

Postprint: Analysis of Trends and Mortality Prediction of Tobacco-Attributable Esophageal Cancer Disease Burden in China, 1990–2019

Authors: Liu Ailing, Zhou Jingjing, Li Chengcheng, He Kaiyue, Liang Shan-shan, Zhou Shangcheng, Zhou Shangcheng

Date: 2023-07-24T00:00:00+00:00

Abstract

Background China faces a substantial disease burden from esophageal cancer, with mounting evidence demonstrating significant adverse effects of tobacco on esophageal cancer incidence. Objective To examine mortality and disease burden trends of esophageal cancer attributable to tobacco in China from 1990 to 2019, providing data to inform public health policy and intervention development. Methods This study utilized GBD 2019 data, extracting age- and sex-specific data on tobacco-attributable esophageal cancer mortality in China from 1990 to 2019. Mortality rate, disability-adjusted life years (DALYs), years of life lost (YLLs), and years lived with disability (YLDs) were employed to assess the disease burden of tobacco-attributable esophageal cancer in China. Joinpoint regression software and age-period-cohort modeling were applied to analyze temporal trends in disease burden and mortality across age, period, and cohort dimensions. Bayesian age-period-cohort analysis (BAPC) was subsequently used to project mortality from tobacco-attributable esophageal cancer in China from 2020 to 2030. Results From 1990 to 2019, tobacco-attributable esophageal cancer deaths among Chinese residents increased from 76,400 to 123,900 (a 62.17% increase), while the age-standardized mortality rate decreased from 9.30/100,000 to 6.20/100,000 annually (a 33.33% decline). DALYs rose from 1.9725 million to 2.8226 million person-years (a 43.10% increase), and the DALY rate declined from 220.50/100,000 to 134.47/100,000 (a 39.02% decrease). By sex, the disease burden was predominantly borne by males, with tobacco-related esophageal cancer causing 117,700 male deaths (age-standardized mortality rate: 12.82/100,000) and 6,200 female deaths (age-standardized mortality rate: 0.63/100,000) in 2019. In 2019, tobacco-attributable esophageal cancer deaths peaked in the >69-74 age group, while DALYs peaked in the >64-69 age group (23,000 deaths and 510,300 DALYs, respectively). Mortality increased

progressively with age, accelerating markedly after age 50. Joinpoint regression revealed an AAPC of -1.4 [95%CI (-1.6, -1.2)] for tobacco-attributable esophageal cancer mortality in China from 1990-2019, with -3.3 [95%CI (-3.6, -2.9)] for females and -1.3 [95%CI (-1.4, -1.1)] for males. The AAPC for the DALY rate was -1.7 [95%CI (-1.9, -1.5)], with -3.7 [95%CI (-4.0, -3.4)] for females and -1.5 [95%CI (-1.7, -1.3)] for males. Age-period-cohort analysis of tobacco-attributable esophageal cancer mortality demonstrated a negative net drift of -1.690% [95%CI (-2.024%, -1.354%)]. Projections for 2020-2030 indicate relatively stable deaths and mortality rates with modest declines, with male mortality decreasing from 12.64/100,000 in 2020 to 12.63/100,000 in 2030, and female mortality decreasing from 0.6/100,000 in 2020 to 0.46/100,000 in 2030. Conclusion From 1990 to 2019, tobacco-attributable esophageal cancer mortality and DALYs in China initially increased then decreased. The disease burden was predominantly borne by males and primarily affected middle-aged and elderly populations, warranting targeted attention. Projections for 2020-2030 suggest relatively stable deaths and mortality rates with slight declines.

Full Text

Analysis of the Disease Burden Trends and Death Projections for Esophageal Cancer Attributable to Tobacco in China from 1990 to 2019

LIU Ailing, ZHOU Jingjing, LI Chengcheng, HE Kaiyue, LIANG Shanshan, ZHOU Shangcheng*

School of Public Health and Management, Guangzhou University of Chinese Medicine, Guangzhou 510006, China

Corresponding author: ZHOU Shangcheng, Professor/Doctoral supervisor; E-mail: whzsc2008@hotmail.com

Abstract

Background: The disease burden of esophageal cancer is substantial in China, and accumulating evidence demonstrates that tobacco exerts significant adverse effects on esophageal cancer development.

