



Secular trends in incidence and mortality of bladder cancer in China, 1990–2017: A joinpoint and age-period-cohort analysis



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ABSTRACT

Background: Bladder cancer is closely related to occupational carcinogens, and China is undergoing a rapid industrialization. However, trend of bladder cancer incidence and mortality remains unknown in China.

Methods: Incidence and mortality rates of bladder cancer (1990–2017) were collected for each 5-year age group stratified by gender (males/females) from the Global Burden of Disease (GBD) 2017 study. The average annual percentage change (AAPC) of rates were analyzed by joinpoint regression analysis; age, period and cohort effects on incidence and mortality were simultaneously estimated by age-period-cohort model.

Results: Through 1990–2017, age-standardized incidence rates significantly rose in men (AAPC = 0.72%, 95% CI: 0.5%, 0.9%) while decreased in women (-1.25%: -1.6%, -0.9%); age-standardized mortality rates decreased in both men (-1.09%: -1.2%, -0.9%) and women (-2.48%: -2.8%, -2.2%). The joinpoint regression analysis showed the mortality almost decreased in all age groups; while the incidence increased in men for older age groups (from 45 to 49 to 80–84). Moreover, age effect showed the incidence and mortality increased with age; the incidence and mortality increased with time period, while in women period effect stop decreasing and began to increase since 2007; cohort effect showed them decreased with birth cohorts.

Conclusions: The incidence of bladder cancer is increasing in men but mortality decreases in both sexes. Both the incidence and mortality in men substantially increase with age and period, while the rates in women increased with period since 2007. The period effect may indicate the increased risks to bladder cancer in Chinese men. Etiological studies are needed to identify the factors driving these trends of bladder cancer.

1. Introduction

Bladder cancer ranks as the ninth most common cancer worldwide with an estimated 429,800 new cases and 165,100 deaths occurred in 2012, and strong sex disparities are observed in bladder cancer and three-quarters of cases occurring in male [1,2]. More than 60% of all bladder cancer cases and half of its deaths occur in less developed countries [2]. In China alone, previous study reported bladder cancer ranked ninth for all cancers death in 2016 with a 14% proportion of bladder cancer deaths occurred worldwide [3]. According to GBD 2017

[4], there are an estimated 72,992.33 new cases and 30,642.90 deaths of the disease in 2017, accounting for 15.41% of 473,800.11 cases and 15.59% of 196,546.21 deaths worldwide, respectively.

Bladder cancer is closely related to occupational carcinogens [5–8]. With the rapid industrialization in China, the exposure to occupational carcinogens may increase. On the other hand, there have been significant improvements in the screening, diagnosis [9], treatment [10] and possible chemoprevention [11–14] of bladder cancer. Thus, it is necessary to examine the trends of bladder cancer incidence and mortality in China to throw light on policy making regarding occupational

Abbreviations: GBD, Global Burden of Disease; AAPC, average annual percent changes; APC, age-period-cohort model; IE, intrinsic estimator; CI, confidence intervals; CDC, Chinese Center for Disease Control and Prevention; DSPs, Disease Surveillance Points; RR, relative risk; AIC, Akaike Information Criterion; BIC, Bayesian Information Criterion; CIR, crude incidence rate; ASIR, age-standardized incidence rate; CMR, crude mortality rate; ASMR, age-standardized mortality rate; coef., coefficients

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protection.

As incidence and mortality of bladder cancer is influenced by age and gender [2,15], we examined these trends for each 5-year age group stratified by gender. The incidence trend on a national scale remains unknown in China. One study reported a decline of mortality rates with AAPC of -5.0% in men and -3.1% in women [16]. However, China has undergone a rapid aging transmission, medical care and socioeconomic development, all these changes may impact the incidence and mortality rates in China for both males and females among different age groups [17–20]. Thus, we examined trends and the net age, period and cohort effect on incidence and mortality trends of bladder cancer through 1990 to 2017.

