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Changing trends in lung cancer disease burden between China and Australia from 1990 to 2019 and its predictions

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Abstract

Purpose: Lung cancer (LC) is a leading cause of death and presents a substantial societal burden. This article compares its disease burden and risk factors between China and Australia to support health policymakers for LC prevention and treatment.
Materials and Methods: The data from the 2019 Global Burden of Disease Study were used to analyze disease temporal trends using Joinpoint regression model. The Bayesian age-period-cohort model was used for prediction. The population-attributable fraction (PAF) was used to analyze LC risk factors.
Results: In 2019, the age-standardized rates (ASR) of incidence and of mortality of LC in China were 41.71/100 000 and 38.70/100 000, while Australia's rates were 30.45/100 000 and 23.46/100 000. It showed an increasing trend in China but a decreasing trend in Australia. By 2030, the ASR of incidence and mortality are predicted to be 47.21/100 000 and 41.54/100 000 in China, while Australia's rates will reach 30.09/100 000 and 23.3/100 000, respectively. Smoking is the most common risk factor for LC, followed by particulate matter and occupational carcinogenesis. The PAF of smoking dropped in Australia (from 68.38% to 53.75% in females; 77.41% to 58.47% in males) but increased in China (from 19.56% to 26.58% in females; 80.45% to 82.03% in males) from 1990 to 2019.
Conclusions: The disease burden of LC in China is rising, whereas in Australia, it is declining. China still faces a heavy LC burden. Risk factor analysis supported for further improving the compliance and enforcement of polices on tobacco control and environmental management to reduce this disease burden.

KEYWORDS
Australia, burden of disease, China, lung cancer, prediction

INTRODUCTION

Lung cancer (LC) is a highly dangerous malignant tumor that may spread rapidly and cause serious health problems and death. It also results in an enormous burden on both individual and social health. According to the World Health Organization's International Agency for Research on Cancer, there were 2.21 million new cases of LC globally in 2020, making it the second most common malignant tumor after breast cancer.[1,2] The number of deaths from LC was 1.8 million worldwide, making it the leading cause of cancer death. According to the Global Cancer Statistics 2020,[1] the incidence rate of LC was high in Asian and some European countries, while it was relatively low in some African and Oceanian countries. Over the past decades, many countries have committed to explore the prevention and treatment of LC through raising people's awareness, implementing health education and policies, and improving early diagnosis and advanced therapies/cares.[1–3] In 2020, LC accounted for approximately 820 000 of the approximately 4.57 million new cancer cases in China. China's LC incidence and deaths accounted for 37% and 39.8% of the world's total numbers, respectively, while China's proportion of the global population was only 18%, which caused huge economic and social burdens in China.[4,5] The latest data released by China's National Cancer Center in December 2022 showed that from 2000 to 2016, the age-standardized incidence rate for men increased from 48.49 per 100 000 people to 49.78 per 100 000 people, and the age-standardized incidence rate for women increased from 20.17 per 100 000 people to 23.70 per 100 000 people.[6] According to the 2022 statistics released by the Australian Institute of Health and Welfare, the LC age-standardized incidence rate has dropped from 47 per 100 000 people in 1982 to 44 per 100 000 people in 2020. Meanwhile, the age-standardized mortality rate decreased from 42 per 100 000 people to 26 per 100 000 people.[7] Previous literature pointed out that the age-standardized mortality rate of LC in Australia was higher than that in China in 1990, but it was substantially higher in China than in Australia in 2019.[8] As a developed country, the Australian Human Development Index (HDI) is ranked as one of the best in the world, with a high standard of economy, education, medical care, and standard of living, as well as an advanced welfare system. These factors had a significant impact on the incidence and mortality of LC.[9] Based on the Global Cancer Survival Trends Monitoring Report 3rd Edition (CONCORD3), Australia's 5-year cancer survival rate ranked among the best in the world, ranking first in survival rates for breast, colon, prostate, pancreatic, esophageal, and LC.[3] Australia has had a long history of tobacco control, which has led to a decrease in the burden of LC.[10] However, it has not been well understood what factors caused these differences in LC disease burden between the two countries. Therefore, this study used the Joinpoint regression model and the Bayesian age-period-cohort (BAPC) model to analyze trends in China and Australia and to predict the future disease burden. We also compared the differences in the risk factors of LC between the two countries and explored the factors affecting the trends in disease burdens in the next 10 years to support health policymaking for LC prevention and treatment in these countries.

MATERIALS AND METHODS

Data extraction

Data were sourced from the Global Burden of Disease (GBD) 2019 study, which conducted a scientific and comprehensive assessment of diseases, injuries, and risk factors across different regions, genders, and age groups. It estimated the disease burden of 369 diseases or injuries and 86 risk factors in 204 countries and regions from 1990 to 2019. It provided a large amount of data for research, such as data on the incidence, mortality, and disability-adjusted life years (DALYs) of different diseases around the world[11]; data on risk factors for various diseases,[12] such as smoking, alcoholism, high blood pressure, obesity, and unhealthy diet; as well as population data by age group and sex from all over the world, used to calculate the burden of disease indicators. By studying these data, it is possible to assess disease incidence, mortality, and disability and to quantify its impact on population health. Simultaneously, it is possible to evaluate the contribution of smoking, alcoholism, obesity, and other risk factors to the disease burden, which will assist in developing disease prevention and control strategies, enhancing public awareness of risk factors, promoting positive health behaviors, and reducing the impact of these risk factors. Data were queried and downloaded using the Global Health Data Exchange (GHDx).[13] GBD 2019 classified diseases according to the *International Classification of Diseases, Tenth Revision* (ICD-10), and the ICD-10 codes of LC are C33 and C34.[14,15] The GBD classified modifiable risk factors associated with the etiology of LC into four levels. First-level risk factors included environmental/occupational risks, behavioral risks, and metabolic risks; Level 2 risk factors included air pollution, occupational risks, other environmental risks, tobacco, dietary risks, and high fasting plasma glucose; Level 3 risk factors included particulate matter pollution, ambient particulate matter pollution, occupational carcinogens, residential radon, smoking, secondhand smoke, and diet low in fruit; and Level 4 risk factors included household air pollution from solid fuels and occupational exposure to asbestos, arsenic, beryllium, cadmium, chromium, diesel engine exhaust, nickel, polycyclic aromatic hydrocarbons, and silica.

Disease burden evaluation indicators

Incidence, mortality, and DALYs were used as indicators to evaluate the disease burden of LC in China and Australia. To eliminate the influence of population composition in different ages and regions, the incidence rate, mortality rate, and DALYs rate were standardized using the GBD 2019 global standard population. The age-standardized rate (ASR; per 100 000 population) was calculated using the following formula[16]:

$$\mathrm{ASR} = \frac{\sum_{i=1}^{A} a_i w_i}{\sum_{i=1}^{A} a_i} \times 100000,$$

where α_i refers to the incidence of the ith age-group and w_i denotes the number of persons (or weight) in the same age subgroup i of the assigned reference standard population.

