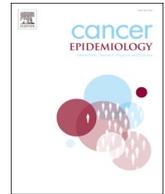




ELSEVIER

Contents lists available at ScienceDirect

## Cancer Epidemiology

journal homepage: [www.elsevier.com/locate/canep](http://www.elsevier.com/locate/canep)

## Trends in disability-adjusted life years of lung cancer among women from 2004 to 2030 in Guangzhou, China: A population-based study



Xiao Lin<sup>a</sup>, Michael S Bloom<sup>b</sup>, Zhicheng Du<sup>a</sup>, Yuantao Hao<sup>a,c,\*</sup>

<sup>a</sup> Department of Medical Statistics and Epidemiology, Health Information Research Center, Guangdong Key Laboratory of Medicine, School of Public Health, Sun Yat-sen University, Guangzhou, 510080, China

<sup>b</sup> Department of Environmental Health Sciences & Epidemiology and Biostatistics, School of Public Health, University at Albany, State University of New York, New York, 12222, United States

<sup>c</sup> Sun Yat-sen Global Health Institute, Sun Yat-sen University, Guangzhou 510080, China

## ARTICLE INFO

## Keywords:

Forecast  
Disease burden  
Lung cancer  
Disability-adjusted life year  
Bayesian age-period-cohort models

## ABSTRACT

**Background:** Forecast of disease burden in lung cancer is an important health agenda. One of the main challenges is to predict the evolution of trends in disability-adjusted life year (DALY) of lung cancer so as to anticipate the future burden and to coordinate the supply of sufficient health services and care.

**Methods:** Using 2004–2013 cancer registry data in Guangzhou, we fitted Bayesian age-period-cohort models with age, period, and cohort effects to analyze trends of lung cancer among women, and then made forecast for DALY of lung cancer until 2030.

**Results:** During 2004–2013, there was an annual average of 10,582 DALYs for lung cancer (15.84% of total DALY). In 2014–2030, DALY is expected to reach 234,752 person-years for lung cancer (12.25% of total DALY), with an annual mean of 13,809 DALYs. Lung cancer crude DALY rate is projected to rise steadily from 257.56 (95% uncertainty interval: 165.97–361.22) in 2014 to 316.99 (219.96–419.41) per 100,000 women in 2030, and the rise is mainly seen in 45–64 years age group. Lung cancer DALY rate remains the highest in the 65–89 years age group.

**Conclusions:** Women at 65–89 years carry the highest lung cancer burden among other age groups in Guangzhou. The DALY rate of lung cancer is projected to increase most precipitously for the 45–64 years age group. This indicates that concerted efforts are needed to develop adequate cancer services, and to reassess health resources for control and care of lung cancer in these populations.

### 1. Introduction

Cancer is one of the leading causes of mortality worldwide, with nearly 18.1 million new cases and 9.6 million cancer-related deaths in 2018 [1–3]. Its rank shifted from the third leading cause of death in 1990 to the second leading cause of death in recent years [3], having caused substantial health and financial burdens to patients around the globe. Of the 213 million disability-adjusted life-years (DALYs) attributed to cancer in the latest global burden of disease (GBD) study, 17.1% have been ascribed to lung cancer [3]. In China, cancer led to over 2.6 million total deaths in 2017; more than 26.5% could be attributed to lung cancer [4]. Indeed, lung cancer ranks the fourth place in the leading causes of DALYs, while also remaining at the top among other neoplasms. The lung cancer burden has only increased in recent years,

reaching almost 15.3 million DALYs [3,5,6]. In a previous GBD study, tobacco smoking and industrially emitted ambient matter pollution were reported to be the leading risk factors for lung cancer [7]. Thus, the incidence of lung cancer in China is expected to grow in the future, given the consistent high consumption of tobacco [8], and a vast and expanding industry capacity [9]. Lung cancer also entails a substantial financial burden, with per-patient costs estimates as \$43,000 and rising, for treatment and care in China [10]. The impact may be even more substantial in urban areas [11], possibly a side effect of rapid growth, industrialization and poor air quality [12]. Indeed, lung cancer was the leading malignant cancer for women's mortality in Guangzhou, a typical mega city in China [11]. Since lung cancer contributes substantially to women's death, it is of public health and financial importance to clearly characterize the lung cancer burden among urban

**Abbreviations:** DALY, disability-adjusted life year; YLL, years of life lost; YLD, years lived with disability; APC model, age-period-cohort model; ICD codes, International Classification of Diseases codes; DIC, deviance information criterion; pD, effective number of parameters; CV<sub>10</sub>, 10-fold cross validation deviance

\* Corresponding author.

E-mail address: [haoyt@mail.sysu.edu.cn](mailto:haoyt@mail.sysu.edu.cn) (Y. Hao).

<https://doi.org/10.1016/j.canep.2019.101586>

Received 6 May 2019; Received in revised form 22 July 2019; Accepted 14 August 2019

1877-7821/ © 2019 Elsevier Ltd. All rights reserved.

women.

DALY, which combines premature mortality, incidence and disability, is the most widely used summary metric for disease burden [3,13]. Studies of cancer disease burden report DALY to offer insight for prioritizing prevention and treatment of cancer [14]. Yet, to date, such studies have focused on evaluating past or present DALYs, seldom giving attention to the prediction of future DALY. But prediction of cancer DALY is critical: a) for purposes of public health and clinical planning, b) for appropriately assigning limited resources to screening, diagnosis, treatment, rehabilitation and palliative care, and c) also for helping to monitor the effectiveness of health tactics [15]. Predicting cancer DALY requires projecting cancer mortality and incidence. A less common method proposed by the GBD study [16] used multilevel model to estimate the trend of cancer mortality (or incidence). It requires multilevel covariates and thus is suitable for use with hierarchical data, but it lacks generalizability and is currently only used in the GBD study. The other more common method is the aggregated method, for which the age-period-cohort (APC) model is most widely used. This approach can predict cancer incidence (or mortality) trends across several decades, in terms of age, period and cohort effects [17]. Equipped with Bayesian priors, the APC model generally yields more stable future values than non-Bayesian APC models [18]. However, to the best of our knowledge, a Bayesian APC model has not previously been used for prediction of lung cancer DALY in literature. Given that, we intended to introduce Bayesian APC modeling to the long-term prediction of DALY in this study.