Objective: To examine trends in mortality and disease burden of esophageal cancer attributable to tobacco among Chinese residents from 1990 to 2019, providing data to inform public health policy and intervention development.

Methods: This study utilized Global Burden of Disease 2019 (GBD 2019) data, extracting age- and sex-specific data on esophageal cancer deaths attributable to tobacco in China from 1990 to 2019. Mortality, disability-adjusted life years (DALYs), years of life lost (YLLs), and years lived with disability (YLDs) were employed to assess the disease burden. Joinpoint regression software and age-period-cohort modeling were applied to analyze temporal trends in disease bur-

den and mortality across age, period, and cohort dimensions. Bayesian age-period-cohort analysis (BAPC) was subsequently used to project mortality rates for esophageal cancer attributable to tobacco from 2020 to 2030.

Results: From 1990 to 2019, deaths from esophageal cancer attributable to tobacco among Chinese residents increased from 76,400 to 123,900 cases (a 62.17% rise), while the age-standardized mortality rate declined from 9.30/100,000 to 6.20/100,000 (a 33.33% decrease). DALYs increased from 1.9725 million to 2.8226 million person-years (a 43.10% increase), and the DALY rate decreased from 220.50/100,000 to 134.47/100,000 (a 39.02% decline). By sex, the disease burden was overwhelmingly borne by males, with 117,700 deaths and an age-standardized mortality rate of 12.82/100,000 in 2019, compared to 6,200 deaths and a rate of 0.63/100,000 among females. In 2019, deaths peaked in the >69–74 years age group (23,000 cases), while DALYs peaked in the >64–69 years group (510,300 cases). Mortality increased progressively with age, particularly after age 50. Joinpoint regression revealed an average annual percent change (AAPC) of -1.4 [95%CI (-1.6, -1.2)] for mortality, with -3.3 [95%CI (-3.6, -2.9)] for females and -1.3 [95%CI (-1.4, -1.1)] for males. The AAPC for DALY rates was -1.7 [95%CI (-1.9, -1.5)], with -3.7 [95%CI (-4.0, -3.4)] for females and -1.5 [95%CI (-1.7, -1.3)] for males. Age-period-cohort analysis showed a net drift of -1.690% [95%CI (-2.024%, -1.354%)]. Projections for 2020–2030 indicate that deaths and mortality rates will remain relatively stable with modest declines, with male rates decreasing from 12.64/100,000 in 2020 to 12.63/100,000 in 2030, and female rates from 0.6/100,000 to 0.46/100,000.

Conclusion: From 1990 to 2019, mortality and DALY rates for esophageal cancer attributable to tobacco initially increased then declined. Males and middle-aged/elderly populations bore the primary disease burden, warranting targeted attention. Projections suggest stable mortality with slight decreases from 2020 to 2030.

Keywords: Esophageal neoplasms; Smoking; Mortality; Disability-adjusted life years; Burden of illness; Bayesian age-period-cohort analysis

Introduction

According to the International Agency for Research on Cancer (IARC), esophageal cancer accounted for 604,000 new cases globally, ranking as the eighth most common malignancy and the sixth leading cause of cancer-related death worldwide. Approximately one-third of disability-adjusted life years (DALYs) from digestive system cancers are attributable to esophageal cancer. The disease exhibits pronounced geographic heterogeneity, with Asia—particularly East Asia—bearing the highest incidence and mortality, and over 50% of cases occurring in China. Epidemiological studies have identified that 39% of the global esophageal cancer burden is attributable to smoking, 33.8% to alcohol consumption, 19.5% to high BMI, 19.1% to low fruit intake,

and 7.5% to chewing tobacco. While previous analyses have examined the overall burden of esophageal cancer, few have specifically isolated the burden attributable to tobacco. Given China's accelerating population aging and persistent tobacco use, assessing the tobacco-attributable burden is critical for advancing prevention strategies. This study analyzes the disease burden of esophageal cancer attributable to tobacco by sex, age, and risk factor (including smoking and chewing) using GBD 2019 data, providing evidence to inform esophageal cancer prevention policies in China.