Statistical analysis and the Joinpoint regression model

R software (Version 4.3.0) was used for statistical analysis, and the packages of Tidyverse, easyGBDR, BAPC, and integrated nested Laplace approximation (INLA) were used for data reading, sorting, modeling, and graphic visualization. The Tidyverse package was used for data processing, including data import, data organization, and data exploration (visualization, statistical analysis). BAPC combined with Poisson model within INLA was used to project future disease burden.[17]

The Joinpoint regression model was used to analyze the temporal trend in the disease burden of LC. The core idea of the model was to perform segmental regression based on the time features of the disease distribution, splitting the research time into different intervals across multiple connection points, and performing trend fitting and optimization for each interval.[18,19] The parameters included modeling method, constraints on the location(s) of the joinpoints, number of joinpoints, model selection method, average annual percentage change (AAPC) ranges, and confidence interval (CI). Before setting parameters, a Kolmogorov–Smirnov test was used to test the normality of the variable. If data were not normally distributed, logarithmic transformation was conducted. For data with a normal distribution, a linear model analysis was used. If data had a Poisson distribution or exponential distribution, a logarithmic linear model was used. Model fitting was performed using Joinpoint software (Version 5.0.2). This software used the incidence, mortality, and DALYs rate of LC to fit the logarithmic linear model, and judged the number of connection points and the connection points by the Monte Carlo permutation test method. We set the maximum number of connection points to 5 and the minimum number to 0. The permutation test started from the number of connection points $k = 0$ and $k\_$ max $= 5$, if $k \neq k\_$ Max, then setting $k = k + 1$ to continue testing until $k = k\_$ max; then the model corresponding to max was optimal APC and AAPC. 95% CI was calculated. APC was used to evaluate the internal trends in independent intervals in piecewise functions. AAPC comprehensively evaluated the global average trend in changes across multiple intervals. The Z test was used to evaluate whether APC was significantly different from 0. Nonsignificant ($p \geq 0.05$) APC were described as stable, whereas significant ($p < 0.05$) positive or negative APC were described as increasing or decreasing.[20]

Predictions of the burden of LC and the BAPC model

The BAPC model[21] was used to predict LC incidence, mortality, and DALYs in China and Australia in 2030. The future standardized population used the number of people predicted by the GBD database in 2017.[22] BAPC is based on age-period-cohort analysis. The age-period-cohort model has been commonly used to analyze the trend in chronic disease morbidity and mortality. In the classic age-period-cohort model, the impact of age, time period, and cohort on incidence or mortality has been taken into account to describe the changing trends in diseases and to make predictions based on the changing trends. However, as there was a linear relationship between the three factors in the age-period-cohort model that made parameter estimation difficult, a Bayesian model has been added based on the age-period-cohort model. To avoid overfitting or underestimation of the BAPC model, the model was calibrated by the following methods: selecting appropriate distribution models that were suitable for data characteristics, ensuring that the data used were clean and properly preprocessed before calibration (e.g., exclude zero count data, because zero count in observation data causes problems in model fitting[23]), and finally evaluating the fit of the model through posterior prediction testing. Therefore, the BAPC model estimated comprehensively the prior information of the unknown parameters and the sample information to obtain the posterior distribution and infer the unknown parameters based on the posterior distribution. The integrated nested Laplace approximation (INLA) algorithm has been commonly used for model estimation, directly approximating the posterior edge. As the expected effects of adjacent time might be similar, the second-order random walk (RW2) model was used to study the impact of age-period and cohort and to estimate the number of incidences, age-specific incidence rates, and standardized incidence rates.

Risk factor analysis

This process involved one secondary risk factor and six tertiary risk factors, including high fasting plasma glucose, particulate matter pollution, ambient particulate matter pollution, occupational carcinogens, residential radon, smoking, and secondhand smoke. The population-attributable fraction (PAF) was used to analyze the attributable disease burden of risk factors.

RESULTS

Comparison of changes in the burden of LC between China and Australia in 1990 and 2019

As presented in Table 1, the number of LC cases in China was 832 920 in 2019. Compared with Australia, China had a much higher ASR of incidence (China 41.71 per 100 000 people vs. Australia 30.45 per 100 000 people), ASR of mortality (China 38.70 per 100 000 people vs. Australia 23.46 per 100 000 people), and the ASR of DALYs (China 831.27 per 100 000 people vs. Australia 491.56 per 100 000 people). Compared with 1990, the ASR of incidence, mortality, and DALYs of LC in China have increased by 38.11%, 24.11%, and 6.9%, respectively. On the other hand, the ASR of incidence, mortality, and DALYs of LC have declined by 19.59%, 29.08%, and 35.94%, respectively, in Australia.

Comparison of trends in the burden of LC by gender in China and Australia from 1990 to 2019

As presented in Table 1 and Figure 1, there were gender differences in the LC burden in China and Australia in 1990. The ASR of incidence (Figure 1a,b), mortality (Figure 1c,d), and DALYs (Figure 1e,f) of males were significantly higher

TABLE 1 Comparison of changes in the burden of lung cancer (LC) between China and Australia in 1990 and 2019.

		China			Australia		
Sex		1990	2019	AAPC (%, 95% CI)	1990	2019	AAPC (%, 95% CI)
Males	Incidence						
	Number (×1000, 95% CI)	178.99 (213.93, 145.48)	576.19 (709.27, 451.4)	4.10 (4.07, 4.14)	5.42 (5.61, 5.22)	7.52 (9.59, 5.76)	1.18 (1.06, 1.26)
	ASR (per 100 000, 95% CI)	44.29 (52.43, 36.72)	61.74 (75.20, 48.93)	1.16 (1.02, 1.30)	61.01 (63.16, 58.67)	37.97 (48.53, 29.16)	−1.79 (−2.05, −1.53)
	Mortality						
	Number (×1000, 95% CI)	177.93 (214.39, 145.87)	523.19 (647.41, 413.19)	3.78 (3.75, 3.82)	4.79 (4.94, 4.62)	6.01 (6.45, 5.54)	0.81 (2.74, 0.87)
	ASR (per 100 000, 95% CI)	46.33 (55.03, 38.78)	58.10 (70.89, 46.53)	0.81 (0.64, 0.97)	54.66 (56.51, 52.68)	30.13 (32.31, 27.88)	−2.01 (−2.23, −1.79)
	DALYs						
	Number (×1000, 95% CI)	4864.23 (5914.77, 3954.89)	11967.77 (14952.33, 9374.37)	3.15 (3.12, 3.18)	109.31 (112.64, 105.82)	116.65 (124.84, 108.46)	0.24 (0.18, 0.30)
	ASR (per 100 000, 95% CI)	1084.53 (1310.23, 891.58)	1203.78 (1495.10, 950.19)	0.36 (0.18, 0.54)	1204.51 (1241.12, 1164.55)	608.52 (650.17, 567.62)	−2.31 (−2.54, −2.08)
Females	Incidence						
	Number (×1000, 95% CI)	78.05 (91.71, 65.13)	256.74 (314.16, 205.68)	4.19 (4.14, 4.24)	2.07 (2.17, 1.96)	5.28 (6.61, 4.11)	3.23 (3.17, 3.31)
	ASR (per 100 000, 95% CI)	18.01 (21.04, 15.12)	24.76 (30.26, 19.89)	1.12 (0.94, 1.30)	19.46 (20.36, 18.45)	24.01 (30.31, 18.84)	0.68 (0.54, 0.82)
	Mortality						
	Number (×1000, 95% CI)	78.40 (91.66, 65.03)	233.98 (282.75, 189.18)	3.84 (3.80, 3.88)	1.77 (1.84, 1.67)	4.02 (4.40, 3.56)	2.84 (2.78, 2.91)
	ASR (per 100 000, 95% CI)	18.63 (21.64, 15.62)	22.86 (27.52, 18.52)	0.72 (0.55, 0.89)	16.38 (17.06, 15.52)	17.80 (19.34, 15.93)	0.27 (0.03, 0.51)
	DALYs						
	Number (×1000, 95% CI)	2096.64 (2468.93, 1730.33)	5160.82 (6353.14, 4138.83)	3.16 (3.12, 3.20)	40.30 (41.84, 38.52)	79.77 (86.58, 72.37)	2.36 (2.29, 2.43)
	ASR (per 100 000, 95% CI)	456.89 (535.53, 377.41)	492.17 (604.27, 393.74)	0.26 (0.04, 0.47)	393.89 (408.94, 376.90)	387.14 (418.90, 353.31)	−0.13 (−0.23, −0.02)
Both	Incidence						
	Number (×1000, 95% CI)	257.04 (293.65, 221.29)	832.92 (981.63, 700.29)	4.17 (4.13, 4.21)	7.49 (7.72, 7.21)	12.8 (16.14, 10.03)	1.90 (1.80, 1.99)
	ASR (per 100 000, 95% CI)	30.20 (34.26, 26.20)	41.71 (48.80, 35.22)	1.16 (0.93, 1.18)	37.87 (39.06, 36.46)	30.45 (38.45, 23.87)	−084 (−1.05, −0.64)
	Mortality						
	Number (×1000, 95% CI)	256.33 (294.56, 221.06)	757.17 (887.75, 638.74)	3.81 (3.78, 3.85)	6.55 (6.74, 6.34)	10.03 (10.72, 9.21)	1.51 (1.47, 1.57)
	ASR (per 100 000, 95% CI)	31.18 (35.52, 27.14)	38.70 (45.03, 32.80)	0.78 (0.56, 1.01)	33.08 (34.00, 31.97)	23.46 (24.97, 21.67)	−1.24 (−1.19, −1.31)
	DALYs						
	Number (×1000, 95% CI)	6960.87 (8039.13, 5966.96)	17128.58 (20231.34, 14340.49)	3.17 (3.13, 3.22)	149.61 (153.68, 145.39)	196.42 (208.12, 183.26)	0.98 (0.92, 1.03)
	ASR (per 100 000, 95% CI)	760.68 (875.37, 654.28)	831.27 (979.99, 699.11)	0.33 (0.10, 0.56)	767.39 (788.12, 745.95)	491.56 (520.06, 461.18)	−1.50 (−1.72, −1.27)

Abbreviations: AAPC, average annual percentage change; ASR, age-standardized rate; CI, confidence interval; DALYs, disability-adjusted life years.