The objectives of this study were: a) to use cancer registry data to provide an estimate of the burden of lung cancer among women residing in Guangzhou, China, and b) to forecast the future lung cancer burden to provide detailed age-sex-specific DALY estimates. In response to the recently announced *Healthy China 2030 plan*, which emphasizes cancer prevention and treatment over the next two decades [19], forecast was made till the year 2030. This study complies with the Guidelines for Accurate and Transparent Health Estimates Reporting statement.

## 2. Materials and methods

### 2.1. Study area and data sources

Guangzhou city, covering an area of 7434 km<sup>2</sup>, held a total number of 8.3 million registered household population in 2013. Age-specific incidence and mortality datasets were obtained from the Guangzhou Cancer Registry, for all-cancer (sum of all registered cancers) and lung cancer cases (defined according to the tenth version of the International Classification of Diseases (ICD) codes as ICD-10 C33-C34), in women residing at urban areas of Guangzhou, from 2004–2013. The cancer registry data were annually collected from cancer surveillance sites by the government, and covered all administrative districts for the whole city [20]. Locally estimated scatterplot smoothing was implemented to smooth biased datapoints and describe the deterministic part of the data variation, as implemented in the GBD study [21]. Age-specific registered population data for the study period were also available from cancer registry database for the urban areas of Guangzhou. Estimated female population for 2014 to 2030 in the urban areas of Guangzhou were calculated based on demographic structure projection models as reported by Han and colleagues [22]. The women population are projected to reach 4.7 million by 2030. Also, the China and world population data were used as the standard population in the study and were extracted from the United Nations projections, covering 2004–2030 [23].

### 2.2. Bayesian APC model

We modelled lung cancer mortality and incidence using Bayesian APC model [Eqs. (1) and (2)] [24].

$$y_{ij} \sim \text{Poisson}(n_{ij}) \tag{1}$$

$$\ln(n_{ij}) = \ln(p_{ij}) + \theta_i + \phi_j + \varphi_k \tag{2}$$

We assumed the number of incidence/mortality cases ( $y_{ij}$ ) for the  $i^{\text{th}}$  age group ( $i = 1, 2, \dots, I$ ) and the  $j^{\text{th}}$  year ( $j = 1, 2, \dots, J$ ) followed a Poisson distribution, with average  $n_{ij}$ . We also used equation  $k = 5 \times (I - i) + j$  to counteract the unequal interval effect presented by age period [25]. Then, the natural logarithm of  $n_{ij}$  was further decomposed into population offset  $\ln(p_{ij})$ , an age effect  $\theta_i$ , a period effect  $\phi_j$  and a cohort effect  $\varphi_k$  shown in Eq. (2). The age effect accounted for biological or sociological characteristics changed along with aging. The period effect reflected factors that simultaneously impact all individuals, regardless of their individual differences, such as impact of war, famine and environmental pollution. The cohort effect represented a comprehensive profile of exposures specific to each generation [26].

Next, constrained Poisson-link APC models were implemented to account for identification problems [27]. We set constraints on the first-order differences for the period and cohort effects, and on the second-order difference for age. A Gaussian distribution prior was set for  $\theta_i$ ,  $\phi_j$  and  $\varphi_k$ , precision parameters of which had a gamma-distributed flat hyper-prior. Next, each Bayesian model was generated by three Markov Chain Monte Carlo chains for 60,000 iterations. We used Gelman and Rubin's convergence diagnostic to check for convergence [28] and posterior mean deviance for model goodness-of-fit. We compared models using the deviance information criterion (DIC) and a smaller DIC implies a better model fit [29]. We further checked model predictive performance using the Bayesian  $P$ -value [30] and 10-fold cross-validation [31]. More desirable model performance is indicated by Bayesian  $P$ -values closer to 0.5 [32], and smaller bias-corrected 10-fold cross validation deviance ( $CV_{10}$ ) [31]. The resulting models were used to forecast median age-specific lung cancer incidence and mortality for 2014-2030. We derived 95% uncertainty intervals (UI) from the parameter posterior distributions (using 2.5% and 97.5% of the iterated samples).

### 2.3. Calculation of DALY

In the study, we adopted the incidence-mortality DALY approach [13,33] to estimate the Guangzhou lung cancer burden among women. DALY estimates premature death as years of life lost (YLL), and non-fatal health outcomes as years lived with disability (YLD). One DALY indicates one-year of "healthy" life lost [33].

To estimate YLL for sex-specific ( $s$ ) health outcomes ( $c$ ) that could lead to premature death, the number of fatal cases ( $d$ ) for a specific health outcome ( $c$ ) at age ( $a$ ) was multiplied by the remaining life expectancy ( $e$ ) at age  $\tilde{a}$  [Eq. (3)]. Next, incident YLD was calculated for sex-specific ( $s$ ) health outcomes ( $c$ ) by multiplying the number of incidence cases without fatality ( $n$ ), with the duration of the disabling condition ( $t$ ), and the disability weight ( $w$ ) specified for a specific health outcome ( $c$ ) [see Eq. (4)]. DALY rate was calculated using age-specific standard population.

$$YLL = \sum_c d_c^{a,s} \times e_c^{\tilde{a},s} \tag{3}$$

$$YLD = \sum_c n_c^{a,s} \times t_c^{\tilde{a},s} \times w_c^{\tilde{a},s} \tag{4}$$

We employed the Coale and Demeny West Level 26 Life Table for calculating YLL. We generated average age-specific durations of lung cancer by Dismod-II software (See Table A.1). A detailed description of Dismod-II can be found elsewhere [34]. Terminal phase of lung cancer disability weights were extracted from the 2017 GBD Study to account for the heaviest disease burden brought by lung cancer [35]. Projected YLL and YLD were calculated with predicted mortality and incidence that were derived from the Bayesian APC model. Annualized rate of change was used to depict the annual percentage change for DALY

