**Original Paper** 

# Secular Trends in Gastric and Esophageal Cancer Attributable to Dietary Carcinogens From 1990 to 2019 and Projections Until 2044 in China: Population-Based Study

Hui-Xiao Guo<sup>\*</sup>, MSc; Qi Wang<sup>\*</sup>, MSc; Can Wang, MSc; Qing Chen Yin, BA; Hua Zhi Huo, BA; Bing Hua Yin, BA

Handan Central Hospital, Handan, China \*these authors contributed equally

**Corresponding Author:** 

Bing Hua Yin, BA Handan Central Hospital Num 59, Congtai Road Congtai District Handan, 056001 China Phone: 86 03102118383 Email: <u>553050711@qq.com</u>

## Abstract

**Background:** Little is known about trends in or projections of the disease burden of dietary gastric and esophageal cancer (GEC) in China.

**Objective:** We aim to report GEC deaths and disability-adjusted life years (DALYs) from 1990 to 2019, predict them through 2044, and decompose changes in terms of population growth, population aging, and epidemiological changes.

**Methods:** We retrieved dietary GEC data from the Global Burden of Disease (GBD) online database and used joinpoint regression and age-period-cohort models to analyze trends in dietary GEC deaths and DALYs from 1990 to 2019 in China. We used a Bayesian age period cohort model of integrated nested Laplace approximations to predict the disease burden of GEC through 2044 and obtained the estimated population of China from 2020 to 2050 from the Global Health Data Exchange website. Finally, we applied a recently developed decomposition method to attribute changes between 2019 and 2044 to population growth, population aging, and epidemiological changes.

**Results:** The summary exposure values and age-standardized rates decreased significantly from 1990 to 1999, with percentage changes of -0.06% (95% CI -0.11% to -0.02%) and -0.05% (95% CI -0.1% to -0.02%), respectively. From 1990 to 2019, for dietary esophageal cancer, the percentage change in age-standardized mortality rate (ASMR) was -0.79% (95% CI -0.93% to -0.58%) and the percentage change in age-standardized DALY rate (ASDR) was -0.81% (95% CI -0.94% to -0.61%); these were significant decreases. For dietary stomach cancer, significant decreases were also observed for the percentage change in ASMR (-0.43%, 95% CI -0.55% to -0.31%) and the percentage change in ASDR (-0.47%, 95% CI -0.58% to -0.35%). In addition, data from both the joinpoint regression and annual percentage change analyses demonstrated significantly decreasing trends for the annual percentage change in ASMR and ASDR for GEC attributable to dietary carcinogens. The overall annual percentage change (net drift) was -5.95% (95% CI -6.25% to -5.65%) for dietary esophageal cancer mortality and -1.97% (95% CI -2.11% to -1.83%) for dietary stomach cancer mortality. Lastly, in 2044, dietary esophageal cancer deaths and DALYs were predicted to increase by 192.62% and 170.28\%, respectively, due to age structure (121.58\% and 83.29\%), mortality change (76.81\% and 92.43\%), and population size (-5.77% and -5.44%). In addition, dietary stomach cancer deaths and DALYs were predicted to increase by 118.1% and 54.08\%, with age structure, mortality rate change, and population size accounting for 96.71\% and 53.99\%, 26.17\% and -3.88% of the change, respectively.

**Conclusions:** Although the predicted age-standardized rates of mortality and DALYs due to dietary GEC show downward trends, the absolute numbers are still predicted to increase in the next 25 years due to rapid population aging in China.

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#### **KEYWORDS**

esophageal cancer; gastric cancer; dietary carcinogens; prediction; temporal trends; China

## Introduction

Gastric and esophageal cancer (GEC) are common cancers of the upper gastrointestinal tract, with estimates of 1.69 million new cases and 1.31 million deaths in 2020 worldwide, and 47.42% of them occur in China [1]. Primary preventive measures, such as limiting tobacco and alcohol use and maintaining a healthy lifestyle and diet, have important public health implications for reducing the disease burden of GEC and thus remain a high priority [2]. For dietary factors, habitually consuming fruits and vegetables is associated with a lower risk of esophageal cancer [3], and high sodium consumption is a well-established risk factor for gastric cancer [4].