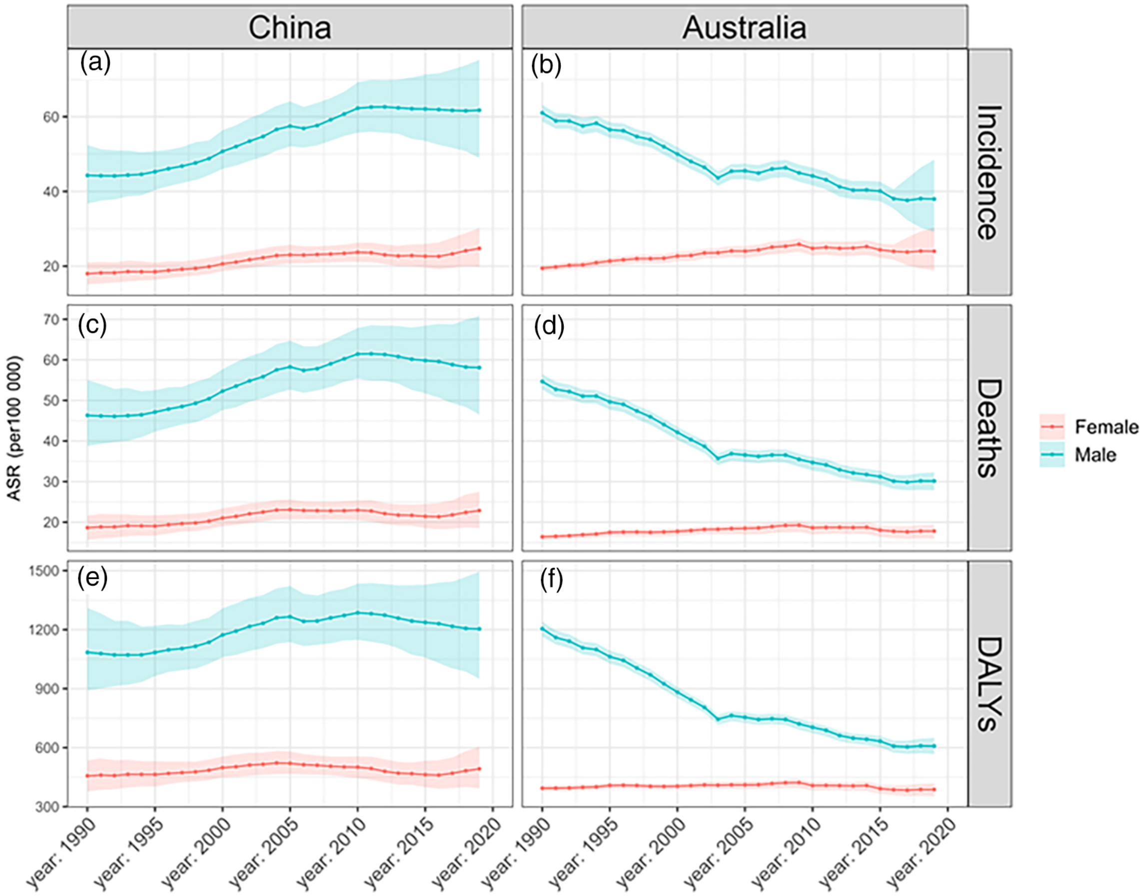

FIGURE 1 Trends in age-standardized incidence rates (a, b), mortality rates (c, d), and disability-adjusted life years (DALYs) rates (e, f) by gender in China and Australia from 1990 to 2019. ASR, age-standardized rate.

than those of females. Over time, in Australian males, there was a significant downward trend, with AAPC at −1.79%, −2.01%, and −2.31%, respectively, whereas in Australian females, the ASR of incidence and mortality increased slightly, and the ASR of DALYs decreased slightly, with AAPC at 0.68%, 0.27%, and −0.13%, respectively. In contrast, both Chinese males and females showed an upward trend, more significant in males, with AAPC at 1.16%, 0.81%, and 0.36%, respectively.

Comparison of trends in the burden of LC by age in China and Australia between 1990 and 2019

As shown in Figure 2, the LC incidence rate gradually increased from age 40. The older the age, the higher the incidence rate, and the change was more apparent between the ages of 60 and 85 years. In both countries, incidence peaked at 80 years of age in 1990 and then began to decline. The incidence rate of 55–85 years old in Australia was higher than that in China. In 2019, the incidence rate in both countries peaked at 85 years old, but still has not reached the inflection point. Among the Australian residents aged 55–75 years, the incidence rate of LC dropped compared with 1990. Starting from the age of 70, the incidence of LC among Chinese residents has increased significantly, and the curve was steep. Compared with 1990, the incidence rate increased significantly. LC mortality rates started to rise from the age of 50. In 1990, the death rate of Australian residents peaked at 80 years and then declined, but the death rate of Chinese residents continued to rise with age, and the inflection point has not yet appeared at the age of 85. The mortality rate among Chinese residents aged 65–80 was lower than in Australia. In 2019, the death rate in the two countries had reached the age of 85, but not yet peaked. The death rate of Chinese residents aged 75–85 was significantly higher than in 1990. The death rate for Australians aged 55–80 was lower than in 1990. The rate of DALYs started to rise from the age of 35. In 1990, the DALYs rate of LC among residents aged 40–55 in China was slightly higher than that in Australia, but from the age of 60, the DALYs rate in Australia was higher than that in China, reached a peak at the age of 75, and then declined. In 2019, the DALYs of the two countries rose in a straight line, peaked at the age of 80, and began to decline. The increase in China was more significant than that in Australia. Compared with 1990, China's DALYs began to rise sharply from age 70, and