**Table 1**  
Goodness-of-fit for age-period-cohort (APC) models for lung cancer, among women in Guangzhou, 2004–2013.

Dataset	Model <sup>a</sup>	Deviance (95% uncertainty interval)	pD <sup>b</sup>	DIC <sup>c</sup>	Bayesian P-value (95% uncertainty interval)	CV <sub>10</sub> <sup>d</sup>
Incidence data	Age	846.78 (838.50, 858.90)	12.48	859.26	0.2857 (0.1339, 0.4062)	17 334
	Age-period	795.71 (775.50, 858.50)	29.72	825.44	0.3393 (0.1964, 0.4241)	11 996
	Age-cohort	814.54 (789.50, 886.15)	39.76	854.30	0.2812 (0.1741, 0.3929)	13 359
	APC with age-cohort interaction term	869.78 (758.20, 1 340.52)	135.21	1004.98	0.3482 (0.2411, 0.4062)	11 527
Mortality data	APC	794.71 (756.20, 924.50)	58.64	853.34	0.3571 (0.2411, 0.4241)	10 024
	Age	907.07 (899.70, 917.20)	11.49	918.56	0.1964 (0.0759, 0.3214)	18 260
	Age-period	716.53 (696.40, 781.55)	29.25	745.78	0.2902 (0.1786, 0.3973)	7 651
	Age-cohort	843.10 (764.20, 1 180.52)	92.65	935.75	0.2500 (0.1786, 0.3304)	12 542
	APC with age-cohort interaction term	760.93 (661.50, 1 168.10)	122.38	883.30	0.3438 (0.2589, 0.4062)	7 502
	APC	697.14 (660.15, 822.26)	54.25	751.39	0.3527 (0.2500, 0.4330)	5 509

<sup>a</sup> Each model was fitted in a Markov Chain Monte Carlo run of three chains for 60,000 iterations, including 10,000 burn-ins and sampling from every 10<sup>th</sup> iteration.

<sup>b</sup> pD, posterior mean deviance.

<sup>c</sup> DIC, deviance information criterion.

<sup>d</sup> CV<sub>10</sub>, 10-fold cross validation test.

rates. We assumed constant life expectancy, cancer durations and disability weights to predict DALY for the projected period. All analyses were performed using R (version 3.4) and WinBugs (version 14).

### 3. Results

#### 3.1. Evaluation of projection models

Table 1 shows the goodness of fit statistics from the model selection procedure for the APC analysis. Age, period and cohort effects were fitted sequentially, and different models were then compared in terms of deviance, DIC and Bayesian P-value, and CV<sub>10</sub>. In all, the full APC model provided the best fit. Firstly, the full APC model fit with smaller values of deviance compared with the other partial models. Secondly, the full APC model fit better than the APC model with interaction term because the interaction-free model had lower DIC. Thirdly, even though the interaction-free full APC model yielded higher DIC values than some partial models, the Bayesian P-values were much closer to 0.5 and with greater precision. Finally, the full APC model produced the lowest cross-validation deviance in the 10-fold cross validation test. Dissection of age, period, and cohort effects in the final model was shown in Figure A.1 and Figure A.2.

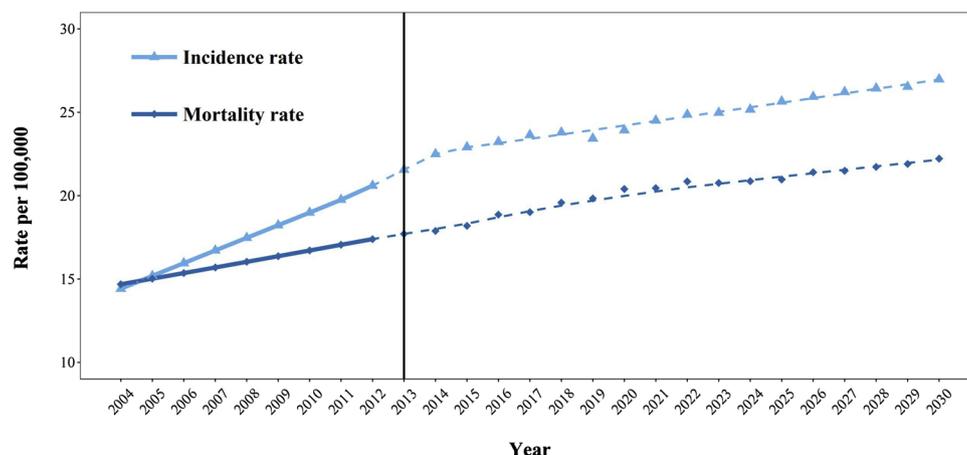
#### 3.2. Characteristics of observed incidence and mortality rates

In Guangzhou, a total of 9049 incident lung cancer cases (with a rate of 24.36 per 100,000) and 6351 lung cancer deaths (with a rate of

17.10 per 100,000) were observed among women during 2004–2013. Fig. 1 shows the age-standardized incidence and mortality rates for observed (2004–2013) and projected (2014–2030) lung cancer cases among women. The figure shows that rates for both lung cancer incidence and mortality are projected to rise through 2030, although with a higher rate for incidence than for mortality. Upward trends of incidence rate for the elder age groups (75 and 85 age-groups) were also decomposed and depicted in Figure A.1.

#### 3.3. Projected DALY and DALY rate of lung cancer

Table 2 shows the trend over time for lung cancer DALY and its crude DALY rates. Overall, there was a total of 105,819 DALYs for lung cancer (15.84% of total DALY) for 2004–2013, averaging to an annual DALY of 10,582 person-years. For 2014–2030, there will be a total of 234,752 DALYs for lung cancer (12.25% of total DALY), which can be averaged to an annual DALY of 13,809 person-years. Crude DALY rate of lung cancer is projected to rise from 257.56 (95% UI: 165.97 to 361.22) in 2014, to 316.99 (219.96 to 419.41) per 100,000 women in 2030. Next, lung cancer crude DALY rate increased for all age groups in the observed period 2004–2013 (with an annualized change rate of 3.59%), but will decline slowly from 2014 to 2030 (with an annualized change rate of -0.31%). Besides, the age-standardized DALY rate for lung cancer increased in 2004–2013 (with an annualized change rate of 3.06%), but it is expected to remain stable for 2014–2030, and therefore resulting in an overall annualized change rate of 1.12% from 2004 to 2030.