Methods

Data Sources This study utilized GBD 2019 data, which employs standardized methods to assess disease burden across 369 diseases and 87 risk factors in 204 countries and territories. Data sources for GBD estimation include censuses, household surveys, civil registrations, disease registries, health service utilization records, air pollution monitoring, and satellite imagery. We selected “esophageal cancer” as the disease outcome and “tobacco” as the risk factor, extracting “Deaths,” “DALYs,” “YLLs,” and “YLDs” metrics. Age- and sex-specific data for China from 1990–2019 were extracted, including 95% confidence intervals.

Measurement Indicators Mortality, DALYs, YLLs, and YLDs were used to evaluate the disease burden of esophageal cancer attributable to tobacco. DALYs represent the total healthy life years lost due to morbidity and mortality, comprising YLLs (years of life lost due to premature death) and YLDs (years lived with disability).

Statistical Methods Joinpoint Regression Analysis. The log-linear model in Joinpoint regression was employed to analyze population-based cancer mortality trends. The default grid search method (GSM) identifies optimal turning points by partitioning data into grids and calculating performance metrics at each intersection. Joinpoint detects inflection points in disease trends, segmenting the overall trajectory into periods with distinct annual percent changes (APC). APC and average annual percent change (AAPC) with 95% confidence intervals were calculated as: $APC = [\exp(\beta) - 1] \times 100$, where β is the regression coefficient; $AAPC = [\exp(w \beta / w) - 1] \times 100$, where w represents the interval width (in years) and β the corresponding regression coefficient for each segment.

Age-Period-Cohort Model Analysis. Based on Poisson distribution, this model addresses collinearity among age, period, and cohort effects, enabling independent evaluation of each factor's impact—an established tool in epidemiology. Given the characteristics of GBD 2019 data and the APC web tool (<https://analysistools.cancer.gov/apc/>), we constructed 5-year intervals for analysis. Data below age 30 were excluded due to zero cases, yielding 14 age groups.

The period 1990–2019 was divided into six 5-year intervals. Birth cohorts were calculated as cohort = period - age, with values derived according to data characteristics.

Bayesian Age-Period-Cohort Analysis (BAPC). BAPC integrates sample information with prior distributions to estimate posterior distributions for unknown parameters, implemented via the BAPC and INLA packages in R. This approach was used to project mortality rates for esophageal cancer attributable to tobacco from 2020 to 2030, based on GBD 1990–2019 data, using the projected standard population from GBD 2019.

Results

Trends in Deaths and Disease Burden from Esophageal Cancer Attributable to Tobacco, 1990–2019 From 1990 to 2019, deaths from esophageal cancer attributable to tobacco among Chinese residents increased from 76,400 to 123,900 cases (62.17% increase), while the age-standardized mortality rate declined from 9.30/100,000 to 6.20/100,000 (33.33% decrease). DALYs rose from 1.9725 million to 2.8226 million person-years (43.10% increase), with the DALY rate decreasing from 220.50/100,000 to 134.47/100,000 (39.02% decline). YLDs increased from 19,200 to 35,000 person-years (82.29% increase), while the YLD rate decreased from 2.22/100,000 to 1.70/100,000 (23.42% decline). YLLs rose from 1.9533 million to 2.7876 million person-years (42.71% increase), with the YLL rate decreasing from 218.28/100,000 to 132.78/100,000 (39.17% decline).

By sex, males accounted for the overwhelming majority of the disease burden. In 2019, tobacco-attributable esophageal cancer caused 117,700 male deaths (age-standardized mortality rate: 12.82/100,000) versus 6,200 female deaths (rate: 0.63/100,000)—18.98 times and 20.35 times higher, respectively. DALYs were similarly dominated by males. Overall, deaths and DALYs increased from 1990–2005, decreased from 2005–2015, then rose slowly after 2015. Age-standardized mortality and DALY rates peaked around 2005 before declining progressively [Figure 1: see original paper][Figure 2: see original paper].