2. Materials and methods

2.1. Data source

The incidence and mortality rate of bladder cancer were obtained from GBD 2017, which estimated incidence or mortality of bladder cancer [International Classification of Diseases (ICD)-10 code] for 354 causes in 195 countries for all ages in different provinces. The rates were age-standardized by the GBD 2017 global age-standard population [4]. The original data estimated by GBD for bladder cancer in China was mainly from the Cause of Death Reporting System of the Chinese Center for Disease Control and Prevention (CDC), Disease Surveillance Points (DSPs) and the Maternal and Child Surveillance System, which are considered to be nationally representative as it is based on a national scale.

2.2. Joinpoint regression analysis

The identification of changes in secular trend is an important issue in the analysis of cancer mortality and incidence data, and such continuous changes were described by a joinpoint regression model. In the model, logarithmic transformation of the rates was carried out and the standard errors were calculated based on binomial approximation [21]. To determine the magnitude of the secular trends, the average annual percent changes (AAPC) and corresponding 95% confidence interval (CI) were evaluated by joinpoint regression analysis [22]. Each p-value is found using Monte Carlo methods, and the overall asymptotic significance level is maintained through a Bonferroni correction. AAPC was calculated as a geometrically weighted average of various annual percent change values from this analysis [23]. Joinpoint analysis was performed using ‘Joinpoint’ software from the Surveillance Research Program of the US National Cancer Institute.

2.3. Age-period-cohort analysis with intrinsic estimator method

Generally, the epidemiological characteristics of diseases are usually related to socioeconomic distribution, geographical position and population factors. Age effect on diseases were affected by biological factors. Period effect reflected factors with immediate effects on diseased incidence or mortality, such as development of effective treatments and implementation of screening. Cohort effect reflected the impact of different risk factors for diseases in different generations. APC analysis is popularly used to estimate net age, period and cohort effects on diseases incidence and mortality [23,24]. Based on the study of Kupper et al., APC model with intrinsic estimator (IE) method can be used to decompose the three temporal trends simultaneously and provides unbiased and relatively efficient estimation results [25,26], which could provide epidemiology evidences for understand on reasons of the increasing trends of bladder cancer.

In APC model with IE method, the age-specific rates were appropriately recoded into successive 5-year age groups (20–24, 25–29, ..., 80–84), consecutive 5-year periods from 1990 to 2017, and correspondingly consecutive 5-year birth cohort groups (1912–1916,

1917–1921, ..., 1992–1996, 1997–2001) to estimate net age, period, and cohort effects of bladder cancer incidence and mortality. In this model, the groups under 15 years old and groups above 80 years old were excluded. The APC model can be expressed as:

$$Y_j = \mu + \alpha \text{age}_j + \beta \text{period}_j + \gamma \text{cohort}_j + \varepsilon_i$$

where Y_j denoted the response variable—the effect on bladder cancer incidence/mortality for group j , α , β and γ denoted the coefficient of age, period and cohort of APC model, respectively, and μ denoted the intercept of the model. ε_i denoted the residual of the APC model.

When it refers to the estimation of cancer rates, the model can be written as a log-linear Poisson model:

$$\ln[E(M_{ij})] = \ln(D_{ij}/P_{ij}) = \mu + \alpha_i + \beta_j + \gamma_k + \varepsilon_{ij}$$

Where $E(M_{ij})$ denotes the expectation of death rate for the i th age group for $i = 1, \dots, a$ age group at the j th time period for $j = 1, \dots, p$ time period born in the k th cohort for $k = 1, \dots, a + p - 1$ birth cohort of observed data; M_{ij}/D_{ij} and P_{ij} denote the observed death rate, death number and size of population of that group, respectively; μ denotes the intercept or adjusted mean death rate; α_i denotes the i th throw age effect or the coefficient for the i th age group; β_j denotes the j th column period effect or the coefficient for the j th time period; γ_k denotes the k th diagonal cohort effect or the coefficient for the k th cohort; ε_{ij} denotes the random error with expectation $E(\varepsilon_{ij}) = 0$.