**Fig. 1.** Observed (2004–2013) and projected (2014–2030) lung cancer incidence and mortality rates, among women in Guangzhou. Notes: Both incidence and mortality rates were age-adjusted by the Chinese population [23].

**Table 2**  
DALY<sup>a</sup> rate (per 100,000 women) of all-cancer and lung cancer in the female population in Guangzhou, 2004–2030.

Cancer	Observed (95% uncertainty intervals)					Projected(95% uncertainty intervals)					
	2004-2005	2006-2007	2008-2009	2010-2011	2012-2013	2013-2015	2016-2018	2019-2021	2022-2024	2025-2027	2028-2030
Overall DALY for all-cancer	93,636 (69,013, 118,097)	95,214 (69,561, 120,029)	107,879 (79,245, 135,138)	203,754 (163,244, 241,098)	134,355 (103,752, 163,061)	252,091 (199,350, 302,918)	344,122 (277,080, 404,746)	342,629 (270,614, 407,394)	317,832 (246,338, 382,273)	318,871 (250,929, 383,321)	342,714 (270,906, 408,463)
Overall DALY for lung cancer	18,021 (11,317, 25,272)	18,526 (11,660, 26,277)	19,623 (12,532, 27,339)	29,911 (20,477, 39,905)	19,685 (12,448, 27,550)	31,930 (20,557, 44,356)	35,923 (23,513, 49,300)	39,368 (25,953, 53,473)	42,255 (28,241, 57,482)	45,831 (31,079, 61,310)	49,538 (34,006, 65,751)
Overall DALY rate <sup>b</sup> for all-cancer	1846.84 (1461.24, 2218.55)	2175.28 (1749.86, 2583.56)	2501.27 (2036.19, 2946.47)	2814.08 (2310.30, 3296.51)	2961.97 (2441.72, 3456.28)	2911.07 (2398.99, 3393.23)	2613.05 (2140.61, 3058.99)	2475.95 (2027.49, 2895.93)	2479.15 (2037.92, 2890.15)	2495.72 (2060.00, 2899.38)	2521.46 (2090.06, 2918.77)
Overall DALY rate <sup>b</sup> for lung cancer	268.59 (167.71, 381.95)	299.55 (192.04, 421.27)	330.68 (216.21, 460.84)	360.85 (239.24, 499.41)	382.26 (254.84, 525.71)	385.42 (256.71, 526.68)	360.51 (238.73, 494.38)	351.52 (234.37, 479.46)	355.01 (239.48, 480.40)	359.92 (245.69, 483.14)	365.70 (252.57, 487.00)
DALY rate <sup>b</sup> for lung cancer by age											
20-44	38.01 (13.21, 73.52)	41.58 (14.86, 79.07)	46.05 (17.20, 85.96)	50.52 (19.79, 92.87)	63.01 (22.86, 119.40)	62.16 (27.35, 110.38)	53.16 (21.85, 97.25)	47.90 (18.41, 89.58)	46.27 (17.75, 86.85)	45.19 (17.79, 84.84)	44.44 (18.17, 83.22)
45-64	358.23 (223.12, 506.66)	375.79 (240.23, 522.97)	398.03 (260.78, 545.57)	423.44 (283.98, 572.08)	448.33 (305.65, 598.29)	488.41 (339.70, 644.36)	447.57 (311.86, 587.63)	423.85 (298.07, 553.91)	417.41 (297.39, 541.88)	413.92 (298.80, 532.98)	412.18 (301.44, 526.17)
65-89	1081.38 (727.52, 1459.07)	1139.01 (768.76, 1537.08)	1197.23 (809.67, 1616.03)	1254.64 (848.50, 1695.16)	1272.36 (858.63, 1716.76)	1249.78 (836.92, 1683.54)	1147.57 (762.15, 1556.25)	1084.41 (721.31, 1467.94)	1061.47 (708.92, 1431.69)	1043.37 (699.90, 1401.90)	1027.87 (692.71, 1375.44)
Standardized overall DALY rate <sup>c</sup> for all-cancer	2.55 (2.01, 3.05)	2.92 (2.34, 3.47)	3.29 (2.67, 3.90)	3.64 (2.99, 4.30)	3.83 (3.15, 4.50)	3.79 (3.12, 4.41)	3.31 (2.71, 3.87)	3.15 (2.58, 3.69)	3.22 (2.65, 3.76)	3.31 (2.73, 3.84)	3.40 (2.82, 3.94)
Standardized overall DALY rate <sup>c</sup> for lung cancer	0.37 (0.24, 0.52)	0.41 (0.26, 0.57)	0.44 (0.29, 0.61)	0.48 (0.31, 0.65)	0.50 (0.33, 0.68)	0.51 (0.34, 0.68)	0.46 (0.30, 0.62)	0.45 (0.30, 0.61)	0.46 (0.31, 0.62)	0.48 (0.32, 0.64)	0.50 (0.34, 0.66)
Standardized DALY rate <sup>c</sup> for lung cancer by age											
20-44	0.05 (0.02, 0.09)	0.06 (0.02, 0.11)	0.07 (0.02, 0.12)	0.08 (0.02, 0.14)	0.10 (0.03, 0.17)	0.08 (0.03, 0.13)	0.06 (0.02, 0.11)	0.05 (0.02, 0.09)	0.05 (0.02, 0.09)	0.05 (0.02, 0.09)	0.05 (0.02, 0.09)
45-64	0.50 (0.31, 0.71)	0.53 (0.34, 0.75)	0.57 (0.38, 0.80)	0.62 (0.41, 0.85)	0.65 (0.44, 0.89)	0.71 (0.49, 0.95)	0.68 (0.47, 0.89)	0.68 (0.47, 0.88)	0.69 (0.49, 0.90)	0.72 (0.52, 0.92)	0.74 (0.55, 0.94)
65-89	1.63 (1.09, 2.19)	1.69 (1.14, 2.30)	1.75 (1.19, 2.41)	1.79 (1.24, 2.51)	1.76 (1.22, 2.47)	1.69 (1.16, 2.33)	1.51 (1.01, 2.07)	1.44 (0.96, 1.95)	1.42 (0.95, 1.92)	1.41 (0.95, 1.90)	1.40 (0.95, 1.88)

<sup>a</sup> Disability-adjusted life-year.