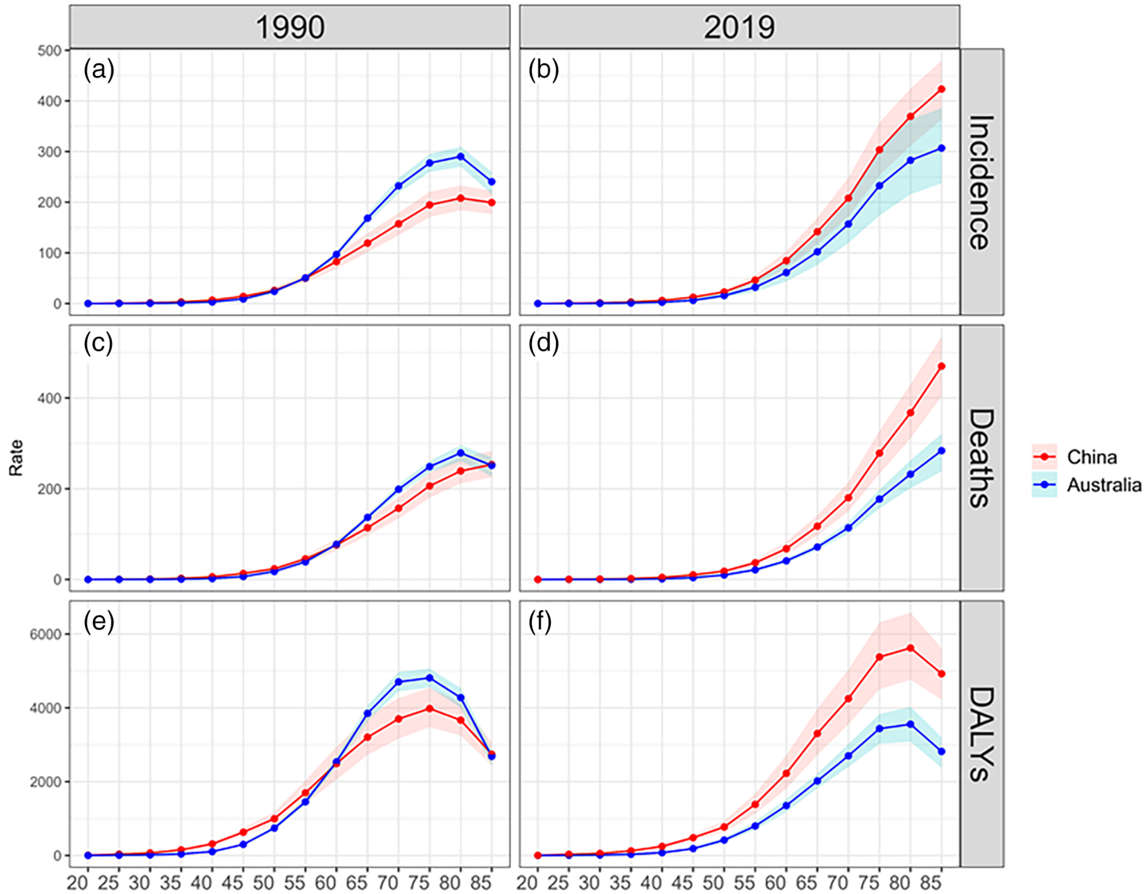

FIGURE 2 Trends in lung cancer (LC) incidence rate (a, b), mortality rate (c, d), and disability-adjusted life years (DALYs) rate (e, f) by age in China and Australia.

Australia's DALYs began to rise slightly from age 50 to a sharp decline at age 80.

Comparison of trends in overall LC burden between China and Australia from 1990 to 2019

There was an overall increasing trend in the age-standardized incidence rate of LC in China (AAPC = 1.16, $p < 0.05$; Figure 3a). It grew rapidly from 1997 to 2004 (APC = 2.84, $p < 0.05$) and increased rapidly again from 2007 to 2010 (APC = 2.01, $p < 0.05$). The standardized incidence rate in Australia showed an overall decreasing trend (AAPC = −0.84, $p < 0.05$; Figure 3b). There was a rapid decline from 1997 to 2003 (APC = −1.81%, $p < 0.05$), a significant increase from 2003 to 2008 (APC = 1.08, $p < 0.05$), and a significant decline from 2008 to 2019 (APC = −1.52, $p < 0.05$). The age-standardized mortality rate of LC in China showed an overall upward trend (AAPC = 0.78, $p < 0.05$; Figure 4a). It rose rapidly from 1997 to 2004 (APC = 2.58, $p < 0.05$), and again from 2007 to 2010 (APC = 1.38, $p < 0.05$), and dropped significantly from 2010 to 2016 (APC = −0.88, $p < 0.05$). The standardized mortality rate of LC in Australia showed an overall downward trend (AAPC = −1.24, $p < 0.05$; Figure 4b). It declined rapidly from 1996 to 2003 (APC = −2.42, $p < 0.05$) and again from 2008 to 2019 (APC = −1.45, $p < 0.05$). The age-standardized DALYs rate of LC in China generally showed an upward trend (AAPC = 0.33, $p < 0.05$; Figure 5a). It rose rapidly from 1997 to 2004 (APC = 1.88, $p < 0.05$) and dropped significantly from 2010 to 2015 (APC = −1.77, $p < 0.05$). The standardized DALYs rate of LC in Australia showed an overall downward trend (AAPC = −1.5, $p < 0.05$; Figure 5b). There was a significant decline from 1990 to 1997 (APC = −1.49%, $p < 0.05$), a rapid decline from 1997 to 2003 (APC = −3.01, $p < 0.05$), and a rapid decline from 2008 to 2017 (APC = −1.76, $p < 0.05$).

Predictions of the burden of LC in China and Australia in 2030

It is estimated that by 2030, the age-standardized incidence rate, mortality rate, and DALYs rate of male LC in China will be 64.44 per 100 000 people, 56.54 per 100 000 people, and 1176.74 per 100 000 people, respectively (Figure 6b,d,f). Compared with 2019, they will increase by 4.37%, decrease

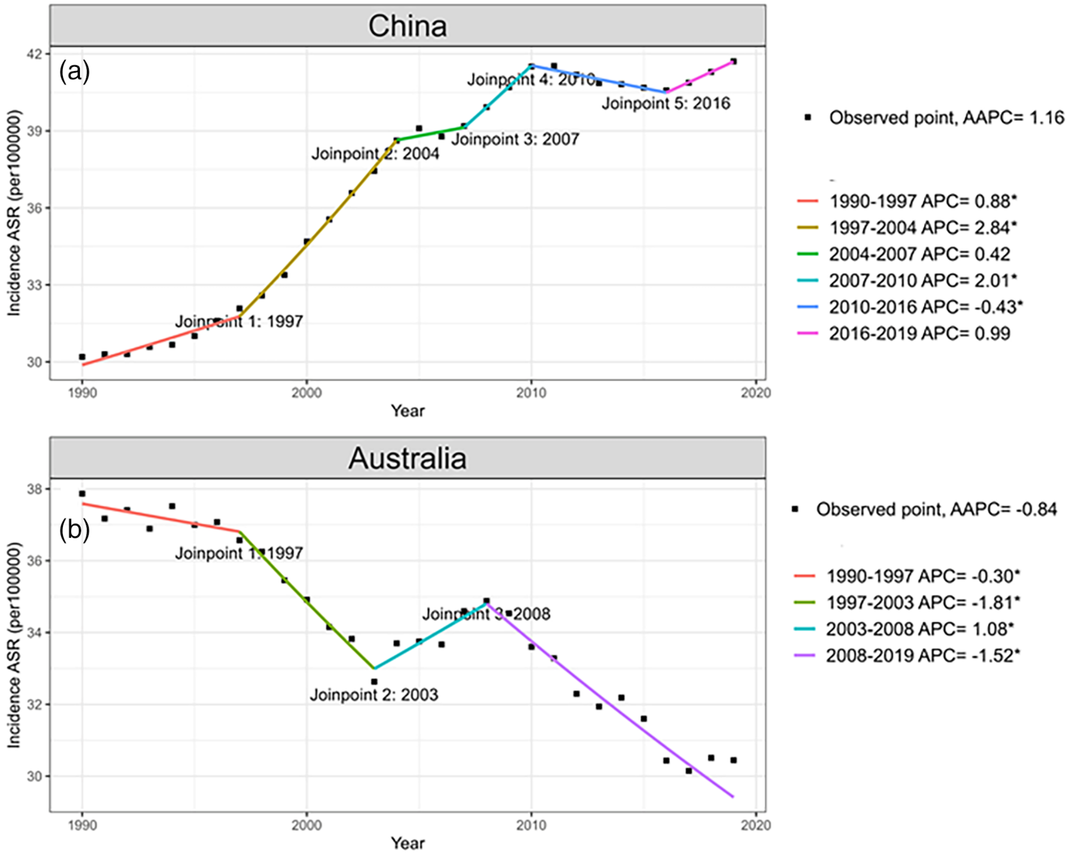

FIGURE 3 Trends in age-standardized incidence rate in China (a) and Australia (b) from 1990 to 2019. AAP, annual percentage change; AAPC, average annual percentage change; ASR, age-standardized rate.

by 2.6%, and decrease by 2.25%, respectively. The age-standardized incidence rate, mortality rate, and DALYs rate of female LC in China will be 31.99 per 100 000 people, 27.5 per 100 000 people, and 584.9 per 100 000 people, respectively (Figure 6a,c,e). Compared with 2019, they will increase by 29.2%, 20.3%, and 18.84%, respectively. The total age-standardized incidence rate, mortality rate, and DALYs rate will be 47.21 per 100 000 people, 41.54 per 100 000 people, and 886.4 per 100 000 people. Compared with 2019, they will increase by 13.19%, 7.34%, and 6.63%, respectively, in China. The age-standardized incidence, mortality rate, and DALYs rates of male LC in Australia will be 37.9 per 100 000 people, 30.42 per 100 000 people, and 603.4 per 100 000 people, respectively (Figure 6b,d,f). Compared with 2019, they will decrease by 0.18%, increase by 0.96%, and decrease by 0.84%, respectively (Figure 6b,d,f). The age-standardized incidence rate, mortality rate, and DALYs rate of female LC will be 21.89 per 100 000 people, 15.92 per 100 000 people, and 371.09 per 100 000 people, respectively (Figure 6a,c,e). Compared with 2019, they will decrease by 8.83%, 10.56% and 4.15%, respectively. The total age-standardized incidence rate, mortality rate, and DALYs rate will be 30.09 per 100 000 people, 23.3 per 100 000 people, and 500.57 per 100 000 people, respectively. Compared with 2019, they will decrease by 1.18% and 0.68%, and increase by 1.83%, respectively, in Australia.

