

## Original Article

# Disease burden of esophageal cancer attributable to low fruit intake in China and globally from 1990 to 2019

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**Abstract:** Objective: To understand the disease burden of esophageal cancer (EC) attributable to inadequate fruit intake in China and global from 1990 to 2019 stratified by age and sex. Methods: Global Burden of Disease Study (GBD 2019) were pooled to calculate the number of deaths, standardized mortality rate, disability-adjusted life years (DALY) and DALY rate of EC attributed to low fruit intake in China and globally by age and sex from 1990 to 2019. The population attributable fractions (PAF) were applied to estimate the proportion of EC caused by low fruit intake. Joinpoint was used to estimate average annual percentage of change (AAPC) to reflect the time change trend of the EC burden attributable to inadequate fruit intake in China and globally. Results: In the Chinese population in 2019, the attributable DALY of EC in males was 356,000 person-years, while it was 80,600 person-years in females. The attributable standardized mortality and DALY rates for different age groups in China increased with age, peaking in the group aged 70 years and above. From 1990 to 2019 in China, the number of deaths, standardized mortality rates, DALY and standardized DALY rates of EC attributable to inadequate fruit intake showed a decreasing trend (AAPCs: -1.62%, -4.54%, -2.10% and -4.88%, respectively), with statistical significance ( $P < 0.001$ ). Conclusion: The overall burden of EC attributed to inadequate fruit intake in China has demonstrated a downward trend. However, due to the aging population, the disease burden in China remains higher than the global average. Hence, prevention and health education efforts should focus on the population with low fruit intake.

**Keywords:** Esophageal cancer, disease burden, China, global, inadequate fruit intake, mortality rate

## Introduction

Esophageal cancer (EC) is a prevalent malignancy, mainly comprising esophageal squamous cell carcinoma and adenocarcinoma according to histologic type. It ranks the 7th among various cancers and 6th among cancer-related deaths. The estimated global incidence and death rates of EC in 2020 were 604,000 new cases and 544,000 mortalities [1]. East Asia, particularly China, bears the highest incidence and mortality rates, counting for over half of the global cases [2]. From 1990-2017, the total number of new EC cases in China increased by 42.7%, from 164,000 to 235,000

[3]. Compared with South Korea and Japan, the age-standardized mortality rate of EC in China was double [4]. These statistics highlight the heavy burden of EC in China, requiring preventive measures to reduce the prevalence of esophageal cancer.

Recent developments such as aging, urbanization, industrialization, and changes in lifestyle have complicated the identification of risk factors for EC, posing a significant challenge to China's public health system. Previous studies have linked low fruit consumption to an increased risk of esophageal cancer [5, 6]. Conversely, a moderate increase in fruit intake

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has been shown to reduce the disease burden of esophageal cancer, thanks to the dietary fiber, vitamins, and antioxidants found in fruits [7]. Global Burden of Disease Study (GBD 2019) showed that in China, insufficient fruit consumption was responsible for 1.046 million deaths and 27.678 million disability-adjusted life years (DALYs). Remarkably, the average fruit intake among the Chinese population was only 55.7 grams per day, substantially below the 200-350 grams recommended in the Chinese Dietary Guidelines for Residents [8]. By identifying trends related to low fruit intake and implementing effective strategies based on these findings, it is possible to develop efficient screening models for esophageal cancer, thereby reducing its incidence, mortality, and associated disability.

Despite the previously reported regional or global burdens of EC, including mortality, incidence rate, DALY rates [9], few studies in China have conducted specific analyses of temporal trends in EC mortality, incidence, and DALY rates attributable to low fruit intake. In addition, some studies only provided a descriptive analysis of the overall burden of EC and did not investigate the long-term trends in impact of risk factors on esophageal cancer in China. Therefore, understanding the epidemic trend of EC in China is crucial for developing health policies that can guide practice to manage and prevent the disease. In this context, this study utilized the latest data from the GBD 2019 database, which offers comprehensive and comparable data on esophageal cancer incidence, mortality, and DALY rates globally and in China. This study presents the updated burden of esophageal cancer attributable to low fruit intake by sex and age globally and in China from 1990 to 2019. The results of this study aim to provide further insight into the management of esophageal cancer, with the goal of reducing its burden in China.