The APC-IE method presented estimated coefficients for the age, period and cohort effects (see Appendix Tables A.1, A.2), and then these coefficients were calculated to their exponential value ($\exp(\text{coef.}) = e^{\text{coef.}}$) that denoted the incidence and mortality relative risk (RR) of a particular age, period, or birth cohort relative to each average level [27] (see Appendix Table A.3). For example, for the period effect in men, the RR of bladder cancer incidence in 2017 was $\exp(\beta_{2017} - \beta_{\text{mean}}) = \exp(\beta_{2017})$, i.e., the risk during this period was 2.04 times greater than the risk for all periods combined; for the period effect of males, the risk of bladder cancer incidence in 2017 was 2.04 ($\exp(\beta_{2017} - \beta_{\text{mean}}) - (\beta_{1992} - \beta_{\text{mean}}) = \exp(\beta_{2017} - \beta_{1992}) \approx 2.04$) times the risk in 1992. Thus from 1992 to 2017, the bladder cancer incidence risk increased by 1.04-fold. APC model was performed through the Stata 12.0 software (StataCorp, College Station, TX, USA). Deviance, Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC) were used to estimate the degree of model fitting.

3. Results

3.1. Descriptive analysis of incidence and mortality rates

Trends of the crude incidence rate (CIR), age-standardized incidence rate (ASIR), crude mortality rate (CMR) and age-standardized mortality rate (ASMR) at all ages for bladder cancer from 1990 to 2017 are shown in Fig. 1. The ASIR in men significantly increased from 2007 to 2017 while no material changes were observed during 1990–2007. The ASIR in women decreased through 1990 to 2017. The ASMR experienced a decrease in both men and women over the past decades.

3.2. Joinpoint regression analysis

Table 1 shows the average annual percent changes of bladder cancer incidence and mortality rates from 1990 to 2016. ASIR significantly decreased in women (AAPC = -1.25%; 95% CI = -1.6, -0.9) but increased in men (AAPC = 0.72%; 95% CI = 0.5, 0.9). ASMR decreased in both men (AAPC = -1.09%; 95% CI = -1.2, -0.9) and women (AAPC = -2.48%; 95% CI = -2.8, -2.2). For age-specific rates, mortality almost decreased in all age groups in both men and women; incidence almost decreased in women, however, incidence significantly increased in men in older age groups (45–49, 50–54, 55–59, 60–64, 65–69, 70–74, 75–79 and 80–84 age group).

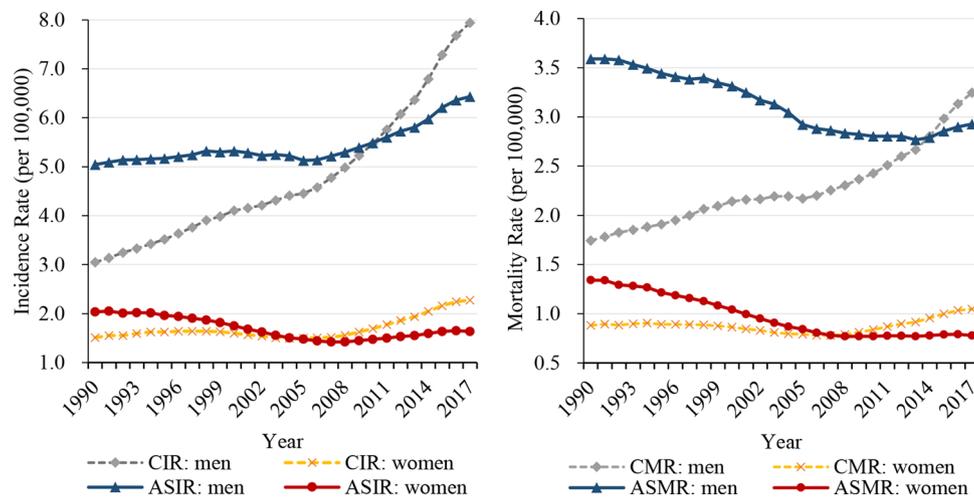


Fig. 1. Trends of the crude rates and age-standardized rates for bladder cancer in men and women from 1990 to 2017, at all ages. CIR, crude incidence rate; ASIR, age-standardized incidence rate; CMR, crude mortality rate; ASMR, age-standardized mortality rate.