Risk factors for LC mortality in China and Australia

In 1990, the main risk factors for LC in Chinese women were particulate matter pollution (33.53%), smoking (19.56%), and secondhand smoking (12.33%), while the main risk factors in Australian women were smoking (68.38%) and occupational carcinogens (13.34%; Figure 7a). In 1990, smoking was the main risk factor in both Chinese (80.45%) and Australian (77.41%) men. In addition, Chinese men had a higher particulate matter pollution risk (32.71%) than Australian men (4.27%), while Australian men had a higher occupational carcinogen risk (48.25%) than Chinese men (7.89%; Figure 7b). In 2019, the high risk factors for Chinese women were particulate matter pollution (27.94%) and smoking (26.58%), followed by secondhand smoking (11.47%; Figure 7c); however, smoking (53.75%) and occupational carcinogens (15.67%) were high risk factors for LC in Australian women (Figure 7c). In 2019, Chinese men had higher smoking (82.03%) and particulate matter pollution (27.31%) risks than Australian men (58.47% and 3.1%, respectively), while Australian men had a higher occupational carcinogen risk (46.72%) than Chinese men (8.77%; Figure 7d). The attributable coefficients of fasting hyperglycemia in China and Australia were higher in 2019 than in 1990.

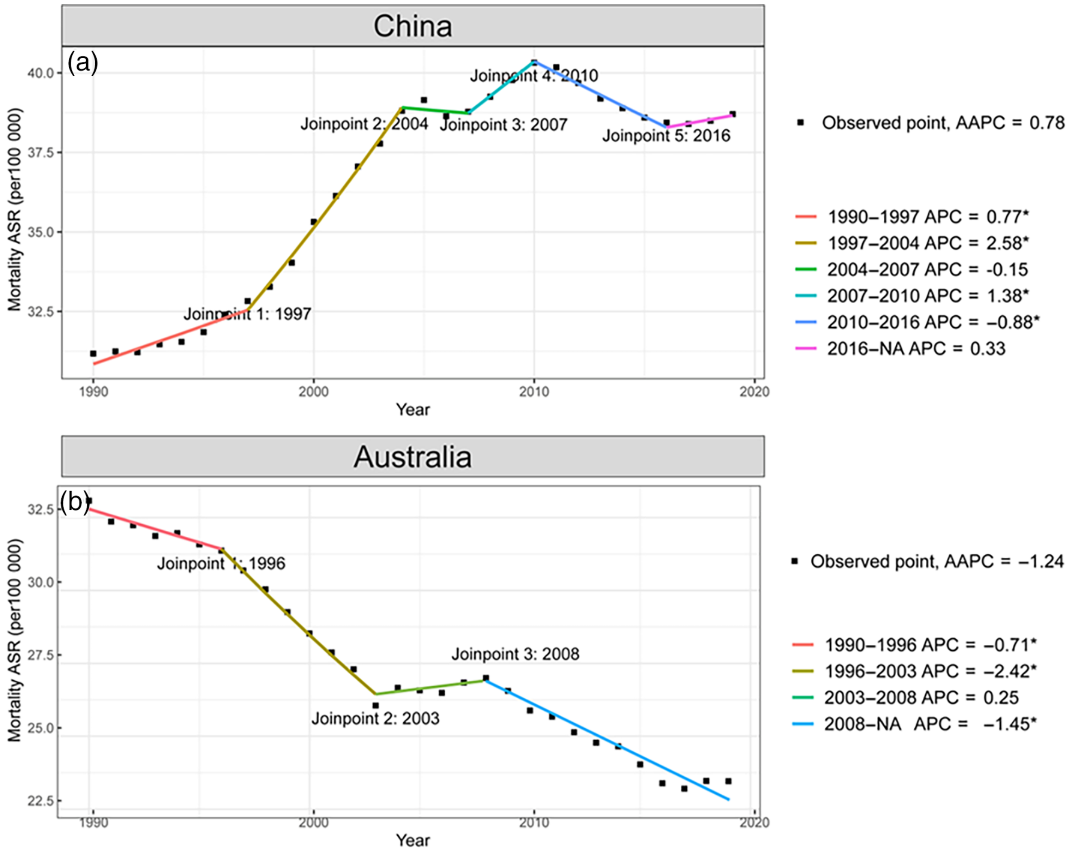

FIGURE 4 Trends in age-standardized mortality rate in China (a) and Australia (b) from 1990 to 2019. AAP, annual percentage change; AAPC, average annual percentage change; ASR, age-standardized rate.

DISCUSSION

This study found that, in the past 30 years, LC numbers of incidence, death, and DALYs in Australia have increased, but ASR of incidence, death, and DALYs have decreased substantially. The number of incidences, death, DALYs, and ASR of incidence, death, and DALYs all increased significantly in China. The 2030 prediction results have showed that the ASR of incidence, death, and DALYs in China will continue to rise. In contrast, in Australia, the ASR of incidence and mortality will continue to decline in 2030. It indicates that the burden of LC in China is heavy, and the situation is still very serious. The reasons for these differences may be related to multiple risk factors such as smoking rates, environmental pollution, occupational exposures, dietary structure and health habit, age structure, genetic factors, as well as levels of socioeconomic development, health education and policies on prevention and management of LC, and access to advanced LC therapies/healthcare.[24,25]

This study analyzed the disease burden of LC in China and Australia from a gender perspective and found that the age-standardized incidence rate, mortality rate, and DALYs rate of males were significantly higher than those of females in both Australia and China. This is largely due to the relatively high smoking rate in men and their higher likelihood of being exposed to some occupational carcinogens.[26] In addition, men are more inclined to unhealthy lifestyles and lack health awareness, and they are a group that needs to be the focus of LC prevention and control.[27] This study also compared and analyzed the trend in gender changes in LC patients between the two countries over time. It showed that the burden of LC among Chinese men has been increasing over the past 30 years, while the burden in Australian men has been decreasing. One possible reason for this discrepancy is that smoking rates in Chinese men have been relatively high. Although China has enforced some tobacco control policies and measures, men's smoking habits are still prevalent. Examination of the predicted 2030 data shows that the ASR of incidence, death, and DALYs for Chinese women are all increasing; the rate of increase in women is significantly greater than that of Chinese males. In contrast, the LC burden in Australian women is declining. Although the smoking rate among Chinese women is still relatively low compared to European and other countries, unfortunately there is a slowly increasing trend in Chinese women's smoking rate.[28] Smoking is more harmful to women's bodies, since women are more sensitive to the harm caused by tobacco.[29] China has had the most severe secondhand smoke problem in the world, with 71% of women over 15 years old suffering from passive smoking daily.[30] Additionally, the exposure risk of females to household and occupational harmful substances and environmental pollutants