### Methods

#### *Sources of data*

By sourcing data from the GBD 2019 (<https://www.healthdata.org/research-analysis/gbd>), we comprehensively analyzed the incidence, mortality, and DALY of EC attributable to low fruit intakes in China and globally. The GBD 2019, conducted by the Institute for Health

Metrics and Evaluation (IHME), aimed to evaluate the global, regional, and national disease burdens, injuries and the impact of 87 risk factors across 369 diseases in 204 countries and regions. It offers annual age-sex-specific incidence, mortality, and DALY rates. The original data for estimating the impact of low fruit intake in China were obtained from fresh foods market statistics, China National Nutrition Survey, China Chronic Disease and Risk Factor Surveillance and other scientific literature. For this study, the parameters selected from the database included “China” and “global” for location, “esophageal cancer” for the cause, and “death”, “incidence”, and “disability-adjusted life-years (DALY)” for outcomes. We report mortality and DALY rates for EC in China by age and sex, using percentage changes from 1990 to 2019 to reflect the trends in cancer burden.

#### *Statistical analysis*

Descriptive analyses were performed on the incidence, mortality, and DALY data by age and sex. Cases were classified into three age groups (15-49, 50-69, 70+) to describe the age-related incidence, mortality, and DALY rates of EC for the years 1990, 2000, 2010 and 2019. The detailed methods for the calculation of mortality and DALY are available in previous studies [10]. To reflect the trends in EC burden, we also calculated the population attributable factor (PAF), which quantifies the extent of risk posed by these factors to the population [11]. The trend analysis was performed using Joinpoint regression program software (version 4.7.0.0), employing Joinpoint regression model. Additionally, a logarithmic linear regression model was used to calculate the average annual percentage change (AAPC) and its 95% confidence interval (CI), and the trends were also analyzed [12].  $P < 0.05$  was considered to be significant. Data analysis was carried out using R software version 3.6.2.

### Results

#### *The burden of esophageal cancer attributable to low fruit intake across gender groups in China and globally from 1990 to 2019*

As shown in **Tables 1** and **2**, in 2019, the number of deaths from esophageal cancer among Chinese men attributable to low fruit intake was 15,200, representing 42.46% of the global

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**Table 1.** Trends in esophageal cancer deaths attributable to low fruit intake in different genders in China and globally from 1990 to 2019

Gender	PAF (%)		Number of deaths (per 10,000)		Standardized death rates (per 100,000)	
	China	Global	China	Global	China	Global
<b>Male</b>						
1990	0.18	0.16	2.03	3.39	5.27	1.86
2000	0.15	0.14	2.31	3.92	4.54	1.72
2010	0.10	0.11	1.83	3.57	2.76	1.22
2019	0.08	0.10	1.52	3.58	1.72	0.94
Rate of change (%)	0.55	0.37	-0.25	0.06	-0.67	-0.49
<b>Female</b>						
1990	0.18	0.18	1.06	1.80	2.61	0.86
2000	0.15	0.16	1.13	1.99	2.12	0.75
2010	0.10	0.13	0.66	1.55	0.94	0.46
2019	0.07	0.13	0.44	1.57	0.44	0.35
Rate of change (%)	0.60	0.28	-0.59	0.13	-0.83	-0.59

**Table 2.** Trends of esophageal cancer DALY attributable to low fruit intake in different genders in China and globally from 1990 to 2019

Gender	DALY (10,000 person years)		Standardized DALY rates (per 100,000)	
	China	Global	China	Global
<b>Male</b>				
1990	55.03	92.41	123.63	46.68
2000	60.76	104.64	103.92	42.25
2010	45.71	92.52	59.32	29.15
2019	35.60	89.25	35.85	22.31
Rate of change (%)	-0.35	-0.03	-0.71	-0.52
<b>Female</b>				
1990	24.41	43.44	55.64	20.12
2000	25.35	47.24	44.04	17.58
2010	13.34	36.29	17.57	10.55
2019	8.06	35.73	7.78	8.23
Rate of change (%)	-0.67	-0.18	-0.86	-0.59