<sup>b</sup> Crude DALY rate, using the Guangzhou population.

<sup>c</sup> Standardized DALY rate, using the world population [23].

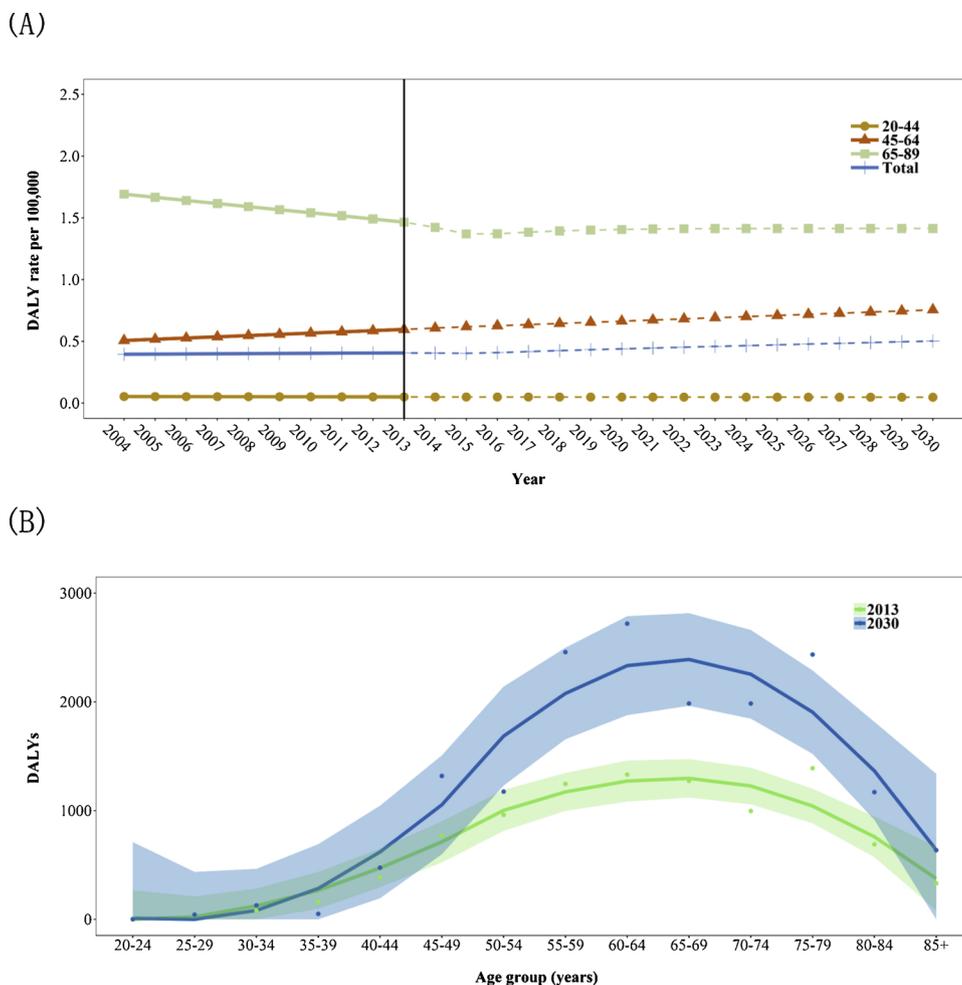


Fig. 2. Trends for lung cancer DALY<sup>a</sup>, among women residing in Guangzhou during 2004–2030.

<sup>a</sup>Disability-adjusted life-year.

Notes: (A) Trends for world-population-adjusted lung cancer DALY rate from 2004 to 2030 by year and age. The DALY rate was age-adjusted by the world population. The world population was extracted from the population report [23] published by the United Nations. (B) Age-specific trends of lung cancer DALY among women for 2013 and 2030.

With regards to age-specific results, the age-standardized DALY rate for lung cancer is expected to rise with an annualized change rate of 1.46% for 45–64 age group in 2004–2030. However, age-standardized DALY rates are predicted to remain stable for 20–44 age group, and decline gradually for 65–89 age group. The DALY burden of lung cancer is the highest among women aged 65–89 years, for both crude rate and age-standardized rate (Table 2).

Fig. 2A shows the temporal trends for world-population-adjusted lung cancer DALY rate from 2004 to 2030 by year and age. Specifically, among women aged 45–64 years, lung cancer DALY rate is projected to increase from 0.60 (0.40 to 0.81) to 0.76 (0.55 to 0.96) per 100,000 women for 2013 and 2030 (with an annualized change rate of 1.32%). However, for 65–89 years, lung cancer DALY rate is projected to decline from 1.47 (0.97 to 1.98) to 1.41 (0.95 to 1.88) per 100,000 women, for 2013 and 2030 (with an annualized change rate of -0.23%). Fig. 2B shows the trend of age-specific DALY numbers for lung cancer among women for 2013 and 2030. Among women aged under 45 years, DALY uncertainty interval was showed to overlap between the years, indicating that time trend for the 20–44 age group is expected to remain stable throughout the projected period. For women aged 45–64 years, the number of lung cancer DALY is expected to rise significantly, with non-overlapping uncertainty intervals.

#### 4. Discussion

This study shows that overall lung cancer DALY is gradually increasing throughout 2004–2030, and most precipitously for the middle-age women (45–64 years). To our knowledge, this is the first study to predict the disease burden of lung cancer using APC models. This study is also the first study to report the lung cancer burden for Guangzhou, China, measuring with DALY and DALY rate. In measuring disease burden, we used DALY and DALY rate because they outperform incidence and mortality in two ways. Firstly, incidence and mortality are conventionally implemented as measurement indices of disease frequency. But these traditional indicators only concern observed cases and basic population data in a less comprehensive manner. The DALY considers both survival time and quality of life attributed to a specific disease, with its calculation requiring age and gender specific data for incidence, fatalities, severity and life expectancy. Therefore, DALY can depict the threat of disease to the whole population, providing a more synthesized picture than incidence and mortality [36]. Secondly, it is convenient to compare DALY and DALY rate from different geographic areas and different times directly, because they are calculated based on comparable age-gender-specific population data as well as standard life expectancies and disability weights [37]. In addition, we adopted the earlier mortality-incidence-based DALY approach [13] to estimate the lung cancer disease burden, rather than the recent mortality-

prevalence-based method [37]. Under the earlier mortality-incidence-based approach, DALY measures a year of healthy life lost either through premature death or through health loss connected with cancer occurring in a specific time. To account for trends, and to set priorities for preventive interventions, incidence is a more appropriate input to the prediction of DALY than prevalence because: a) incidence is more sensitive to temporal trend; and b) incidence data are readily available from the Guangzhou cancer registries. Thus, the mortality-incidence-based DALY was adopted for this study.