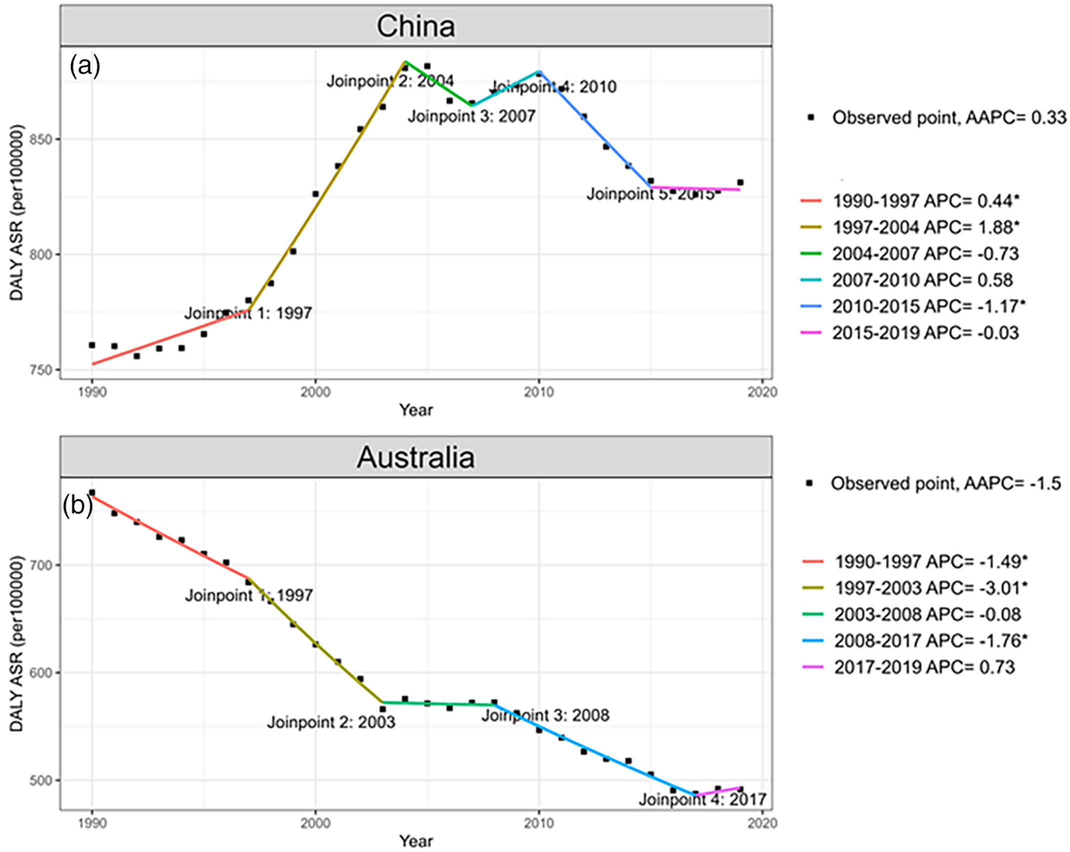

FIGURE 5 Trends in age-standardized disability-adjusted life years (DALYs) rate in China (a) and Australia (b) from 1990 to 2019. AAP, annual percentage change; AAPC, average annual percentage change; ASR, age-standardized rate.

was higher than that of males.[31] These findings suggest that we need to pay more attention to the health of Chinese women in the future. Moreover, gender differences in LC are closely related to pathological types and gene mutations. Small cell LC and squamous cell carcinoma are more common in male smokers, while adenocarcinoma is more common in female patients.[10] Compared with Asian women, the incidence rate of lung adenocarcinoma in Australian women is lower; however, the mutation frequency of Kirsten rat sarcoma oncogenes (KRAS) is relatively high (Asian women with lung adenocarcinoma mainly have EGFR and ALK gene mutations).[32–34] Understanding these differences will be beneficial in the selection of treatment plans. In recent years, significant progress has been made in the field of LC treatment, especially in the areas of immunotherapy and targeted therapy.[35] These treatment methods provided new hopes for previously "difficult to treat" LC patients and have significantly improved their survival rate and quality of life.

This study also analyzed the changes in the disease burden of LC in different age groups in China and Australia from 1990 to 2019. In terms of incidence and mortality rates, they gradually increased with age. In 1990, it peaked at the age of 80, while in 2019, it had not yet reached the peak at the age of 85. One reason for these differences could be that, due to socioeconomic development, improvement in medical conditions and living standards, the average life span of the population has been extended, leading to an older population.[27] In this study, a comparative analysis of Chinese and Australia population aged 60–85 showed that in 1990, Australia's disease burden was higher than that of China, but was markedly surpassed by China in 2019. The main reason lies in the differences between China and Australia in terms of population aging, elderly care services, and medical security. China is one of the most populous countries in the world and has a prominent aging problem. However, elderly care services and medical security are relatively weak, which may lead to inadequate treatment and management of LC, thereby increasing the burden of LC. In contrast, the number of elderly people in Australia is relatively small, and the government has invested a lot of resources in the issue of aging, effectively reducing the health burden on elderly people by providing high-quality medical services, actively carrying out health promotion and education, and providing adequate elderly care facilities.[36] Overall, to reduce the burden of LC, China needs to strengthen response measures to the aging problem, improve elderly care services and medical security, and strengthen LC prevention and early screening.

Smoking is a major risk factor leading to a high incidence of LC,[37,38] and it is also the main risk factor for death from LC.[39] Harmful substances released from smoking, such

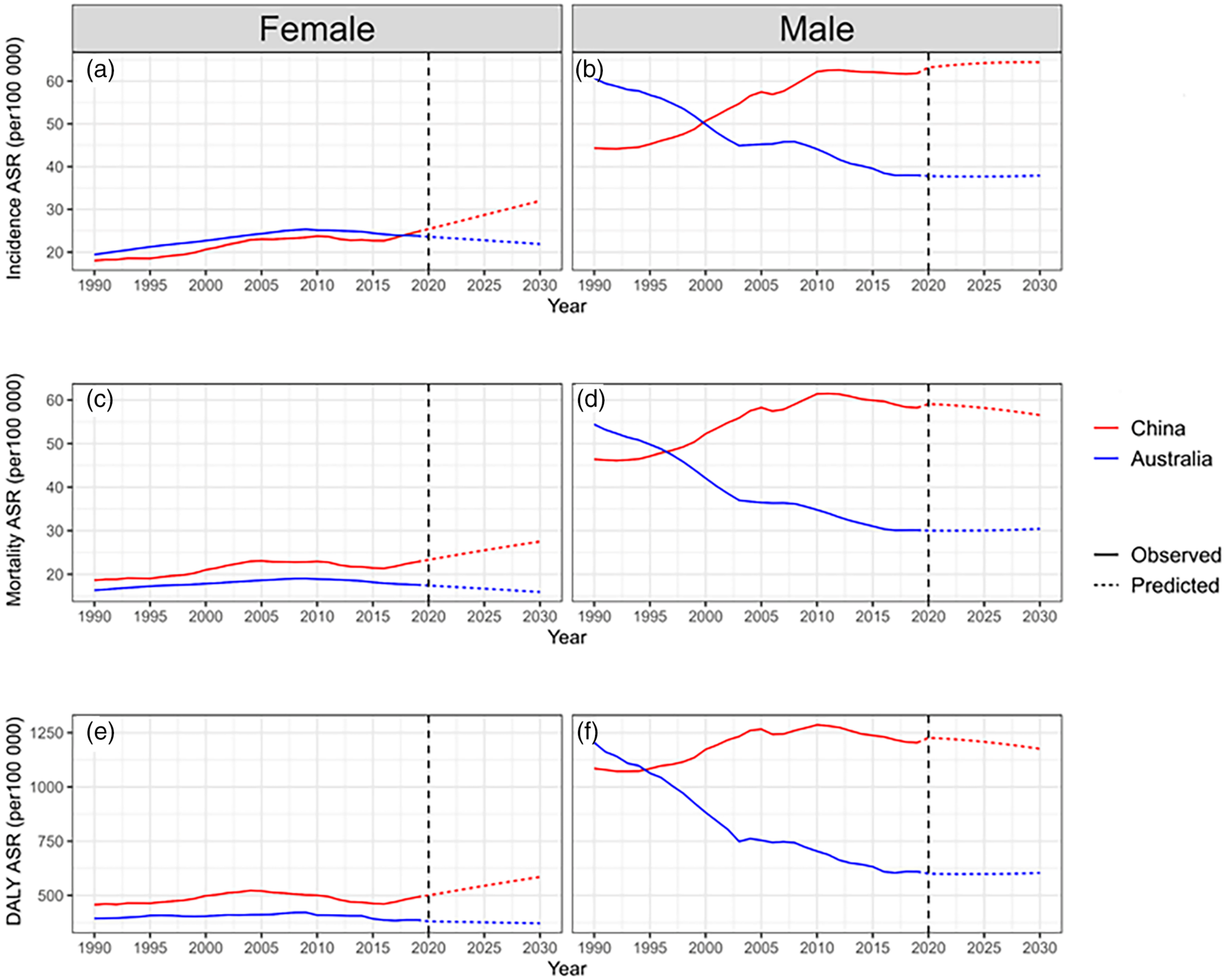

FIGURE 6 Predictions of age-standardized incidence rate (a, b), mortality rate (c, d), and disability-adjusted life years (DALYs) rate (e, f) of lung cancer (LC) in China and Australia in 2030. ASR, age-standardized rate.