Comparison of Deaths and Disease Burden Between 1990 and 2019

In 2019, deaths peaked in the >69–74 years age group (23,000 cases), while DALYs peaked in the >64–69 years group (510,300 cases). Mortality increased continuously with age, rising sharply after age 50 and peaking in the >84–89 years group. The DALY rate peaked in the >69–74 years group before declining. Trends in age-specific mortality and DALY rates were similar between 1990 and 2019, though rates in 2019 were lower across all age groups [Figure 3: see original paper][Figure 4: see original paper].

Joinpoint Regression Analysis of Mortality Trends, 1990–2019 Joinpoint regression identified five distinct segments in mortality trends: stable from 1990–1998, increasing from 1998–2004 ($P < 0.05$), decreasing from 2004–2017 ($P < 0.05$), and stable from 2017–2019. The overall AAPC was -1.4 [95%CI (-1.6, -1.2)], with -3.3 [95%CI (-3.6, -2.9)] for females and -1.3 [95%CI (-1.4, -1.1)] for males. Across age groups (excluding 0–29 years with no cases), most exhibited declining trends ($P < 0.05$), with the steepest decline in the >39–44 years group (AAPC: -3.0 [95%CI (-3.3, -2.8)]). Only the >84–89 years group showed an increase (AAPC: 0.2 [95%CI (0, 0.5)]).

Age-Period-Cohort Analysis of Mortality, 1990–2019 The age-period-cohort model revealed a negative net drift of -1.690% [95%CI (-2.024%, -1.354%)]. Local drift declined from ages 30–42, reaching a minimum of -3.710% [95%CI (-4.279, -3.138)] at age 42, then increased gradually. After adjusting for period and cohort effects, age effects showed mortality increasing substantially with age, peaking around age 92 before declining. Period effects fluctuated: mortality decreased from 1990–1997, increased to 2002 (reference: RR=1.00), then fell to its lowest level [RR=0.6538, 95%CI (0.617, 0.6931), $P < 0.05$]. Cohort effects were relatively stable, rising slowly from 1905–1920, peaking in 1920 [RR=1.377, 95%CI (1.305, 1.453), $P < 0.05$], then declining to 1985 [RR=0.342, 95%CI (0.159, 0.732), $P < 0.05$] [Figure 5: see original paper].

Projections for 2020–2030 Projections indicate that deaths and mortality rates will remain relatively stable with modest declines from 2020–2030. Mortality will increase among those aged 30–49, decrease among those aged >49–74, and increase again among those >74–95. The largest increases will occur in the 30–34 years group (40.00% increase) and >34–39 years group (28.21% increase), while the steepest decline will be in the >54–59 years group (from 12.24/100,000 in 2020 to 11.08/100,000 in 2030) [Figure 6: see original paper][Figure 7: see original paper].

Discussion

From 1990–2019, mortality and DALY rates for esophageal cancer attributable to tobacco initially increased then declined. The disease burden was overwhelmingly concentrated among males and middle-aged/elderly populations, necessitating targeted interventions. Projections for 2020–2030 suggest stable mortality with slight decreases.

The increase in absolute deaths and DALYs likely reflects demographic shifts, including population growth and aging. China's elderly population (>65 years) rose from 5.6% in 1990 to 12.6% in 2019, reaching 267 million (18.9% of the total population) by 2021. Declining mortality rates may be attributed to socioeconomic development, dietary improvements, and tobacco control initiatives

following China's 2003 Framework Convention on Tobacco Control. The mortality and DALY rate peak in 2004 followed by decline suggests early success of tobacco control policies. The AAPC of -1.4 overall, with a more pronounced decline among females (-3.3) than males (-1.3), likely reflects lower female smoking prevalence and reduced secondhand smoke exposure.