3.3. APC analysis with IE method

Appendix Table A3 showed bladder cancer incidence and mortality relative risks due to age, period, and cohort effects, and Fig. 1 was also drafted to reflect the age, period, and cohort effect.

3.3.1. Age effect

After controlling for period and cohort effects, the age effect on bladder cancer showed that RR of incidence slightly increased with advancing age in both men and women, and mortality showed a substantially increasing trend (see Fig. 2a), which indicated that incidence and mortality of bladder cancer increased with advancing age. From age group 20–24 to 80–84, the RR of incidence increased by 53.81 and 30.56 times in men and women, respectively, and that of mortality increased by 229.51 and 124.19 times in men and women, respectively. These four values were computed by their own coefficients.

3.3.2. Period effect

The period effect on incidence and mortality presented different trends between men and women (see Fig. 2b). Both incidence and mortality in men significantly increased with advancing time period, and the RR of incidence in men is increasing at an alarming rate; while

for women, the period effect showed V-shape polylines for incidence and mortality, both of which decreased from 1992 to 2007 and subsequently increased from 2007 to 2017. From 1992 to 2017, the risk of incidence and mortality increased by 2.04, 1.11, 1.42, and 0.79 times in men and women, respectively.

3.3.3. Cohort effect

The cohort effect presented that incidence and mortality substantially decreased from earlier to later birth cohort (see Fig. 2c). From 1912 to 1916 to 1997–2001 birth cohort, the risk of incidence significantly decreased by 90.92% and 82.90% in men and women, respectively; and the risk of mortality decreased by 95.55% and 91.13% in men and women, respectively.

4. Discussion

This study observed that the ASIR of bladder cancer significantly increased from 2007 to 2017 in men while no material changes were observed during 1990–2007. The ASIR in women decreased and the ASMR also experienced a decrease in both men and women through 1990 to 2017. These findings aren't consistent with previous study which reported bladder cancer incidence is significantly decreasing in

Table 1

The average annual percent changes (AAPC) in bladder cancer incidence and mortality.1990–2017.

Age-group (year)	Incidence (95% CI)		Mortality (95% CI)		
	Men	Women	Men	Women	Women
ASR	0.72 [*] (0.5, 0.9)	-1.25 [*] (-1.6, -0.9)	-1.09 [*] (-1.2, -0.9)		-2.48 [*] (-2.8, -2.2)
	1990-2006: 0.14 (-0.0, 0.3)				
	2007-2017: 2.23 (2.0, 2.4)				
20 - 24	-2.85 [*] (-3.3, -2.4)	-3.96 [*] (-4.7, -3.2)	-5.77 [*] (-6.4, -5.2)		-6.87 [*] (-7.7, -6.0)
25 - 29	-2.45 [*] (-3.3, -1.6)	-4.76 [*] (-5.8, -3.7)	-5.48 [*] (-6.4, -4.6)		-7.62 [*] (-8.8, -6.5)
30 - 34	-2.02 [*] (-2.9, -1.2)	-4.56 [*] (-5.6, -3.6)	-4.99 [*] (-5.9, -4.1)		-7.35 [*] (-8.4, -6.3)
35 - 39	-1.25 [*] (-1.7, -0.8)	-3.43 [*] (-4.0, -2.9)	-4.12 [*] (-4.5, -3.7)		-6.19 [*] (-6.7, -5.6)
40 - 44	-1.14 [*] (-1.5, -0.8)	-3.29 [*] (-3.8, -2.8)	-3.75 [*] (-4.2, -3.3)		-5.79 [*] (-6.3, -5.3)
45 - 49	0.38 (-0.1, 0.8)	-2.55 [*] (-3.2, -1.9)	-2.25 [*] (-2.7, -1.8)		-5.04 [*] (-5.7, -4.4)
50 - 54	1.28 [*] (1.0, 1.6)	-1.16 [*] (-1.5, -0.9)	-1.32 [*] (-1.6, -1.1)		-3.62 [*] (-3.9, -3.3)
55 - 59	1.00 [*] (0.9, 1.1)	-0.80 [*] (-0.9, -0.7)	-1.35 [*] (-1.4, -1.3)		-3.05 [*] (-3.2, -2.9)
60 - 64	1.79 [*] (1.4, 2.1)	-0.74 [*] (-1.2, -0.3)	-0.52 [*] (-0.8, -0.2)		-2.89 [*] (-3.3, -2.5)
65 - 69	1.88 [*] (1.5, 2.2)	-0.32 (-0.8, 0.2)	-0.30 (-0.6, 0.0)		-2.35 [*] (-2.8, -1.9)
70 - 74	0.68 [*] (0.5, 0.9)	-1.05 [*] (-1.3, -0.8)	-1.30 [*] (-1.5, -1.1)		-2.70 [*] (-2.7, -3.0)
75 - 79	0.78 [*] (0.7, 0.9)	-0.53 [*] (-0.8, -0.3)	-1.00 [*] (-1.1, -0.9)		-1.94 [*] (-2.2, -1.7)
80 - 84	0.40 [*] (0.3, 0.5)	-0.74 [*] (-1.0, -0.5)	-0.96 [*] (-1.1, -0.9)		-1.65 [*] (-1.9, -1.4)