Diet is considered an important modifiable factor for preventing cancer, and understanding and planning for the burden of cancers attributable to dietary carcinogens is of great public health significance. Thus, we searched PubMed and the China National Knowledge Infrastructure database with the terms ("gastric cancer") OR ("stomach cancer") AND ("esophagus cancer") AND ("disease burden") AND ("China") AND ("diet") OR ("dietary factors") for previous studies published between January 1, 1990, and April 17, 2023, about trends and projections of deaths and disability-adjusted life years (DALYs) due to gastric and esophageal cancer attributable to dietary factors in China. We found previous research that reported current trends in the disease burden and attributable risk factors of gastric and esophageal cancer in China [5-7]. The research also predicted future changes and trends for the above two cancers separately [8-10]. However, there were no available data on trends and projections for the disease burden of dietary gastric and esophageal cancer in the Chinese population. Finally, summarizing a comprehensive time trend of the GEC burden caused by specific carcinogenic factors in China is of great significance for developing precise population prevention strategies.

The 2019 Global Burden of Disease (GBD) study was a systematic scientific effort to provide a unique resource on the burden of diseases across causes of disability and death in 204 countries and territories [11]; thus, it also provides a unique opportunity to assess and project long-term trends in the disease burden attributable to various risk factors. Our study aims to present recent trends in GEC deaths and DALYs attributable to dietary factors between 1990 and 2019 and short-term predictions through to the year 2044 in China. We also decompose the estimates in terms of population growth, population aging, and epidemiological changes. This study will provide useful information to optimize the allocation of health resources to reduce the dietary GEC burden in China.

## Methods

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#### **Study Design and Time Frame**

The data used in this study were derived from the 2019 GBD, specifically focusing on the disease burden of dietary esophageal

and stomach cancers in China. The detailed methodology of the GBD estimation process has been fully described elsewhere [11]. In this study, we present the secular trends in gastric and esophageal cancer attributable to dietary carcinogens between 1990 and 2019 and also project the disease burden until 2044 in China.

#### **Location and Population**

In this study, we chose *China* from the database as the location, *esophageal cancer* and *stomach cancer* as the causes, *dietary risks* as the risk, and *death* and *DALYs* as the measures. Data were downloaded from the Global Health Data Exchange website [12].

#### **Dietary Factors and Disease Information**

A total of 11 dietary factors associated with 5 cancer types were assessed in the GBD. In this study, we focused on the disease burden of dietary GEC. For esophageal cancer, dietary factors included low consumption of fruits and vegetables; stomach cancer was only attributed to a diet high in sodium. The indices of disease burden included summary exposure values (SEV), deaths, DALYs, age-standardized mortality rate (ASMR), age-standardized DALY rate (ASDR), and population-attributable fraction (PAF). In addition, attributable deaths and DALYs were estimated using the total resulting death rate or DALYs multiplied by the PAF for the risk-outcome pair for age, sex, cause, and location. The SEV and the number, rate, and PAF for dietary GEC were also obtained directly from the Global Health Data Exchange website.

#### **Statistical Analysis**

Descriptive analyses were conducted and the temporal trends were expressed as annual percentage change (APC) and average annual percentage change (AAPC). Trends for age-standardized SEV, ASMR, ASDR, and age-standardized PAF (ASPAF) were further assessed by joinpoint regression analysis on a log scale since these measures followed a Poisson distribution.

Furthermore, we present the age period cohort results as follows [13]: (1) net drift, which represents the APC of the expected age-adjusted rates over time; (2) local drifts, which assess the age period cohort of the expected age-specific rates over time; (2) the longitudinal age curve, which shows the fitted longitudinal age-specific rates in the reference cohort, adjusted for period deviations; (3) period rate ratios (RRs), the ratio of age-specific rates in each period relative to the reference period; and (4) cohort RRs, the ratio of age-specific rates in each cohort.

Then, we used a Bayesian age period cohort model of integrated nested Laplace approximations (with the R packages *BAPC* and *INLA*) to predict the number of deaths, DALYs, ASMR, and ASDR of dietary carcinogen–attributable GEC cases from 2019 to 2044 [14]. Briefly, we assumed the inverse gamma prior and applied a second-order random walk (RW2) to adjust for excessive dispersion [15]. Additionally, we obtained the estimated population of China from 2020 to 2050. This approach

used inputs of population by age and sex in 2017, sex ratios at birth in 2017, and forecasted for age-specific fertility rates, age-specific mortality rates, and net migration for all locations through 2100. This analysis complied with the Guidelines on Accurate and Transparent Health Estimate Reporting [16,17].