Males experienced a 20-fold higher mortality rate than females, consistent with higher male smoking prevalence. A prospective cohort study reported that smoking accounted for 19.4% of esophageal cancer deaths in men versus 1.6% in women—findings that align with our results. Prevention efforts should prioritize males and middle-aged/elderly populations, as mortality increases with age due to cumulative tobacco exposure, peaking in the 70–80 years group. Period effects showed overall declining mortality, likely reflecting national tobacco control policies and economic development. Smoking cessation significantly reduces esophageal cancer risk within five years, with risk approaching that of never-smokers after 20 years.

The “Healthy China 2030” initiative prioritizes tobacco control. Our projections indicate modest mortality declines from 2020–2030, with concerning increases among younger adults (30–49 years), who represent a critical demographic for national development. This underscores the need for intensified tobacco control among youth, alongside continued prevention efforts targeting high-risk male and elderly populations through health education, smoking cessation support, and lifestyle modification.

This study has limitations. GBD 2019 lacks incidence data for tobacco-attributable esophageal cancer in China; incorporating incidence would strengthen future analyses. Additionally, GBD's multi-model estimation approach may deviate from actual conditions, potentially affecting projection accuracy.

Author Contributions

LIU Ailing: Conceptualization, original draft preparation. ZHOU Jingjing: Data collection and collation. LI Chengcheng: Statistical analysis and visualization. HE Kaiyue: Manuscript revision. LIANG Shanshan: Literature review. ZHOU Shangcheng: Quality control.

Conflicts of Interest: None declared.

References

[1] LAGERGREN J, SMYTH E, CUNNINGHAM D, et al. Oesophageal cancer[J]. *Lancet*, 2017, 390(10110): 2383-2396. DOI: 10.1016/s0140-6736(17)31462-9.

- [2] BRAY F, FERLAY J, SOERJOMATARAM I, et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries[J]. *CA Cancer J Clin*, 2018, 68(6): 394-424. DOI: 10.3322/caac.21492.
- [3] Global Burden Of Disease Cancer Collaboration, FITZMAURICE C, ABATE D, et al. Global, regional, and national cancer incidence, mortality, years of life lost, years lived with disability, and disability-adjusted life-years for 29 cancer groups, 1990 to 2017: a systematic analysis for the global burden of disease study[J]. *JAMA Oncol*, 2019, 5(12): 1749-1768. DOI: 10.1001/jamaoncol.2019.2996.
- [4] GBD 2017 Oesophageal Cancer Collaborators. The global, regional, and national burden of oesophageal cancer and its attributable risk factors in 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017[J]. *Lancet Gastroenterol Hepatol*, 2020, 5(6): 582-597. DOI: 10.1016/S2468-1253(20)30007-8.
- [5] GBD Risk Factors Collaborators. Global burden of 87 risk factors in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019[J]. *Lancet*, 2020, 396(10258): 1223-1249. DOI: 10.1016/S0140-6736(20)30752-2.
- [6] COLLABORATORS G 2 D A I. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019[J]. *Lancet*, 2020, 396(10258): 1204-1222. DOI: 10.1016/S0140-6736(20)30925-9.
- [7] KIM H J, FAY M P, FEUER E J, et al. Permutation tests for joinpoint regression with applications to cancer rates[J]. *Stat Med*, 2000, 19(3): 335-351. DOI: 10.1002/(sici)1097-0258(20000215)19:3<335:aid-sim336>3.0.co;2-z.
- [8] ZENG S Q. Joinpoint regression model and its application in infectious disease trend analysis[J]. *Chinese Journal of Health Statistics*, 2019, 36(5): 787-791.
- [9] ZENG S Q, LI Y, LIU J, et al. Comparison of trend characteristics between two sequential datasets using Joinpoint regression model[J]. *Chinese Journal of Health Statistics*, 2021, 38(2): 307-311. DOI: 10.3969/j.issn.1002-3674.2021.02.039.
- [10] LI H Z, DU L B. Application of Joinpoint regression model in time trend analysis of cancer epidemiology[J]. *Chinese Journal of Preventive Medicine*, 2020, 54(8): 908-912. DOI: 10.3760/cma.j.cn112150-20200616-00889.
- [11] LIU X, YU C, BI Y, et al. Trends and age-period-cohort effect on incidence and mortality of prostate cancer from 1990 to 2017 in China[J]. *Public Health*, 2019, 172: 70-80. DOI: 10.1016/j.puhe.2019.04.016.
- [12] WANG L, YU C H, ZHANG G S, et al. Comparison of secular trends in road injury mortality in China and the United States: an age-period-cohort

analysis[J]. *Int J Environ Res Public Health*, 2018, 15(11): 2508. DOI: 10.3390/ijerph15112508.

