 2 Trends in risk for esophageal cancer incidence mortality and DALY rates for esophageal cancer by SDI and GBD regions, 1990–2019. The size of the point indicates a logarithmic transformation after normalization to age-standardized mortality and DALY rates. The color of the point indicates the average annual percent change of age-standardized mortality and DALY rates. (A) Trends in risk-attributable age-standardized mortality rates for males. (B) Trends in risk-attributable age-standardized DALY rates for males. (C) Trends in risk-attributable age-standardized mortality rates for females. (D) Trends in risk-attributable age-standardized DALY rates for females. DALY, disability-adjusted life-years; SDI, socio-demographic index; GBD, global burden of diseases; AAPC, average annual percent change.

was predominantly found in countries in Europe and North America[20]. The burden of EC differs widely among countries and populations due to variations in risk factors and subtype distribution[21]. The main risk factors for EAC include obesity and metabolic syndrome, while the main risk factors for ESCC are more likely to be overconsumption of alcohol, dietary habits, such as low intake of fruits and vegetables, hot beverages, and pickled foods, and lower socioeconomic status[7,18,22-29]. Significant differences in the burden of EC between genders, with a greater burden in males, may be attributed to both biological differences and environmental factors. These factors include higher exposure to occupational risks, elevated levels of social stress, and unhealthy lifestyles among males. Gender disparities in the burden of EC may arise from the differential distribution of exposure factors between the genders.

EC is a complex, multifactorial disease influenced by various risk factors, which can be broadly categorized into behavioral, environmental, metabolic, and genetic factors. Behavioral risk factors include smoking, alcohol consumption, and dietary factors, including the consumption of pickled foods, a low intake of fruits and vegetables, and consumption of hot drinks. Smoking is the leading attributable risk factor for EC, accounting for 40.8% of all EC deaths. The proportion of EC deaths attributable to smoking is highest among men, representing 51.2% of all male EC deaths. This disparity may be associated with the substantially higher prevalence of smoking among men, which is often > 10-fold that among women in many Asian countries[30]. Dietary factors also significantly contribute to the risk of EC. Studies have demonstrated that the consumption of pickled foods and hot foods increases the risk of EC 2.10- and 1.90-fold, respectively[31,32]. This finding is further evidenced by the increased prevalence of EC in regions where such dietary habits are common, particularly in developing countries in Asia[32]. Environmental risk factors for EC include exposure to radiation and bitumen[33]. However, attributable deaths due to environmental risk factors were not analyzed due to the low prevalence in the population and the lack of sufficient data. Metabolic factors, especially obesity, have a crucial role in the development of EAC. Obese individuals have been shown to have a higher risk of EAC, with an odds ratio of approximately 1.50[27]. Biologically, visceral obesity may contribute to the pathogenesis of EAC by directly influencing the development of gastroesophageal reflux disease and Barrett's esophagus. Moreover, visceral obesity can affect the progression of EAC through mechanisms independent of reflux, involving adipokines, growth factors, insulin resistance, and alterations in the microbiome[26]. Over the past four decades, there has been a significant increase in the global prevalence of obesity. Previous studies have reported a corresponding increase in the incidence of EAC, which may partly reflect the obesity epidemic[34]. The increasing trends in obesity are theorized to be significant contributors to the increased incidence of EAC. The global obesity epidemic may lead to a shift in the pathologic distribution pattern of EC[35].

Demographic characteristics significantly influence the EC burden. As a chronic, non-communicable, age-related disease, changes in the population size and age structure can drive the burden of EC. The United Nations General Assembly declared 2021–2030 the United Nations Decade of Healthy Aging with an aim to foster global collaborative efforts to promote longer and healthier lives[36]. With increasing life expectancy, the pace of population aging is accelerating more rapidly than in previous times. Between 2015 and 2050, the proportion of the world's population ≥ 60 years of age is projected to nearly double, increasing from 12% to 22%[36]. Greater than 90% of EC deaths occur in individuals > 50 years of age, with individuals > 70 years of age accounting for approximately 50% of all EC deaths[37]. Both incidence and mortality from EC are higher in older populations, and population aging contributes to an increased disease burden from EC. Our findings indicate that 24.1% and 18.5% of the increases in EC deaths and DALYs, respectively, between 1990 and 2019 were attributed to population aging. Population aging is thus poised to pose a significant challenge to the prevention and control of EC. Trends in the burden of EC are also influenced by economic development and advances in medical technology. With economic development and social progress, the population has witnessed rapid growth, leading to an increase in population