Finally, we also used a recently developed decomposition method to attribute changes in the total number of GEC deaths and DALYs from dietary factors due to population growth, population aging, and age-specific changes between 2019 and 2044 [18,19]. Compared with previous studies [20-22], the recently developed method was insensitive to the decomposition order and the choice of reference group [19], enhancing the stability of our results. More details are provided in Multimedia Appendix 1 [13-22]. All statistical analyses were performed using R (version 3.6.0; R Core Team).

#### **Ethical Considerations**

This study used data from the GBD study, which was approved by the institutional review board of the University of Washington School of Medicine. The original data collection obtained informed consent from study participants or was granted exemptions by the institutional review board. As this is a secondary analysis of existing data, no additional human participant research ethics review or informed consent was required. Study data were anonymized and deidentified to protect the privacy and confidentiality of study participants. Our analysis complied with the Guidelines on Accurate and Transparent Health Estimate Reporting [16].

## Results

#### **Temporal Trends in GEC Attributable to Dietary Factors Between 1990 and 2019**

As shown in Table 1, the SEV and age-standardized rates both decreased significantly from 1990 to 1999, with percentage changes of -0.06% (95% CI -0.11% to -0.02%) and -0.05% (95% CI -0.1% to -0.02%). The indices of cancer burden included the estimated number, all-age PAF and ASPAF,

mortality, and DALYs. For dietary esophageal cancer, except for the estimated number of deaths, other indices showed a significantly decreasing trend. For dietary stomach cancer, although the percentage changes for the number of deaths increased significantly from 1990 to 2019 (0.36%, 95% CI 0.08% to 0.68%), significant decreases were observed for ASMR (-0.43%, 95% CI -0.55% to -0.31%) and ASDR (-0.47%, 95% CI -0.58% to -0.35%). There were no significant changes in other disease burden indices. More details are shown in Table 1.

Table 2 shows the results of the joinpoint regression model. Between 1990 and 2019, for esophageal cancer attributable to dietary carcinogens, the AAPC for ASMR and ASDR and the ASPAF for death rates and ASPAF for DALYs were -5.28% (95% CI -5.48% to 5.08%), -5.63% (95% CI -5.84% to -5.43%), -3.51% (95% CI -3.59% to -3.42%), and -3.58% (95% CI -3.67% to -3.5%), respectively. Furthermore, for dietary stomach cancer, the ASMR decreased by an average of 1.95% (-2.18% to -1.72%) per year. The average decline in ASDR was 2.21% (-2.46% to -1.96%). AAPCs in the ASPAF for death rates and ASPAF for DALYs were -0.04% (95% CI -0.03%) and -0.02% (95% CI -0.03% to -0.02%), respectively.

In addition, the declining trends in above 4 indices differed between dietary esophageal cancer and stomach cancer. For dietary esophageal cancer, although the magnitude of the decline in these 5 trends varied across different periods, all of them demonstrated a significantly decreasing trend. A rapid downward trend appeared during 2004 to 2014 in both ASMR (-9.38%, 95% CI -9.61% to -9.14%) and ASDR (-9.99%, 95% CI -10.22% to -9.75%). In general, the ASMR and ASDR for dietary stomach cancer showed declining trends. However, during 1998 to 2004, there were significant upward trends in ASMR (2.92%, 95% CI 2.37% to 3.46%) and ASDR (2.63%, 95% CI 2.15% to 3.12%). The ASPAF for both mortality and DALYs of dietary stomach cancer showed a slow and smooth decline.



Table 1. The summary exposure values and burden of esophageal cancer and stomach cancer attributable to dietary carcinogens.