CI, Confidence interval; ASR, age-standardized rate. Incidence and mortality for bladder cancer was age-standardized by the GBD 2017 global age-standard population. *Significantly different from 0 at alpha = 0.05 (p < 0.05).

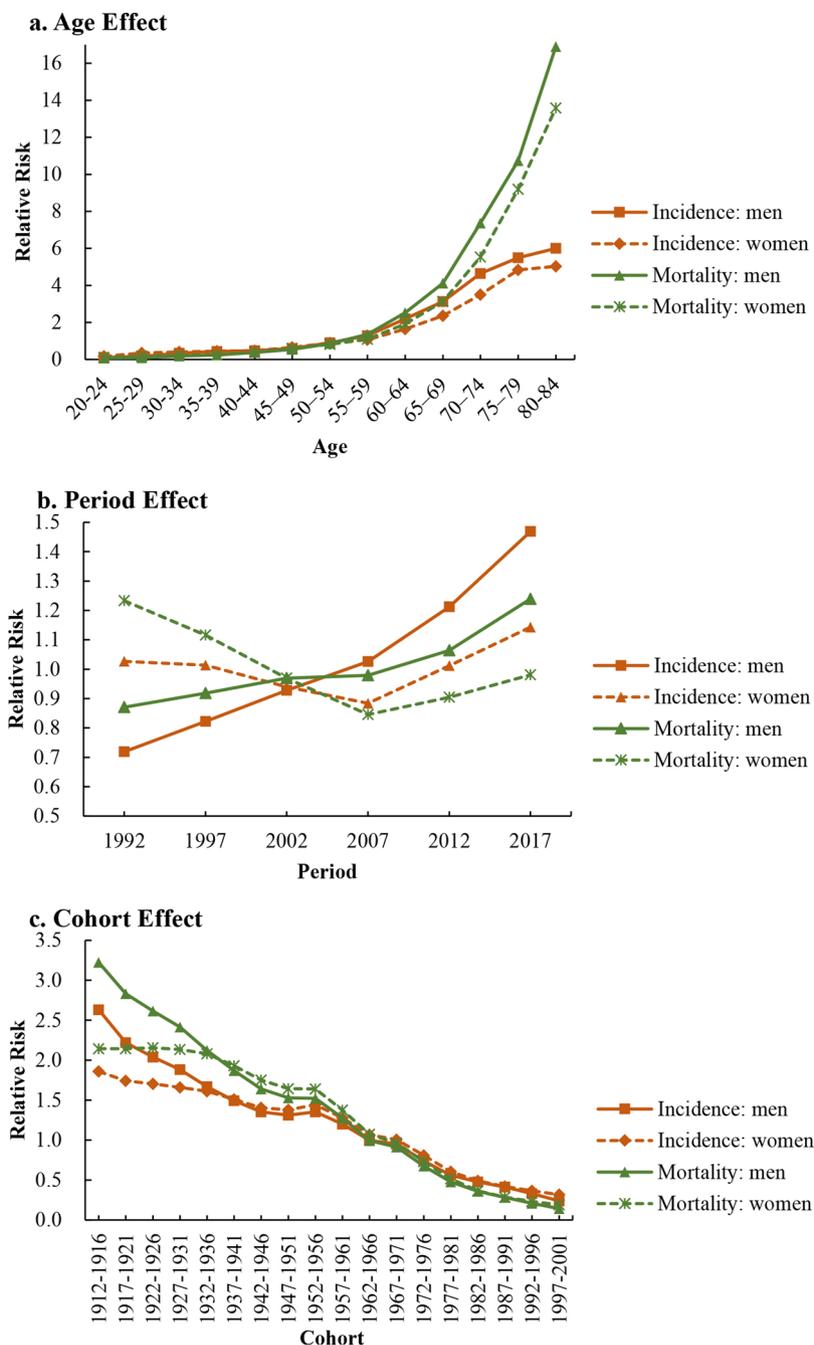


Fig. 2. Bladder cancer incidence and mortality relative risks due to (a) age; (b) period; and (c) cohort effects.

men and women from 1993 to 2007 and that rates are projected to decrease in China through 2030 according to GLOBOCAN 2012 [16]. These differences in trends in the present and previous paper was attributable to the different source and completeness of cancer incidence and mortality data for China. The incidence data of China reported by GLOBOCAN 2012 were extracted from the Cancer Incidence in Five Continents series Volumes I-X20; for the mortality data, they extracted from Hospital Authority. The original data estimated by GBD 2017 for bladder cancer in China was mainly from the Cause of Death Reporting System of the Chinese Center for Disease Control and Prevention (CDC), Disease Surveillance Points (DSPs) and the Maternal and Child Surveillance System, which are considered to be nationally representative as it is based on a national scale, and data from GBD study are used worldwide. The differences in the present and previous paper may be related to the rate in men increases observed after 2007 in our study,

because the previous study of bladder cancer rates worldwide, using data from GLOBOCAN 2012, only presented a shorter period 1993–2007.

This study presented that the trends in bladder cancer incidence and mortality by estimated their percent changes of rates and the net age, period and cohort effect over the past decades. Joinpoint regression analysis presented mortality rates decreased in all age groups in both men and women, while incidence rates increased in men mainly in older age groups (> 45 years