[13] LIANG S S, ZHOU Z H, LI C C, et al. Analysis of disease burden and incidence prediction of diabetes in China from 1990 to 2019[J]. *Chinese General Practice*, 2023, 26(16): 2013-2019. DOI: 10.12114/j.issn.1007-9572.2023.0009.

[14] XU Q Q, YAN Y F, CHEN H, et al. Prediction of sustainable development goals for mortality of four major chronic diseases in China[J]. *Chinese Journal of Epidemiology*, 2022, 43(6): 878-884. DOI: 10.3760/cma.j.cn112338-20211028-00830.

[15] CHEN F, WANG Y Q. Analysis of disease burden and changing trends of esophageal cancer in China from 1990 to 2019[J]. *China Cancer*, 2021, 30(6): 401-407. DOI: 10.11735/j.issn.1004-0242.2021.06.A001.

[16] LIU J S, WU Y J, YUAN Y. Population aging, public expenditure, and ecological sustainability[J]. *Economic Issues*, 2023(4): 37-44. DOI: 10.16011/j.cnki.jjw.2023.04.010.

[17] COOK M B, DAWSEY S M, FREEDMAN N D, et al. Sex disparities in cancer incidence by period and age[J]. *Cancer Epidemiol Biomarkers Prev*, 2009, 18(4): 1174-1182. DOI: 10.1158/1055-9965.EPI-08-1118.

[18] EDGREN G, LIANG L M, ADAMI H O, et al. Enigmatic sex disparities in cancer incidence[J]. *Eur J Epidemiol*, 2012, 27(3): 187-196. DOI: 10.1007/s10654-011-9647-5.

[19] GU D F, KELLY T N, WU X G, et al. Mortality attributable to smoking in China[J]. *N Engl J Med*, 2009, 360(2): 150-159. DOI: 10.1056/NEJMsa0802902.

[20] WANG Q L, XIE S H, LI W T, et al. Smoking cessation and risk of esophageal cancer by histological type: systematic review and meta-analysis[J]. *J Natl Cancer Inst*, 2017, 109(12): 10.1093/jnci/djx115. DOI: 10.1093/jnci/djx115.

[21] Healthy China Action (2019–2030)[EB/OL]. (2019-07-15)[2023-03-02]. https://www.gov.cn/xinwen/2019-07/15/content_{5409694}.htm.

Figures and Tables

[Figure 1: see original paper] Changes in deaths, DALYs, YLDs, and YLLs for esophageal cancer attributable to tobacco in China, 1990–2019

[Figure 2: see original paper] Changes in standardized mortality rate, DALY rate, YLD rate, and YLL rate for esophageal cancer attributable to tobacco in China, 1990–2019

[Figure 3: see original paper] Age- and sex-specific disease burden trends for esophageal cancer attributable to tobacco in China, 2019

[Figure 4: see original paper] Age- and sex-specific disease burden trends for esophageal cancer attributable to tobacco in China, 1990 vs. 2019

[Figure 5: see original paper] Age-period-cohort effects on esophageal cancer mortality attributable to tobacco in China, 1990–2019

[Figure 6: see original paper] Projected esophageal cancer deaths attributable to tobacco in China, 2020–2030

[Figure 7: see original paper] Projected age-specific esophageal cancer deaths attributable to tobacco in China, 2020–2030

Trends in esophageal cancer mortality attributable to tobacco in China, 1990–2019

Age-specific mortality trends for esophageal cancer attributable to tobacco in China, 1990–2019

Note: Figure translations are in progress. See original paper for figures.

Source: ChinaXiv — Machine translation. Verify with original.