Metric/measure	1990 values (95% CI)	2019 values (95% CI)	Percentage change (95% CI)
Summary exposure values			
All ages, %	82.76 (76.67 to 85.98)	77.67 (69.95 to 82.22)	-0.06 (-0.11 to -0.02)
Age-standardized, %	81.86 (75.44 to 85.15)	77.37 (69.58 to 81.93)	-0.05 (-0.10 to -0.02)
Esophageal cancer			
Deaths			
Deaths, n	40,514 (17,911 to 66,618)	20,509 (4338 to 52,321)	-0.49 (-0.84 to 0.01)
PAF <sup>a</sup> (all ages), %	0.23 (0.10 to 0.36)	0.08 (0.02 to 0.20)	-0.65 (-0.89 to -0.35)
ASPAF, <sup>b</sup> %	0.23 (0.10 to 0.36)	0.08 (0.02 to 0.21)	-0.64 (-0.88 to -0.34)
Mortality (all ages) 1/10 <sup>5</sup>	3.42 (1.51 to 5.63)	1.44 (0.31 to 3.68)	-0.57 (-0.87 to -0.16)
ASMR, <sup>c</sup> 1/10 <sup>5</sup>	5.07 (2.23 to 8.32)	1.07 (0.24 to 2.73)	-0.79 (-0.93 to -0.58)
DALYs <sup>d</sup>			
DALYs, n	1,034,489 (449,013 to 1,696,655)	455,090 (90,540 to 1,163,817)	-0.56 (-0.87 to -0.08)
PAF (all ages), %	0.23 (0.10 to 0.36)	0.08 (0.02 to 0.20)	-0.66 (-0.89 to -0.35)
ASPAF, %	0.23 (0.10 to 0.36)	0.08 (0.02 to 0.21)	-0.65 (-0.89 to -0.35)
All-age rate, 1/10 <sup>5</sup>	87.40 (37.93 to 143.34)	32.00 (6.37 to 81.82)	-0.63 (-0.89 to -0.35)
ASDR, <sup>e</sup> 1/10 <sup>5</sup>	116.66 (51.12 to 190.9)	22.22 (4.54 to 56.38)	-0.81 (-0.94 to -0.61)
Stomach cancer			
Deaths			
Numbers, n	27,227 (613 to 101,649)	37,131 (833 to 138,479)	0.36 (0.08 to 0.68)
PAF (all ages), %	0.09 (0.01 to 0.33)	0.09 (0.01 to 0.33)	-0.01 (-0.12 to 0.01)
ASPAF, %	0.09 (0.01 to 0.33)	0.09 (0.01 to 0.33)	-0.01 (-0.11 to 0.01)
Mortality (all ages), 1/10 <sup>5</sup>	2.30 (0.05 to 8.59)	2.61 (0.06 to 9.74)	0.13 (-0.10 to 0.4)
ASMR, 1/10 <sup>5</sup>	3.34 (0.08 to 12.56)	1.90 (0.04 to 7.12)	-0.43 (-0.55 to -0.31)
DALYs			
DALYs, n	734,448 (16,388 to 2,731,936)	873,813 (19,283 to 3,220,231)	0.19 (-0.06 to 0.48)
PAF (all ages), %	0.09 (0.01 to 0.33)	0.09 (0.01 to 0.33)	0.01 (-0.10 to 0.01)
ASPAF, %	0.09 (0.01 to 0.33)	0.09 (0.01 to 0.33)	-0.01 (-0.09 to 0.01)
All-age rate, 1/10 <sup>5</sup>	62.05 (1.38 to 230.80)	61.43 (1.36 to 226.40)	-0.01 (-0.22 to 0.23)
ASDR, 1/10 <sup>5</sup>	80.72 (1.81 to 301.47)	42.52 (0.94 to 157.03)	-0.47 (-0.58 to -0.35)

<sup>a</sup>PAF: population-attributable fraction.

<sup>b</sup>ASPAF: age-standardized population-attributable fraction.

<sup>c</sup>ASMR: age-standardized mortality rate.

<sup>d</sup>DALY: disability-adjusted life year.

<sup>e</sup>ASDR: age-standardized disability-adjusted life year rate.



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Table 2. Joinpoint analysis of trends in disease burden of dietary esophageal cancer and stomach cancer in China, 1990 to 2019.