total (35,800 cases). Additionally, the attributable DALYs amounted to 356,000 person-years, or 39.89% of the global total (892,500 cases). For Chinese women, there were 4,400 attributable deaths, accounting for 28.03% of the global total (15,700 cases), and 80,600 attributable DALYs, representing 22.56% of the global total (357,300 cases). In 2019, the standardized mortality and DALY rates of male esophageal cancer caused by insufficient fruit intake in China (1.72/100,000, 35.85/100,000)

were higher than those in females (0.44/100,000, 7.78/100,000). Similarly, the standardized global mortality and DALY rates for males (0.94/100,000, 22.31/100,000) were higher than those for females (0.35/100,000, 8.23/100,000). The decrease in standardized mortality and DALY rates of EC attributed to insufficient fruit intake in Chinese males from 1990 to 2019 (-0.67% and -0.71%) was lower than those in Chinese females (-0.83% and -0.86%), which were higher than the decreasing trend at a global level (Male: -0.49, -0.52 and Female: -0.59, -0.59).

*Trends of esophageal cancer deaths attributable to low fruit intake across gender and age groups in China and globally from 1990 to 2019*

As shown in **Tables 3** and **4**, there were differences in the PAF of EC deaths caused by insufficient fruit intake across various age groups in China in 2019. The age group 15-49 years displayed the highest PAF (10.14%), while the age group 50-69 years displayed the lowest PAF (7.20%). The attributed standardized mortality and DALY rates increased with age, peaking in the group aged 70 years and above (9.53/100,000, 137.41/100,000), significantly higher than global data (4.92/100,000, 71.34/100,000). From 1990 to 2019, the most significant reductions in PAF, standardized mortality, and DALY rates

occurred in the 50-69 year age group, with decreases of 0.58%, 0.79%, and 0.79% respectively. Examining gender-specific trends, the majority of esophageal cancer deaths in China in 2019 due to low fruit intake occurred in individuals aged 75 years and above, with 7,200 cases in males and 3,000 in females. Globally, the highest number of male deaths was in the 50-69 years group (17,500 cases), which also saw the highest DALYs in males aged 50-69 (20,700 person-years) and in females aged 70

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**Table 3.** Trends of esophageal cancer deaths attributable to low fruit intake in different gender and age groups in China and globally from 1990 to 2019

Age groups (years)	Gender	PAF (%)		Number of deaths (10,000)		Standardized death rates (per 100,000)	
		China	Global	China	Global	China	Global
15~49	Male						
	1990	20.32	18.69	0.23	0.40	0.67	0.29
	2000	17.21	16.97	0.29	0.50	0.76	0.31
	2010	12.28	13.92	0.19	0.41	0.48	0.22
	2019	10.19	13.54	0.11	0.34	0.28	0.17
	Rate of change (%)	-0.50	-0.28	-0.55	-0.16	-0.58	-0.42
	Female						
	1990	19.51	19.87	0.05	0.14	0.16	0.11
	2000	17.19	18.70	0.08	0.20	0.23	0.12
	2010	12.38	17.45	0.03	0.15	0.07	0.08
	2019	9.73	17.78	0.01	0.14	0.03	0.07
	Rate of change (%)	-0.50	-0.11	-0.77	-0.01	-0.79	-0.32
	Both of sexes						
	1990	20.16	19.00	0.28	0.54	0.42	0.20
	2000	17.20	17.43	0.37	0.70	0.50	0.22
2010	12.29	14.73	0.22	0.55	0.28	0.15	
2019	10.14	14.60	0.12	0.48	0.16	0.12	
Rate of change (%)	-0.50	-0.23	-0.59	-0.12	-0.62	-0.39	
50~69	Male						
	1990	17.05	15.65	1.14	1.92	14.27	5.70
	2000	14.00	13.89	1.14	2.00	11.50	5.00
	2010	9.17	10.82	0.85	1.77	6.28	3.38
	2019	7.32	9.84	0.69	1.75	3.72	2.60
	Rate of change (%)	-0.57	-0.37	-0.40	-0.09	-0.74	-0.54
	Female						
	1990	17.60	17.45	0.50	0.83	6.70	2.41
	2000	14.90	15.88	0.43	0.80	4.68	1.97
	2010	9.45	12.99	0.22	0.60	1.66	1.12
	2019	6.56	12.69	0.12	0.61	0.67	0.86
	Rate of change (%)	-0.63	-0.27	-0.75	-0.27	-0.90	-0.64
	Both of sexes						
	1990	17.21	16.15	1.64	2.75	10.62	4.03
	2000	14.23	14.40	1.57	2.80	8.20	3.47
2010	9.22	11.29	1.07	2.38	4.01	2.23	
2019	7.20	10.44	0.81	2.36	2.20	1.71	
Rate of change (%)	-0.58	-0.35	-0.51	-0.14	-0.79	-0.58	
70 years and more	Male						
	1990	17.12	15.38	0.66	1.07	39.99	13.00
	2000	14.32	13.59	0.88	1.41	35.82	12.41
	2010	9.70	10.47	0.79	1.40	22.00	9.04
	2019	7.66	9.18	0.72	1.48	14.72	7.27
	Rate of change (%)	-0.55	-0.40	0.10	0.38	-0.63	-0.44
	Female						
	1990	17.79	16.73	0.51	0.82	23.48	6.90