as nicotine and a variety of carcinogens, can lead to damages and mutations of lung tissue and increase the risk of LC. Not only does smoking have direct harmful effects on the smoker, but secondhand smoking can also be harmful to passive smokers.[40] Smoking and secondhand smoking are the largest contributors to LC. According to a recent report,[41] the smoking rate in China is still high, especially among males, while the smoking rate in Australia is relatively low. This may be the fundamental reason for the different trends in LC burden between China and Australia. From 1987 to 2019, Australia enacted strict tobacco control laws, such as the Tobacco Advertising Prohibition Act of 1992, the No Smoking in Public Places Act, the Tobacco Warning Label Act in 2006, and the Tobacco Plain Packaging Act in 2019. Amendments to the Tobacco Sales Act were passed in 2016, raising the minimum age limit for purchasing tobacco products to 18 years. Raising tobacco taxes and the price of tobacco products in Australia also led to a reduction in smoking rates.[42] The Australian government and communities also provide smoking cessation assistance measures, including smoking cessation medications, counseling, and support services to assist smokers to quit smoking.[43] The implementation of these policies has a significant positive impact on reducing the smoking rate and the incidence rate and mortality of LC. However, China's tobacco industry is large and powerful, making a significant contribution to the economy and tax revenues, which gives tobacco companies greater influence and voice in the implementation of tobacco control policies, subject to certain restrictions.[44] Even though China has also promulgated a series of tobacco control regulations and policies, its legislation falls short in raising taxes and tobacco prices.[45,46] Many local governments have not effectively implemented smoke-free policies and have inadequate supervision, leading to problems with smoking in some public places. Even with the restrictions on sales of tobacco products to minors, there are still some flaws in the actual implementation, and it remains common for minors to obtain and consume tobacco

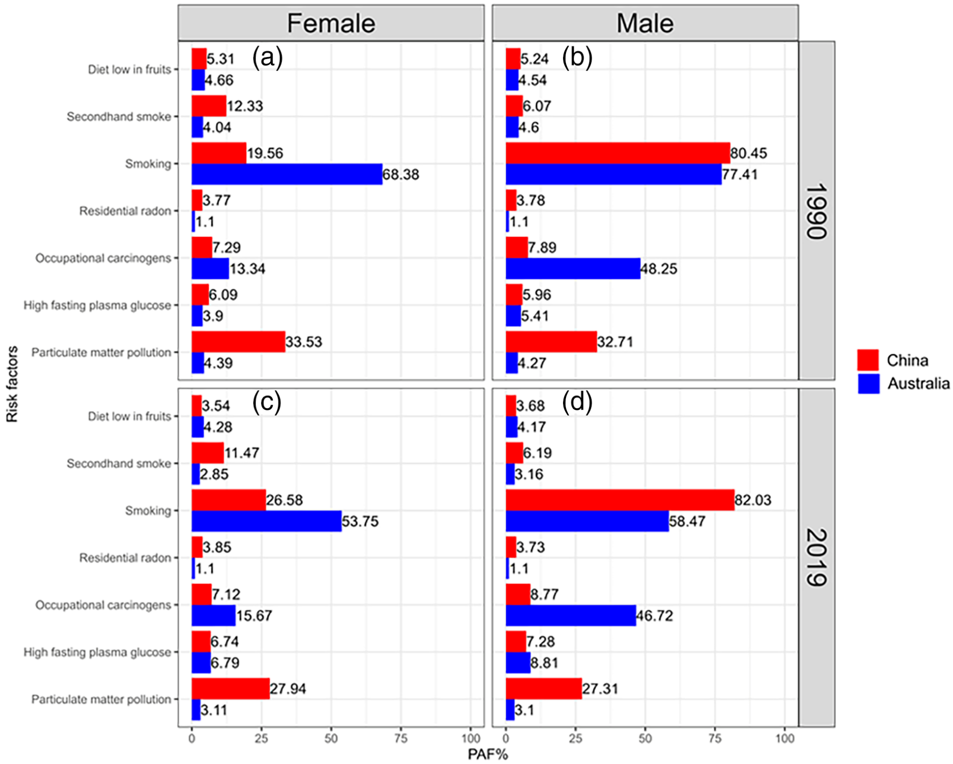

FIGURE 7 Risk factors for lung cancer (LC) death in China and Australia in 1990 (a, b) and 2019 (c, d). PAF, population-attributable fraction.

products in China.[47] In addition, differences in smoking can be attributed to differences in social and cultural backgrounds between the two countries. In Chinese society, smoking is often used as a way to socialize and communicate or may even be regarded as a symbol of masculinity.[48] Because of the existence of this concept, some people are not sufficiently aware of the dangers of smoking, and therefore, it is difficult to change their smoking behaviors. Therefore, smoking is ubiquitous in social life, and the government has adopted a relatively relaxed attitude toward smoking control. In contrast, Australia has experienced a series of antismoking campaigns and information campaigns targeting smoking in the late 20th century. These campaigns highlighted the health hazards of smoking, leading to a gradual change in society's perception of smoking, with smoking being seen as an unhealthy behavior. In combination with these campaigns, the Australian government has adopted strict smoking control policies, such as increasing tobacco taxes and banning smoking in public places.

Environmental pollution is also a major contributor to the high incidence of LC.[49] Pollutants in the air, such as harmful substances in industrial exhaust and automobile exhaust, can increase the risk of LC.[50] The acceleration of industrialization and urbanization is a significant cause of environmental pollution. Although Australia is a developed country, its industrialization process has been relatively slow, focusing mainly on mining and manufacturing.[51] Therefore, its air pollutants mainly come from vehicle exhaust, coal power generation, and soil pollution caused by mining activities. However, China's industrialization scale is much larger, and high-density industrial activities and large coal consumption have led to serious particulate metter 2.5 (PM2.5), sulfur dioxide (SO_2) and nitrogen oxides (NOx) (including NO and NO_2) emissions.[52] Water pollution caused by insufficient treatment of industrial wastewater and urban sewage is also quite serious. Following a range of measures to improve environmental conditions enforced recently in China, the risk of cancer caused by particulate matter pollution in 2019 has decreased compared with that in 1990, but is still the second most important risk factor. China has an approximately nine times higher risk of cancer due to particulate matter than Australia, suggesting the need to further strengthen its environmental governance. Indoor radon exposure is a potential health hazard, while long-term exposure to high levels of indoor radon is likely to increase the risk of LC.[53] The risk of residential radon-induced LC in China is three times greater than in Australia.