Metr	ic	Trend 1		Trend 2		Trend 3		Trend 4		Trend 5		1990-2019
		Period	APC, <sup>a</sup> % (95% CI)	Period	APC, % (95% CI)	Period	APC, % (95% CI)	Period	APC, % (95% CI)	Period	APC, % (95% CI)	AAPC, <sup>b</sup> % (95% CI)
Age-standardized mortality rate												
]	Esophageal cancer	1990- 1993	-2.56 (-3.38 to -1.73)	1993- 1998	-3.9 (-4.47 to -3.32)	1998- 2004	-1.91 (-2.41 to -1.42)	2004- 2014	-9.38 (-9.61 to -9.14)	2014- 2019	-3.87 (-4.56 to -3.18)	-5.28 (-5.48 to -5.08)
5	Stomach cancer	1990- 1998	-2.10 (-2.36 to -1.85)	1998- 2004	2.92 (2.37 to 3.46)	2004- 2011	-4.02 (-4.41 to -3.64)	2011- 2015	-4.43 (-5.56 to -3.29)	2015- 2019	-2.59 (-3.32 to -1.85)	-1.95 (-2.18 to -1.72)
Age-standardized population attributable proportion of death rates												
]	Esophageal cancer	1990- 1995	-2.33 (-2.45 to -2.21)	1995- 2002	-3.79 (-3.90 to -3.69)	2002- 2010	-4.63 (-4.74 to -4.52)	2010- 2014	-3.78 (-4.27 to -3.29)	2014- 2019	-2.24 (-2.48 to -2.00)	-3.51 (-3.59 to -3.42)
:	Stomach cancer	1990- 1995	-0.06 (-0.07 to -0.05)	1995- 1999	0.09 (0.11 to 0.07)	1999- 2010	-0.03 (-0.03 to -0.03)	2010- 2013	0.00 (-0.04 to 0.04)	2013- 2019	-0.02 (-0.02 to -0.01)	-0.04 (-0.04 to -0.03)
Age-standardized DALY <sup>c</sup> rate												
]	Esophageal cancer	1990- 1993	-2.89 (-3.73 to -2.04)	1993- 1998	-4.20 (-4.79 to -3.60)	1998- 2004	-2.18 (-2.69 to -1.67)	2004- 2014	-9.99 (-10.22 to -9.75)	2014- 2019	-3.83 (-4.55 to -3.11)	-5.63 (-5.84 to -5.43)
	Stomach cancer	1990- 1995	-2.50 (-2.96 to -2.03)	1995- 1998	-1.99 (-4.04 to 0.10)	1998- 2004	2.63 (2.15 to 3.12)	2004- 2015	-4.52 (-4.68 to -4.37)	2015- 2019	-2.67 (-3.32 to -2.02)	-2.21 (-2.46 to -1.96)
Age-standardized population attributable proportion of DALY rates												
]	Esophageal cancer	1990- 1995	-2.43 (-2.55 to -2.31)	1995- 2002	-3.96 (-4.07 to -3.85)	2002- 2010	-4.78 (-4.89 to -4.67)	2010- 2014	-3.79 (-4.29 to -3.29)	2014- 2019	-2.10 (-2.34 to -1.86)	-3.58 (-3.67 to -3.50)
:	Stomach cancer	1990- 2000	-0.04 (-0.04 to -0.04)	2000- 2004	0.02 (0.00 to 0.04)	2004- 2010	-0.03 (-0.03 to -0.02)	2010- 2013	-0.01 (-0.04 to 0.03)	2013- 2019	-0.03 (-0.03 to -0.02)	-0.02 (-0.03 to -0.02)

<sup>a</sup>APC: annual percentage change.

<sup>b</sup>AAPC: average annual percentage change.

<sup>c</sup>DALY: disability-adjusted life year.

#### Effects of Age, Time Period, and Cohort on Cancer Burden Between 1990 and 2019

Figure 1 demonstrates the age-period-cohort analysis results on deaths and DALYs from dietary esophageal cancer. The ranges for age and period were 25 to  $\geq$ 95 years and 1990 to 2019, respectively. For dietary esophageal cancer deaths, the overall APC (net drift) was -5.95% (95% CI -6.25% to -5.65%). According to the results for local drifts and net drift (Figure 1A), the data that had a percentage value below 0 suggests that there was a significantly decreasing trend in all age groups. The longitudinal age curve for dietary esophageal cancer mortality showed that the rates increased from the age of 25 years and reached the highest level at about the age of 57 years, then gradually decreased with age (Figure 1B). In addition, there were persistent downward trends in the estimated period and cohort RRs, as illustrated in Figure 1C and D. Similar patterns were observed for the age, time period, and cohort effects on

the DALYs of esophageal cancer associated with dietary carcinogens (Figure 1E-H).