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2000	15.24	15.05	0.61	0.98	20.30	6.29
2010	10.23	11.87	0.42	0.82	10.03	4.03
2019	7.38	10.60	0.30	0.80	5.17	3.08
Rate of change (%)	-0.58	-0.37	-0.41	-0.03	-0.78	-0.55
Both of sexes						
1990	17.39	15.92	1.17	1.89	30.60	9.39
2000	14.67	14.14	1.50	2.40	27.27	8.87
2010	9.87	10.93	1.21	2.22	15.55	6.19
2019	7.58	9.61	1.03	2.28	9.53	4.92
Rate of change (%)	-0.56	-0.40	-0.12	0.21	-0.69	-0.48

**Table 4.** Trends in esophageal cancer DALY attributable to low fruit intake in different gender and age groups in China and globally from 1990 to 2019

Age groups (years)	Gender	DALY (10,000 person years)		Standardized DALY Rates (per 100,000)	
		China	Global	China	Global
15~49	Male				
	1990	10.70	18.37	30.97	13.37
	2000	13.16	22.94	34.35	14.12
	2010	8.81	18.57	21.62	9.99
	2019	4.77	15.40	12.90	7.74
	Rate of change (%)	-0.55	-0.16	-0.58	-0.42
	Female				
	1990	2.39	6.84	7.40	5.11
	2000	3.77	9.29	10.39	5.85
	2010	1.32	6.91	3.37	3.79
	2019	0.54	6.71	1.53	3.45
	Rate of change (%)	-0.78	-0.02	-0.79	-0.33
	Both of sexes				
	1990	13.09	25.21	19.58	9.30
	2000	16.93	32.23	22.70	10.03
2010	10.14	25.48	12.67	6.92	
2019	5.30	22.11	7.36	5.62	
Rate of change (%)	-0.59	-0.12	-0.62	-0.40	
50~69	Male				
	1990	33.54	56.88	420.30	169.03
	2000	33.43	59.21	338.46	147.98
	2010	25.00	52.72	184.96	100.40
	2019	20.07	51.82	108.78	76.65
	Rate of change (%)	-0.40	-0.09	-0.74	-0.55
	Female				
	1990	14.03	24.04	188.99	69.56
	2000	12.25	23.21	132.65	56.88
	2010	6.15	17.68	47.05	32.81
	2019	3.45	17.96	18.70	25.56
	Rate of change (%)	-0.75	-0.25	-0.90	-0.63
	Both of sexes				
	1990	47.57	80.92	308.79	118.63