Comparison with other disease burden studies corroborates our findings. The lung cancer DALY in Guangzhou is much less severe than those reported for China overall and globally [37]. However, both China overall and the world share a similar pattern of increasing lung cancer DALY among women [3], as those in Guangzhou. The uprising trends of lung cancer DALY and DALY rates may mainly be ascribed to the escalating burden in the middle-age group (45–64). After age-standardization, we find that DALY rate for the middle-age group may see a steady rise with an annualized rate of 1.46% over the 2004–2030 period. Next, even though the elderly women (65–89 years) continue to carry the highest lung cancer DALY burden, we find that their DALY rate may be slowly decreasing (Fig. 2A). The reasons may be in part owing to the decreasing trend of age effects among the elderly (Figure A.2). Indeed, as illustrated by Yang and Holford [26,38], varying age and cohort effects can have an influence on the shape of the period trend. The declining age effects among the elderly may reflect the developmental changes of public health intervention in averting lung cancer [39]. Nonetheless, the rising trend for all-age group and the 45–64 age group are consistent with expected trends for China and the world [3]. In China, these patterns may be due in part to high levels of exposure to environmental pollutions in the past, such as ambient PM<sub>2.5</sub> [4,7]. As a rapidly expanding megacity, with a population of more than 8.7 million in 2017 [22], Guangzhou experienced high levels of air pollution problems over the past decade [40] and a previous local burden of disease study reported that over 20% lung cancer DALY burden could be ascribed to ambient PM<sub>2.5</sub> exposure in Guangzhou [41]. Alternative to ambient air pollution, growing smoking prevalence rate in women [42] may also explain the rising incidence trends and escalating lung cancer burden [7]. Therefore, we suspect that Guangzhou's upward trend for DALY of lung cancer may be attributable in part to its air pollutants and the unhealthy behavior in women. However, the quantitative assessment of exposure factors is beyond the scope of the paper.

In the study, the predicted steady growth in the overall crude and age-standardized DALY rates among women, for all-cancers and for lung cancer, reflects a gradual, yet important increase in resource requirements for cancer care services in coming years. However, cancer services in mainland China, especially for supportive and palliative care, are diverse and scarce as less than one in a thousand cancer patients can receive such services [43]. And as our data show, much of the burden will take place in the 65–89 years age group, but most of the projected growth is seen in the 45–64 years age group for lung cancer. Therefore, cancer services should be expanded to cover the shortage. Specifically, the expansion of future cancer services should give special consideration to the unique conditions of an expanding aging patient population, such as increasing surgical expenses, a higher likelihood for treatment-related complications, multiple comorbidities, and special needs for supportive and palliative care, among others.

Some limitations of our work should be acknowledged. First, the time interval in the study only covered a ten-year period, owing to the limited availability of cancer registration data. However, a previous study in Taiwan empirically constructed and validated a Bayesian APC model with only seven years of data (covering 1996–2002) [44]; and a previous age-period-cohort study conducted by Chen and colleagues [45] predicted the long-term trend of lung cancer incidence in China until the year 2020, based merely on a ten-year period of data (1998–2007). Therefore, we believe that our collected data may be

sufficient for fitting and extrapolating the age, period and cohort effects. Second, we did not consider more specific information in our models such as gross domestic product, geography information, individual exposure to hazards, etc., due to the absence of relevant data. Finally, we assumed the life expectancy, disability weights and disease duration to remain constant in the models. This approach allows us to compare the results to previous reports [33], and yet, ongoing evidence suggests a global increase of life expectancy [46], and the future burden of cancer will likely be influenced by increasing life expectancy, unless mortality rate falls drastically [3]. Therefore, changing trends of life expectancy remain to be integrated into the DALY prediction in a future research. Analogously, resulting from changes in public perceptions, public policies and technological innovations, and trends in disease duration, a different set of disability weights is also possible in the future [13]. So, we suggest integrating changes of disability weights and disease duration in a future study, expanding upon our work here. Though limited in some respects, the results of the current study provide a first step in a long-term investigation of DALY trends of lung cancer.

But the study also has some strengths. An APC approach was used in the study, which makes it easier to explain the trends of lung cancer burden among the study population. While APC model is recognized as a highly robust aggregate model for tabular data [24], it allows for decomposing tabular data into three time-related effects: age, period and cohort effects, and each effect reflects an underlying factor such as biological process, etiological factors, and historical changes related to diseases [26]. Therefore, the APC model can depict complex influence of social, historical and environmental factors that may have a simultaneous impact on the population over a long period of time [47]. Besides, under the Bayesian approach, we are able to introduce first-order and second-order differences in the models to smooth out each time effect. As a result, we could achieve better fit, and at the same time, avoid extreme predictions [18]. Another strength of the research is that we simplified the calculation of YLD and avoided interpretation complexity. Specifically, we did not use age weights and time discount in calculating incident YLD, given the controversial nature of these attributes. Previous study showed that incorporating these attributes might underestimate disease burden among the younger groups and lead to morally unacceptable allocations of health resources between generations [13]. The approach to simplification has also been taken in the current GBD study [7], and thus our choice of attributes also ensures comparison with the existing study.