The results of age period cohort models on death and DALYs from dietary stomach cancer are shown in Figure 2. In general, the net drift was -1.97% (95% CI -2.11% to -1.83%) for dietary stomach cancer mortality. The results for local drifts and net drift show that the percentage declined from the age of 25 years and reached the lowest level at about the age of 43 years, then gradually increased with age; the peak point occurred at about the age of 93 years, after which the percentage decreased with age (Figure 2A). For the longitudinal age curve, the maximum value occurred at about the age of 88 years, after which there was a short and rapid declining trend (Figure 2B). As illustrated in Figure 2C, the time-period RRs decreased from 1992 to 1997, increased until 2002, and then showed a continuous downward trend. Finally, there was a persistent downward trend in the estimated cohort RRs (Figure 2D). Similar patterns were observed for the age period cohort analysis of the DALYs for dietary stomach cancer (Figure 2E to H).

**Figure 1.** Effects of age, time period, and cohort on deaths and DALYs due to dietary esophageal cancer from 1990 to 2019 in China. Local drifts with net drift values of (A) deaths and (E) DALYs; fitted longitudinal age curves of (B) deaths and (F) DALYs; relative risks of (C) death and (G) DALYs in each period compared with the reference period (2000-2004); and relative risks of (D) deaths and (H) DALYs in each cohort compared with the reference cohort (1940-1944 cohort). DALY: disability-adjusted life year.





**Figure 2.** Effects of age, time period, and cohort on deaths and DALYs due to dietary stomach cancer from 1990 to 2019 in China. Local drifts with net drift values of (A) deaths and (E) DALYs; fitted longitudinal age curves of (B) deaths and (F) DALYs; relative risks of (C) death and (G) DALYs in each period compared with the reference period (2000-2004); and relative risks of (D) deaths and (H) DALYs in each cohort compared with the reference cohort (1940-1944 cohort). DALY: disability-adjusted life year.



#### Predictions and Changes Between 2019 and 2044

Figure 3 shows the future trends for the disease burden of GEC attributable to dietary carcinogens from 2020 to 2044 in China. For dietary esophageal cancer, there are predicted to be

gradually decreasing trends in the ASMR (Figure 3A) and ASDR (Figure 3B). For dietary stomach cancer, the ASMR is predicted to decrease from 1990 to 1999, increase until 2004, and then show a continuous downward trend (Figure 3C). Similar patterns are seen in the ASDR (Figure 3D).

XSL•FO RenderX Figure 3. Temporal trends of for ASMR and ASDR for esophageal cancer and stomach cancer attributable to dietary carcinogens between 1990 and 2044 in China. The dotted lines represent the observational values from the Global Burden of Disease data set. The predictive mean values are shown as black solids, and the fan is the predictive distribution between the 5% and 95% quintiles. (A) ASMR for esophageal cancer; (B) ASMR for stomach cancer; (C) ASDR for esophageal cancer; (D) ASDR for stomach cancer. ASDR: age-standardized disability-adjusted life year rate; ASMR: age-standardized mortality rate; DALY: disability-adjusted life year.



Table 3 presents decomposition analysis results for the disease burden of dietary esophageal and stomach cancer. In 2044, dietary esophageal cancer ASMR was predicted to increase by 192.62% compared with 2019, which was due to age structure (121.58%), mortality change (76.81%), and population size (-5.77%). Dietary esophageal cancer ASDR was predicted to increase by 170.28% because of age structure (83.29%), mortality change (92.43%), and population size (-5.44%). Furthermore, dietary stomach cancer ASMR in 2044 was predicted to increase by 118.1%, with age structure, mortality change and population size contributing 96.71%, 26.17%, and -4.78%, respectively. Dietary stomach cancer ASDR was predicted to increase by 54.08%, with age structure, mortality rate changes, and population size accounting for 53.99%, 3.97%, and -3.88%, respectively.

**Table 3.** Predicted number and contribution changes for dietary esophageal cancer and stomach cancer deaths and disability-adjusted life years from 1990 to 2044.

		Values, n		Changes between 2019 and 2044, %						
		2019	2044	Total change	Change due to mortality change	Change due to demographics	Change due to age structure	Change due to population size		
Deaths										
	Esophageal cancer	20,492	59,965	192.62	76.81	115.81	121.58	-5.77		
	Stomach cancer	37,112	80,942	118.1	26.17	91.93	96.71	-4.78		
Disability-adjusted life years										
	Esophageal cancer	455,089	1,230,011	170.28	92.43	77.85	83.29	-5.44		
	Stomach cancer	873,813	1,346,403	54.08	3.97	50.11	53.99	-3.88		



## Discussion

The GEC burden attributable to dietary risk factors in China from 1990 to 2044 is systematically summarized in this study. Deaths and DALYs due to dietary esophageal cancer declined by 49% and 56%, respectively, but deaths and DALYs due to dietary stomach cancer grew by 36% and 19%, respectively, over the last 30 years. For esophageal and stomach cancers attributable to dietary carcinogens, although both the ASMR and the ASDR are predicted to decline in the coming 25 years, the numbers of both deaths and DALYs are predicted to continue to increase. The results of decomposition methods supported the finding that the aging population is the main reason for future changes in the GEC burden.