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	2000	45.69	82.42	239.01	101.98
	2010	31.15	70.40	117.18	66.17
	2019	23.52	69.79	63.75	50.61
	Rate of change (%)	-0.51	-0.14	-0.79	-0.57
70 years and more	Male				
	1990	10.80	17.16	653.93	208.70
	2000	14.16	22.49	573.98	197.58
	2010	11.90	21.23	332.68	137.28
	2019	10.76	22.02	218.62	108.27
	Rate of change (%)	0.00	0.28	-0.67	-0.48
	Female				
	1990	7.98	12.56	367.12	105.25
	2000	9.33	14.74	308.45	94.16
	2010	5.87	11.70	140.50	57.29
	2019	4.07	11.06	69.32	42.48
	Rate of change (%)	-0.49	-0.12	-0.81	-0.60
	Both of sexes				
	1990	18.78	29.72	490.87	147.46
	2000	23.50	37.23	427.73	137.71
	2010	17.76	32.93	229.16	91.76
	2019	14.84	33.08	137.41	71.34
	Rate of change (%)	-0.21	0.11	-0.72	-0.52

years and above (40,700 person-years). For both genders worldwide, the majority of DALYs were in the age group of 50-69 years (518,200 person-years for males and 179,600 person-years for females). Additionally, standardized mortality and DALY rates for males in all age groups were consistently higher than those for females, both in China and globally.

### *The temporal trends of burden of esophageal cancer attributable to low fruit intake in China and globally*

As shown in **Table 5**, in 2019, the figures for deaths, standardized mortality rate, DALY and standardized DALY rates of EC attributed to insufficient fruit intake in China were 51,900, 1.32/100,000, 1.3585 million person-years and 32.83/100,000, respectively. These metrics were all higher than the global figures (51,500, 0.63/100,000, 1.2498 million person-years and 14.96/100,000). From 1990 to 2019, China experienced an overall downward trend in the number of deaths, standardized mortality rates, DALYs, and standardized DALY rates in EC attributable to low fruit intake, with AAPCs of -1.62%, -4.54%, -2.10%, and -4.88%, respectively, with statistical significance ( $P < 0.001$ ). In contrast, the global death toll and

DALY remained stable, with AAPCs of -0.10% and -0.33%, respectively, with statistical significance ( $P < 0.001$ ).

### **Discussion**

To our knowledge, this is the most recent study analyzing long-term effects of low fruit intake on mortality and DALY rates of esophageal cancer in China. Based on the Global Burden of Disease Study 2019 (GBD 2019), this analysis examined the burden of esophageal cancer attributable to low fruit intake from 1990 to 2019. It reported that in 2019, there were 51,900 deaths and 1.3585 million person-years lost due to esophageal cancer attributable to insufficient fruit intake in China. These figures are significantly higher than the global averages, aligning with findings from previous relevant studies [13]. Another study identified insufficient fruit intake as the fourth largest risk factor for the burden of EC [14], underlining the need for targeted management and control measures focusing on low fruit intake to reduce EC incidence.

Several studies have demonstrated an inverse association between the EC risk and fruit intake [15]. Fruits are rich in vitamins, antioxidants,

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**Table 5.** The Joinpoint results for esophageal cancer burden attributable to low fruit intake between 1990 and 2019 in China and globally

Indicator	1990	2019	AAPC (%)	95% CI	P value
China					
Numbers of deaths	3.09	5.19	-1.62	(-2.05~-1.20)	<0.001
Standardized death rates	3.86	1.32	-4.54	(-4.81~-4.26)	<0.001
DALY	79.44	135.85	-2.10	(-2.37~-1.84)	<0.001
Standardized DALY rates	89.33	32.83	-4.88	(-5.14~-4.61)	<0.001
Global					
Numbers of deaths	1.95	5.15	-0.10	(-0.23~0.04)	0.160
Standardized death rates	1.02	0.63	-2.57	(-2.71~-2.43)	<0.001
DALY	43.66	124.98	-0.33	(-0.46~-0.21)	<0.001
Standardized DALY rates	21.28	14.96	-2.71	(-2.84~-2.59)	<0.001