In summary, we developed a Bayesian APC model to predict time trends in women lung cancer incidence and mortality. We then described the women lung cancer burden using DALY, which comprehensively reflected both cancer incidence and mortality. In Guangzhou, women at the 65–89 years age group have the highest lung cancer disease burden. Our projected growth for the all-age lung cancer DALY rate, and especially for women at 45–64 years of age, indicates that Guangzhou will face a slight and yet consistent growth in the disease burden of lung cancer for at least the next two decades. We expect our results to be useful for policy-makers, by offering them important insight regarding the forecasted cancer burden and quantitative data upon which to base expansion of more adequate cancer treatment services. Our results also highlight the need for reassessment of the resources allocated to cancer control and care, in order to anticipate the growing burden of cancer in the women community.

## 5. Author contributions statement

XL, MB and YH conceived and designed the research. YH and XL contributed to acquisition of data. XL and DC analyzed the data. XL and MB wrote the paper. All contributors were involved in critical review of the manuscript. YH acts as guarantor. All authors have had full access to all of the data in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis. All authors read and

approved the final manuscript.

## Declaration of Competing Interest

None.

## Acknowledgements

The authors thank Qi Tian, Yu Liao and Long Chen for their help in connection with the Guangzhou Center for Disease Control and Prevention.

## Funding

The research was supported by a funding [5100071020342] from the Center for Statistics and Information of National Health Commission of the People's Republic of China. However, the funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

## Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.canep.2019.101586>.