Occupational exposures are also one of the critical reasons for high LC incidence.[54] The incidence of occupational carcinogenic LC in Australia is higher than that in China, due to differences in occupational exposure. As a developing country, China still has a large number of traditional industries, and these industries pose high occupational exposure risks to workers. For example, Chinese coal miners have been exposed to high concentrations of coal stones and dust for a long time, which is one of the main factors leading to LC.[55,56] The most important occupational carcinogen associated with LC in Australia is asbestos.[57] Although Australia has completely banned the use of asbestos, exposure to asbestos still exists.[58]

The risk of LC is closely related to dietary structure and activity habits. Previous studies have found that obesity, fasting hyperglycemia, and prolonged sitting are the risk factors for cancer.[59] This is also confirmed in this study. Compared with 1990, the risk of LC caused by fasting blood glucose increased in China and Australia in 2019. There are certain differences in the dietary structure and activity habits between China and Australia. In the 1990s, China's industrialized economy was just starting, and the dietary structure was mainly based on traditional rice and noodles. People's dietary habits generally leaned toward vegetarianism. However, with the continuous development of industrialization and urbanization, the income level of the Chinese population has gradually increased, improving the quality of life and dietary conditions, and the dietary structure has also begun to change. High-fat, high-sugar, high-salt, and high-calorie foods have become the daily diet choices of many people, leading to the rising incidence rate of obesity and diabetes.[60] In addition, Chinese people love to eat processed foods, such as smoked meat, and the carcinogens in these foods can increase the risk of LC.[60,61] In contrast, Australia has a relatively healthy dietary structure, mainly consisting of vegetables, fruits, and coarse grains. In addition, Australians place greater emphasis on outdoor activities, especially those with sufficient oxygen supply such as hiking, which are beneficial for the health of the respiratory system. Reducing or eliminating poor living habits may significantly reduce the risk of LC.[62]

The burden of LC is related to levels of socioeconomic development and access to healthcare. As a populous developing country, China has a large urban–rural gap, imbalanced socioeconomic development, and insufficient medical resources, especially in remote regions.[63] In rural areas of China, when noticing early symptoms, many patients often tend to purchase medicines in pharmacies for self-treatment, rather than seeking medical consultation in a timely manner.[64] This behavior may cause patients to miss opportunities for early detection of LC, thereby increasing the burden of LC in China. On the other hand, Australia has had a higher level of socioeconomic development and a comprehensive health system to provide better medical resources.[65] Australian patients may be able to seek more timely medical consultation/treatment, and therefore improve early detection and treatment of LC.

Another risk factor impacting the disease burden of LC is health education and policies on prevention and management. Australia has developed a comprehensive set of policies for the prevention and management of LC, including strengthening smoking control, promoting healthy habit, and improving medical resources.[10] Australia has also strengthened health education for LC, improving public awareness and prevention awareness of LC.[10] On the other hand, although the Chinese government's attention to LC has increased in recent years, further attention needs to be paid to smoking control, environmental pollution control, dietary health education, and medical resource allocation, as well as further improving health education in public awareness of LC early screening and healthy lifestyle.[66,67]

The differences in LC disease burden between China and Australia may be partly due to the different interactions between various risk factors. For example, people with lower socioeconomic status generally face greater health risks, including higher rates of LC incidence and mortality.[68] Risk factors such as environmental pollution, bad health habits, and limited health protection faced by low-income families may lead to an increase in the incidence of LC,[68] thus increasing the disease burden of LC. The development of science and technology and the emergence of new medical technologies/therapies have provided patients with more treatment options and opportunities; however, people of a lower SES have a lower chance to access early LC diagnosis and advanced LC therapies, leading to worse outcomes of LC survival.[68,69] Unfortunately, to date, there are few studies to investigate how interactions between these LC risk factors impact on LC disease burden in China and Australia, which warrants further studies in these interactions to address challenges in reducing the LC disease burden in both countries.

In addition to the abovementioned risk factors, it is worthy to note that several positive factors may partly contribute to an increase in the LC incidence rate in China over the past decades, including an expansion of medical care coverage, advanced development of medical technology, enhancement of health awareness, and an extended average life expectancy among the population. The Chinese government started to establish the basic medical insurance system for urban employees in 1998. In the following 20 years, it successively established the new rural cooperative medical care and basic medical insurance for urban residents. Recently, it integrated them into a basic medical insurance to cover both urban and rural residents, aimed to gradually achieve full coverage for insured persons. According to the "Statistical Express Report on the Development of Medical Security in 2023" released by the National Medical Insurance Administration of China on April 11, 2024,[70] by the end of 2023, the number of people covered by China's basic medical insurance was about 1.334 billion, representing about 95% participation rate. This implies that more and more individuals have been able to access regular health checks and early screening services over the years, leading to increased detections of LC cases at an early stage and thereby contributing to an overall rise in LC incidence. Similarly, advancements in medical technology, especially the development of imaging and molecular biology techniques, have made LC detection and diagnosis accurate and sensitive in detecting smaller tumors or early lesions and, therefore, also increased the diagnosis rate of LC. Moreover, due to an increase in the public attention to health issues, Chinese people have paid more attention to healthy lifestyles, such as quitting smoking, eating healthy food, and exercising regularly. For people with LC risk factors (such as a long history of smoking), increased awareness of physical health may prompt them to actively seek medical examinations, thereby increasing the diagnosis rate of LC. Finally, LC is an age-related disease that increases with age.

With the improvement in medical conditions and living standards, the average life expectancy of the Chinese population has significantly increased. Data from the National Bureau of Statistics show that the average life expectancy of the Chinese population has increased from 72.95 years in 2005 to 77.93 years in 2020.[71] The increase in life expectancy naturally led to an increase in LC incidence. However, in the years ahead, these positive factors such as improved healthcare cover, medical technology, and healthy lifestyle may eventually lead to reduced LC incidence and disease burden.

It is worth noting that this study has several limitations. First, this data source may have some limitations. For example, incomplete and inconsistent data may lead to less accurate estimates of disease burden in low-income countries due to a lack of high-quality data. In addition, cultural, social, and political factors may also affect the reporting of data. These may affect the accuracy of regression analysis and model predictions. Second, the GBD data are mainly estimated by combining system dynamics and statistical models. Therefore, some distortions in the data are inevitable. The predictions for 2030 standardized incidence, mortality, and DALYs rates of LC are based on model predictions. Models may be overfit and underfit, resulting in an inability to predict accurately. In addition, changes in disease epidemic trends, changing epidemics, medical technology, treatment options, and public health policies may affect the disease burden, and these changes are difficult to accurately predict in the model. However, with the development of modeling technology using artificial intelligence,[72] model predictions could be further improved. Additionally, there is an assumption in our study that past trends will continue without considering the latest development of health care practices and environmental factors. In fact, these factors will have an impact on disease burden trends. For example, targeted therapy for LC has significantly improved the survival rate of patients with advanced lung adenocarcinoma.[35] Therefore, the prediction results should be treated with caution. Finally, as some risk factors for LC, including genetic factors, a history of certain lung diseases (such as chronic obstructive pulmonary disease, and tuberculosis), certain viral infections, and immune system suppression, have not been included in the GBD 2019 data, it is important to add the above risk factors in subsequent updates.

In conclusion, the disease burden of LC is on the rise in China but on the decline in Australia. Men and the elderly are high-risk groups for LC needing further attention. However, it cannot be ignored that the future burden of LC in Chinese women will be higher than that in Chinese men. Smoking, particulate matter pollution, and occupational carcinogenesis are the major risk factors for LC, and further measures need to be taken to control these risks. In the near future, China would face a heavy burden of LC disease. Although there are significant challenges, especially for China, to reduce the disease burden of LC, it is crucial to further improve effective interventions, including (1) strengthening tobacco control legislation, implementing no-smoking areas, increasing tobacco taxes and other measures to reduce smoking rates; (2) implementing stringent air quality standards by promoting clean energy and reducing industrial emissions; (3) improving health education through public and social media, school education and community activities to increase public awareness of LC risk factors (such as smoking, air pollution, and occupational exposure); (4) promoting LC early screening programs, especially for high-risk groups; (5) optimizing the diagnosis, treatment, and rehabilitation for LC; (6) and improving the accessibility and quality of medical services, particularly in regional and rural areas. This requires cross-sector collaboration and sustained public policy supports to effectively address these challenges and reduce the disease burden of LC.

AUTHOR CONTRIBUTIONS

HM and CD designed the study. DZ and HM conducted data extraction. DZ, HM, and PY analyzed the data. DZ and HM prepared the initial draft of the manuscript. CD, HM, and PY revised the manuscript. All authors reviewed and approved the manuscript.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflict of interest to declare.

DATA AVAILABILITY STATEMENT

All data used in this study can be freely accessed at GBD 2019 (http://ghdx.healthdata.org/gbd-2019).

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