Dietary modifications are an effective strategy to reduce the GEC burden in terms of deaths and DALYs. In our study, dietary carcinogenic factors were a diet low in fruits and vegetables for esophageal cancer and a diet high in sodium for stomach cancer. Epidemiological studies have found that low intake of fresh fruits and vegetables is associated with a higher risk of esophageal squamous cell carcinoma, which is the dominant histological subtype in China [23]. In addition, accumulating evidence suggests that people who prefer salty food and salt-preserved meat and fish generally have a higher risk of gastric cancer [24]. The World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) report also supports the strong association between high-salt foods and gastric cancer [25]. However, the SEV for dietary carcinogens from 1990 to 2019 only slightly declined, from 82.76% to 77.67%, which is consistent with previous findings from the Chinese Health and Nutrition Survey (CHNS). Nevertheless, data from the CHNS show that intake did not meet the recommended levels (an average of 269.4 g of fresh vegetables and 40.7 g of fruit per day in 2012 vs recommend daily intakes of 300-500 g of vegetables and 200-350 g of fruit for adults in 2016) [26-28]. According to the latest data from the 2020 Report on Chinese Residents' Chronic Diseases and Nutrition, the consumption levels of fruits and vegetables were lower than the recommended intake levels, while the intake of salt was much higher than the standard [29]. These unhealthy dietary habits might be related to a lower awareness of basic knowledge of cancer in China, especially the level of knowledge of primary prevention [30]. Thus, our findings suggest that people should still attach importance to a nutritionally balanced diet and the primary prevention of cancer in the future.

In general, the temporal trends for deaths and DALYs for dietary GEC decreased from 1990 to 2019, even though these trends fluctuated in different time segments over the last 30 years. The joinpoint method describes short-term trends more accurately by dividing the long-term trend line into several segments and analyzing each segment. For dietary stomach cancer, the proportion of deaths and DALYs remained stable from 1990 to 2019, which is also consistent with a previous study [10]. But deaths and DALY rates for stomach cancer attributable to dietary carcinogens declined over the past 30 years, which is similar to the changes for stomach cancer in China reported by other studies [8,9]. This might be related to the increasing coverage of population-based screening projects. From 2001 to 2020, a

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total of 5 cancer screening programs were implemented in high-risk areas of China focusing on screening for stomach cancer [31]. Notably, a significantly increasing trend of dietary stomach cancer deaths and DALY rates occurred in the period from 1998 to 2004, which might be explained by the establishment of the national cancer registry system and the improvement of data quality. In 1982, the Reporting Manual of Cancer Registration was first released by the Office of National Central Cancer Registry. In 2002, the National Central Cancer Registry was launched under the supervision of the former Ministry of Health and was responsible for systematically collecting, analyzing, and interpreting cancer data [23]. Moreover, esophageal and gastric cancer have always been treated as upper gastrointestinal tumors for primary and secondary prevention; thus, initial gastric registry data might derive in part from upper gastrointestinal tumor data.

Our findings show that the rates and percentages of deaths and DALYs due to dietary esophageal cancer declined in China over the past 30 years, which is similar to the trends for esophageal cancer associated with all risk factors [2,5,6]. A previous study also showed that the burden of esophageal cancer associated with a low-fruit diet declined in China from 1990 to 2017 [7]; however, there are no prior studies focusing on low-vegetable diets. These declining trends were associated with long-term, extensive efforts in esophageal cancer etiological prevention and screening in China. Chinese researchers launched a series of prevention projects starting in 1985, including the Linxian general population nutrition intervention trial, a dysplasia population nutrition intervention trial, a chemoprevention trial [32], and a cancer screening program in high-risk areas [31], because the bulk of the burden of esophageal cancer worldwide comes from East Asia, particularly from China [24]. Considering the success of dietary interventions, future efforts should focus on improving dietary habits to reduce the burden of GEC.