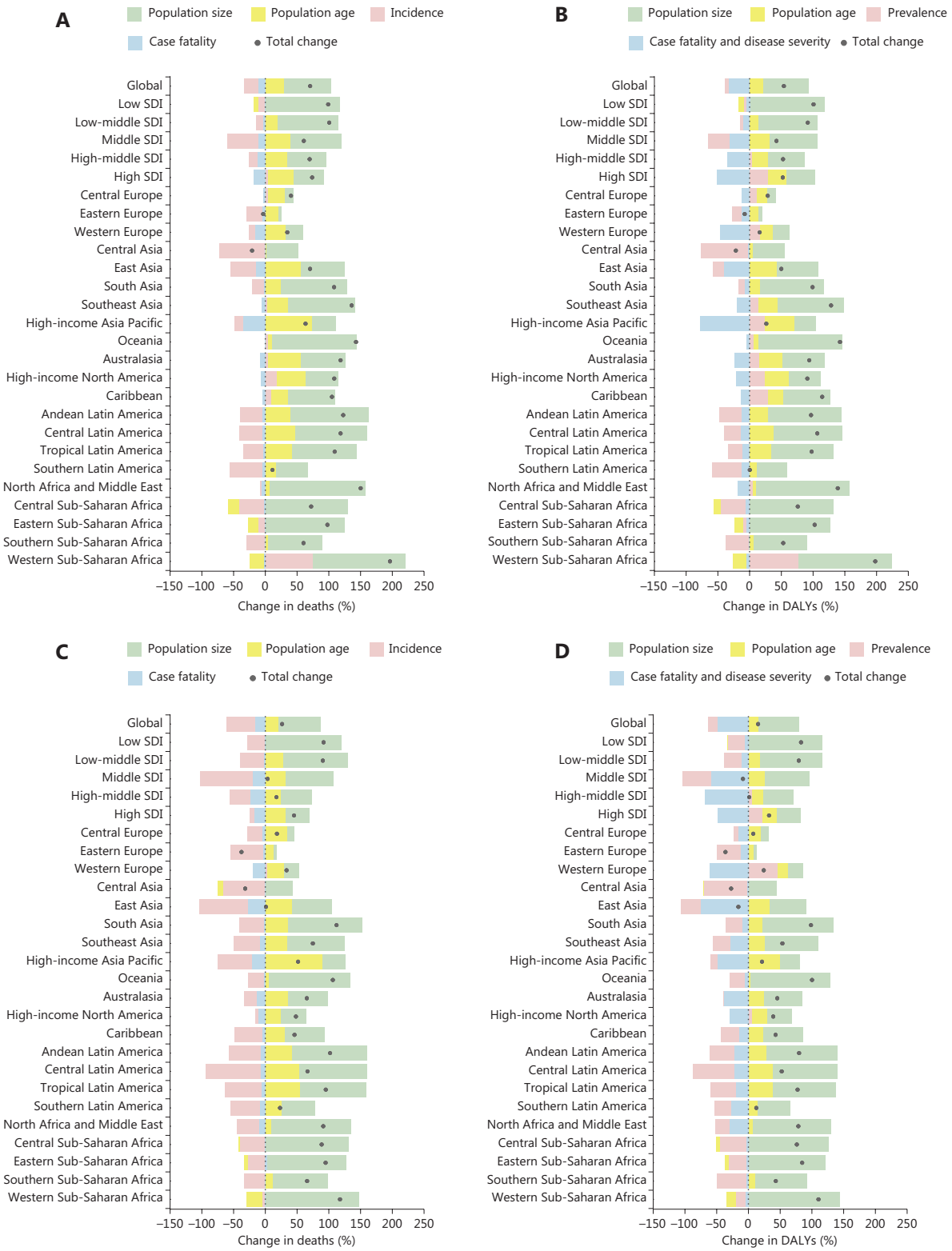

Figure 3 Decomposition of changes in age-related deaths and DALYs due to esophageal cancer between 1990 and 2019, by SDI and GBD regions. (A) Decomposition of changes in age-related deaths for males. (B) Decomposition of changes in age-related DALYs for males. (C) Decomposition of changes in age-related deaths for females. (D) Decomposition of changes in age-related DALYs for females. DALYs, disability-adjusted life-years; SDI, socio-demographic index; GBD, global burden of diseases.

size[38]. This growth in population size also contributes to the burden of EC. Our study found that 72.3% and 69.4% of the increases in EC deaths and DALYs, respectively, over the last three decades were attributed to population growth. In contrast, advances in medical technology have reduced the EC fatality rate, thereby mitigating the burden of EC.

This study had several notable strengths. Our study utilized representative data from GLOBALCAN 2022 and GBD 2019, which facilitated a comprehensive and systematic analysis of the profiles, trends, and contributors to the global burden of EC. However, there were also limitations to consider. First, our analysis was restricted to a limited number of risk factors, as described above. Second, cancer statistics inherently have a lag, and therefore only trends from 1990–2019 could be analyzed in this study.

Conclusions

This study aimed to provide a comprehensive understanding of the global burden of EC. The burden of EC remains substantial and shows an upward trend worldwide, particularly in males. Effective measures to control tobacco use and obesity are critical for addressing the risk-attributable burden of EC. Population growth and aging pose challenges for EC prevention and control efforts.

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Conflict of interest statement

No potential conflicts of interest are disclosed.

Author contributions

Conceived and designed the analysis: Yi Teng, Wanqing Chen.
Collected the data: Yi Teng.
Contributed data or analysis tools: Yi Teng.
Performed the analysis: Yi Teng.
Wrote the paper: Yi Teng, Changfa Xia, Maomao Cao, Fan Yang, Xinxin Yan, Siyi He, Mengdi Cao, Shaoli Zhang, Qianru Li, Nuopei Tan, Jiachen Wang, Wanqing Chen.

Data availability statement

All data used in this study are publicly available from the Global Cancer Observatory (GCO) [https://gco.iarc.fr] and the Global Burden of Disease Study 2019 [https://vizhub.healthdata.org/gbd-results/].

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