and other bio-active compounds that play a crucial role in preventing EC through reducing inflammation and oxidative stress, and enhancing the activity of detoxifying enzymes. Moreover, fruits are good sources of folate, which has been linked to a reduced risk of EC [16]. The results of this study showed that the mortality rate, standardized mortality rate, DALY, and standardized DALY rates of EC attributed to insufficient fruit intake in China and globally were higher in males than those in females, corroborating findings from previous study [17]. The study by Domper Arnal et al. [18] highlighted that these gender differences might be associated with varying lifestyle habits and physiological factors. In terms of lifestyle habits, men had a higher exposure rate to risk factors such as smoking, drinking alcohol, high BMI, and chewing betel nut than women, leading to a higher baseline mortality rate for EC compared to women [14]. Physiologically, women may benefit from the protective effects of endogenous estrogen [19]. Moreover, there are notable differences in the fruit intakes between genders, with the average daily fruit intakes for adult males and females in 2018 being 96.6 g and 133.1 g, respectively [20]. This may be related to women's stronger health awareness and willingness to change unhealthy lifestyles. Therefore, men should be a primary focus in the prevention and control of esophageal cancer, and the government should take measures to strengthen health education, improve the health awareness and behavior of the male population, to reduce the burden of esophageal cancer attributable to insufficient fruit intake in China.

In this study, the attributed standardized mortality and DALY rates in different age groups in China increased with age, peaking in individuals aged 70 years and above. However, the PAF in this age group was relatively low, possibly due to an aging population, metabolic decline and diminished autoimmune function. The elderly population (>65 years old) in China only accounted for 5.63% in 1990, but this figure rose to 12.6% in 2019. Projections suggest that China will experience a rapid increase in aging, expecting to reach a peak of 437 million individuals by 2051. Over time, this demographic shift suggests that the burden of esophageal cancer will worsen. Moreover, some elderly individuals must manage their blood sugar levels, resulting in generally lower fruit consumption compared to younger people [21]. Thus, it is crucial to focus prevention and treatment efforts for esophageal cancer related to inadequate fruit intake on health promotion activities targeted at the elderly, particularly those over 50, guiding them in making informed choices about fruit consumption.

The results of this study showed that in 2019, the number of deaths, standardized mortality rate, DALY, and standardized DALY rates in China were all higher than the global averages. In addition, there was an overall downward trend in these metrics in China, with decline more pronounced than those observed globally. This trend may be related to the Chinese government's implementation of esophageal cancer screening for high-risk populations since 2006, continuous improvement of residents' nutritional status and living environment and improvement of medical technology. In 2012,

China launched a program for the screening, early diagnosis and treatment of EC in urban areas, which had expanded to cover 29 provinces, municipalities, and autonomous regions by 2019 [3]. Efforts by the Chinese Nutrition Society to promote smoking cessation, alcohol moderation, regular physical activity, weight control, and increased fruit intake have effectively reduced the mortality rate of esophageal cancer [22]. Although the daily average fruit intake among the Chinese population has been gradually increasing, it remains below the recommended level in dietary guidelines. Targeted preventive measures should be taken to adjust the nutritional diet structure reasonably, improve the current situation of low fruit intakes in China, reduce the burden of esophageal cancer attributable to insufficient fruit consumption, thus advancing the health aspirations of the Chinese people.

In summary, from 1990 to 2019, China witnessed a reduction in the burden of esophageal cancer attributed to insufficient fruit intake. However, compared to global averages, the disease burden of esophageal cancer in China remains high. Scientifically increasing fruit intakes is of great significance in reducing the burden of esophageal cancer, with the elderly and men identified as key demographic groups for targeted prevention and control measures. Health administrative departments in China should develop targeted strategies for primary prevention, actively promote health education among these key populations, and encourage higher fruit consumption to mitigate the future disease burden of esophageal cancer.

This study has several limitations. Firstly, esophageal cancer includes two main histological subtypes - esophageal squamous cell carcinoma and adenocarcinoma - each associated with different risk factors and the incidence trends. Unfortunately, GBD database does not provide separate data for these subtypes. Secondly, detailed information on the duration and frequency of fruit intakes among the general population in China was not available, which may limit the comprehensive evaluation of the effects of low fruit intake on EC. Thirdly, the results of this study were obtained from the GBD 2019, which integrates data from a variety of data sources such as unpublished and pub-

lished data. The lack of direct examination of low fruit intakes in some datasets could introduce potential biases. Hence, the further studies focusing on esophageal cancer attributable are necessary to enhance the quality and availability of relevant data.

### Disclosure of conflict of interest

None.

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