We further revealed trends for age, period, and cohort effects for deaths and DALYs due to dietary GEC. Regarding the age effect, the top points of the longitudinal age curves for deaths and DALYs for esophageal cancer were 60 years and 72 years, which is similar to the peak ages for deaths and incidence [10]. For dietary stomach cancer deaths and DALYs, the peak of the age curves shifted to 85 years and 70 years, which is also consistent with the highest death and incidence ages reported in a previous study [6]. These age-specific trends in both esophageal and stomach cancer related to dietary carcinogens might be due to both age-related biological factors and the increased level of dietary exposure, as explained by a similar study of occupational lung cancer [33]. Furthermore, the period effect reflected changes in social and economic policy, as well as the impact of major events at specific points in time [34]. In this study, we found that the change trends in period RRs for dietary GEC mortality and DALYs were similar to the results of the joinpoint analysis and were explained by the implementation of the cancer registry system, primary prevention, and screening programs, as mentioned above. Lastly, birth cohort effects represent the influence of physical and social exposures that appear earlier in the life process and accumulate with time [35]. In our study, the cohort RRs for dietary

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carcinogens associated with GEC mortality and DALYs showed gradually decreasing trends for cohorts born since 1895.

We first projected the trends of dietary GEC death and DALYs through to 2044 and used a recently developed decomposition method to attribute changes to population growth, population aging, and age-specific changes [18,19]. Previous studies predicted the burden of GEC attributable to all risk factors and found that there was a persistently decreasing trend in terms of ASMR and ASDR, but the number of new cases was expected to increase in the next decades [8-10,36,37]. Moreover, population aging contributed to most of the additional dietary GEC deaths and DALYs, which could be explained by the continuous increase of the older population and the higher incidence in this age group. As shown in our study, change due to risk factors also deserves attention, as it contributes to increased disease burden. Therefore, considering the persistent increase in case numbers, dietary GEC might be one of the main public health concerns in the near future in China, and it is necessary to increase the promotion of healthy diets.

Our study has several limitations, as mentioned in earlier GBD study reports [38,39]. First, the main histological subtypes of

GEC (esophageal squamous cell carcinoma and esophageal adenocarcinoma, cardia and noncardia stomach cancer) have distinct incidence trends and geographical distributions [40,41], but data for these subtypes are not currently captured independently in the GBD database. Second, although other dietary factors, such as high-sugar drinks and alcohol, are recognized to be related to deaths and DALYs due to GEC in China, the disease burden caused by these dietary carcinogens was not estimated [42]. Lastly, we only estimated the burden of GEC attributable to dietary factors; the combined effects of dietary and other risk factors may increase or complicate the burden of GEC [43,44]. Despite these limitations, using the most up-to-date data and advanced modeling strategies, our study is the first to provide a comprehensive understanding of the burden of dietary GEC from 1990 to 2044.

Although the predicted ASMR and ASDR for dietary GEC generally show downward trends, absolute numbers will still increase in the next 25 years due to the rapid population aging seen in China. China still needs to strengthen the targeted interventions and address modifiable risk factors, such as advocating for a balanced diet.

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#### **Data Availability**

The data sets generated for this study can be found in the Global Burden of Disease repository [12].

#### **Authors' Contributions**

HXG and BHY contributed to conceptualization and design, QW and QCY contributed to data extraction, HXG and QW contributed to formal analysis, HXG and QW contributed to writing of the original draft, and QCY and HZH contributed to review and editing. All authors read and approved the final manuscript.

#### **Conflicts of Interest**

None declared.

#### **Multimedia Appendix 1**

Supplemental information on statistical analysis. [DOCX File , 49 KB-Multimedia Appendix 1]

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#### Abbreviations

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AAPC: average annual percentage change
APC: annual percentage change
ASDR: age-standardized disability-adjusted life year rate
ASMR: age-standardized mortality rate
ASPAF: age-standardized population-attributable fraction
CHNS: Chinese Health and Nutrition Survey
DALY: disability-adjusted life year

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GBD: Global Burden of Disease
GEC: gastric and esophageal cancer
PAF: population-attributable fraction
RR: rate ratio
RW2: second-order random walk
SEV: summary exposure value
WCRF/AICR: World Cancer Research Fund/American Institute for Cancer Research

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