## References

- [1] F. Bray, J. Ferlay, I. Soerjomataram, R.L. Siegel, L.A. Torre, A. Jemal, Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries, *CA Cancer J. Clin.* 68 (6) (2018) 394–424.
- [2] C. Fitzmaurice, D. Dicker, A. Pain, et al., The global burden of Cancer 2013, *JAMA Oncol.* 1 (4) (2015) 505, <https://doi.org/10.1001/jamaoncol.2015.0735>.
- [3] S.I. Hay, A.A. Abajobir, K.H. Abate, C. Abbafati, K.M. Abbas, F. Abd-Allah, R.S. Abdulkader, A.M. Abdulle, T.A. Abebo, S.F. Abera, et al., Global, regional, and national disability-adjusted life-years (DALYs) for 333 diseases and injuries and healthy life expectancy (HALE) for 195 countries and territories, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016, *Lancet* 390 (10100) (2017) 1260–1344.
- [4] M. Zhou, H. Wang, X. Zeng, P. Yin, J. Zhu, W. Chen, X. Li, L. Wang, L. Wang, Y. Liu, et al., Mortality, morbidity, and risk factors in China and its provinces, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017, *Lancet* (2019).
- [5] C.J. Murray, A.D. Lopez, Mortality by cause for eight regions of the world: global Burden of Disease Study, *Lancet* 349 (9061) (1997) 1269–1276.
- [6] M. Zhou, H. Wang, J. Zhu, W. Chen, L. Wang, S. Liu, Y. Li, L. Wang, Y. Liu, P. Yin, et al., Cause-specific mortality for 240 causes in China during 1990–2013: a systematic subnational analysis for the Global Burden of Disease Study 2013, *Lancet* 387 (10015) (2016) 251–272.
- [7] E. Gakidou, A. Afshin, A.A. Abajobir, et al., Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016, *Lancet* 390 (10100) (2017) 1345–1422.a.
- [8] G. Yang, Marketing 'less harmful, low-tar' cigarettes is a key strategy of the industry to counter tobacco control in China, *Tob. Control* 2013 (2012).
- [9] N. Jiang, S. Yin, Y. Guo, et al., Characteristics of mass concentration, chemical composition, source apportionment of PM<sub>2.5</sub> and PM<sub>10</sub> and health risk assessment in the emerging megacity in China, *Atmos. Pollut. Res.* (2017).
- [10] X. Zhang, S. Liu, Y. Liu, et al., Economic burden for lung cancer survivors in Urban China, *Int. J. Environ. Res. Public Health* 14 (3) (2017), <https://doi.org/10.3390/ijerph14030308>.
- [11] H. Liu, G. Lin, J. Shen, et al., Annual Report of Guangzhou Cancer Registry, Guangzhou Center For Disease Control and Prevention, 2014.
- [12] G. Li, L. Jiang, Y. Zhang, et al., The impact of ambient particle pollution during extreme-temperature days in Guangzhou City, China, *Asia Pac. J. Public Health* 26 (6) (2014) 614–621, <https://doi.org/10.1177/1010539514529811>.
- [13] C.J.L. Murray, Quantifying the burden of disease: the technical basis for disability-adjusted life years, *Bull. World Health Organ.* 72 (3) (1994) 429–445.
- [14] S.C. Yu, F. Tan, M.G. Zhou, et al., Global burden of disease, injury and risk factor study 2010: its policy implications for China, *Biomed. Environ. Sci.* 27 (01) (2014) 45–48, <https://doi.org/10.3967/bes2014.013>.
- [15] S. Innvæ, The use of evidence in public governmental reports on health policy: an analysis of 17 Norwegian official reports (NOU), *BMC Health Serv. Res.* 9 (1) (2009) 177.
- [16] C.J. Murray, A.D. Lopez, Alternative projections of mortality and disability by cause 1990–2020: global Burden of Disease Study, *Lancet* 349 (9064) (1997) 1498–1504, [https://doi.org/10.1016/S0140-6736\(96\)07492-2](https://doi.org/10.1016/S0140-6736(96)07492-2).
- [17] B. Møller, H. Fekjaer, T. Hakulinen, et al., Prediction of cancer incidence in the Nordic countries: empirical comparison of different approaches, *Stat. Med.* 22 (17) (2003) 2751–2766, <https://doi.org/10.1002/sim.1481>.
- [18] Qiu Zhenguo, Jiang Zhichang, Wang Mengzhe, et al., Long-Term Projection Methods: Comparison of Age-Period-Cohort Model-Based Approaches: Cancer Projections Network (C-Projections), (2010).
- [19] Daily C. Healthy China 2030. 2016. [http://www.chinadaily.com.cn/opinion/2016-08/30/content\\_26636133.htm](http://www.chinadaily.com.cn/opinion/2016-08/30/content_26636133.htm). (Accessed 1 February 2018).
- [20] W. Chen, R. Zheng, P.D. Baade, et al., Cancer statistics in China, 2015, *CA Cancer J. Clin.* 66 (2) (2016) 115–132.
- [21] R.M. Barber, N. Fullman, R.J.D. Sorensen, T. Bollyky, M. McKee, E. Nolte, A.A. Abajobir, K.H. Abate, C. Abbafati, K.M. Abbas, et al., Healthcare Access and Quality Index based on mortality from causes amenable to personal health care in 195 countries and territories, 1990–2015: a novel analysis from the Global Burden of Disease Study 2015, *Lancet* 390 (10091) (2017) 231–266.
- [22] Z. Han, X. Chen, Forecasting and analysis of the population in Guangzhou City: 2006–2020, *South China Popul.* 21 (3) (2006) 58–64.
- [23] World Population Prospects - Population Division - United Nations. World Population Prospects - Population Division - United Nations. 2017. <https://esa.un.org/unpd/wpp/Download/Standard/Population/>. (Accessed 7 December 2017).
- [24] J. Mork, B. Møller, T. Dahl, et al., Time trends in pharyngeal cancer incidence in Norway 1981–2005: a subsite analysis based on a reabstraction and recoding of registered cases, *Cancer Causes Control* 21 (9) (2010) 1397–1405, <https://doi.org/10.1007/s10552-010-9567-9>.
- [25] L. Luo, J.S. Hodges, Block constraints in age–Period–Cohort models with unequal-width intervals, *Sociol. Methods Res.* 45 (4) (2016) 700–726, <https://doi.org/10.1177/0049124115585359>.
- [26] Y. Yang, K.C. Land, Age-Period-Cohort Analysis, Chapman & Hall/CRC Interdisciplinary Statistics Series, 2013 10(1201):b13902.
- [27] S.E. Fienberg, W.M. Mason, Identification and estimation of age-period-cohort models in the analysis of discrete archival data, *Sociol. Methodol.* 10 (1979) 1–67.
- [28] A. Gelman, D.B. Rubin, Inference from iterative simulation using multiple sequences, *Stat. Sci.* (1992) 457–472.
- [29] D.J. Spiegelhalter, N.G. Best, B.P. Carlin, et al., Bayesian measures of model complexity and fit, *J. R. Stat. Soc. Series B Stat. Methodol.* 64 (4) (2002) 583–639.
- [30] P.M. Altham, The analysis of matched proportions, *Biometrika* 58 (3) (1971) 561–576.
- [31] M.S. Clements, Lung cancer rate predictions using generalized additive models, *Biostatistics* 6 (4) (2005) 576–589, <https://doi.org/10.1093/biostatistics/kxi028>.
- [32] A. Gelman, A bayesian formulation of exploratory data analysis and goodness-of-fit testing, *Int. Stat. Rev.* 71 (2) (2003) 369–382.
- [33] L.P. Yang, S.Y. Liang, X.J. Wang, et al., Burden of disease measured by disability-adjusted life years and a disease forecasting time series model of scrub typhus in Laiwu, China, *PLoS Negl. Trop. Dis.* 9 (1) (2015) e3420, <https://doi.org/10.1371/journal.pntd.0003420>.
- [34] J.J. Barendregt, G.J. Van Oortmarssen, T. Vos, et al., A generic model for the assessment of disease epidemiology: the computational basis of DisMod II, *Popul. Health Metr.* 1 (1) (2003) 4.
- [35] S.L. James, D. Abate, K.H. Abate, S.M. Abay, C. Abbafati, N. Abbasi, H. Abbastabar, F. Abd-Allah, J. Abdela, A. Abdelalim, et al., Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017, *Lancet* 392 (10159) (2018) 1789–1858.
- [36] A. Lopez, C. Mathers, M. Ezzati, et al., Global Burden of Disease and Risk Factors, Oxford University Press and the World Bank, Washington, 2006.
- [37] C.J. Murray, T. Vos, R. Lozano, et al., Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010, *Lancet* 380 (9859) (2012) 2197–2223, [https://doi.org/10.1016/S0140-6736\(12\)61689-4](https://doi.org/10.1016/S0140-6736(12)61689-4).
- [38] T.R. Holford, Understanding the effects of age, period, and cohort on incidence and mortality rates, *Annu. Rev. Public Health* 12 (1991) 425–457.
- [39] D.T. Jamison, J.G. Breman, A.R. Measham, G. Alleyne, M. Claeson, D.B. Evans, P. Jha, A. Mills, P. Musgrove, Disease Control Priorities in Developing Countries, The World Bank, 2006.
- [40] G.H. Dong, Ambient Air Pollution and Health Impact in China, Springer, 2017, p. 1017.
- [41] Y. Liao, L. Xu, X. Lin, et al., Temporal Trend in Lung Cancer Burden Attributed to Ambient Fine Particulate Matter in Guangzhou, China, *Biomed. Environ. Sci.* 30 (10) (2017) 708–717.
- [42] CHS (Centre for Health Statistics), Information of National Health Commission of the People's Republic of China, National Health Services Survey, 2018 2019. (Unpublished results).
- [43] J. Liu, M. Yuan, History, current status, problems and prospective of palliative service system in mainland China, *J. Soc. Work.* (02) (2016) 34–49.
- [44] C. Chien, T.H. Chen, A bayesian model for age, period, and cohort effects on mortality trends for lung cancer, in association with gender-specific incidence and case-fatality rates, *J. Thorac. Oncol.* 4 (2) (2009) 167–171.
- [45] W.Q. Chen, R.S. Zheng, H.M. Zeng, Bayesian age-period-cohort prediction of lung cancer incidence in China, *Thorac. Cancer* 2 (4) (2011) 149–155.
- [46] C.J. Murray, R.M. Barber, K.J. Foreman, O.A. Abbasoglu, F. Abd-Allah, S.F. Abera, V. Aboyans, J.P. Abraham, I. Abubakar, L.J. Abu-Raddad, et al., Global, regional, and national disability-adjusted life years (DALYs) for 306 diseases and injuries and healthy life expectancy (HALE) for 188 countries, 1990–2013: quantifying the epidemiological transition, *Lancet* 386 (10009) (2015) 2145–2191.
- [47] K.S. Markides, Encyclopedia of Health and Aging, Sage Publications, 2007.