old). Through APC model with IE method, the age effect showed both incidence and mortality increased with advancing age; period effect presented incidence and mortality in men significantly increased with advancing period, while women showed increasing trends through 2007 to 2017; cohort effect showed incidence and mortality decreased from earlier to more recent birth cohort. Therefore, the trends of three different temporal effects on incidence

and mortality of bladder cancer were discussed preliminarily in the following section.

Age effect on bladder cancer explained incidence and mortality increased with advancing age, the burden of bladder cancer was mainly increased by China's aging transition [28]. Previous studies have demonstrated that older people have a lower 5-year overall survival rate [29], and Chinese aging rose rapidly from 1980 to 2010 [30]. Additionally, older adults usually experience worse prognosis and are often under-treated [31,32]. All these factors may cause the increasing age trends on incidence and mortality of bladder cancer in China, as well as Philippines and Iceland where increasing age trends in mortality rate were observed [16]. Aging or treatment management may still be urgent measures to be improved for controlling bladder cancer mortality.

Cohort effect reflected influencing factors that arise earlier in life course and accumulate with life course [33]. Cohort effect on bladder cancer incidence and mortality showed continuously decreasing trends from 1912 to 1916 to 1997–2001 birth cohort in both men and women. The possible reason was that more recent birth cohorts, receiving better education, had a stronger awareness of health and disease prevention than earlier birth cohorts [34]. National survey reported, for boys and girls among adolescents, the prevalence rate of experimenting smoking was 47.8% in 1998 [35], and the prevalence of smoking was 38.8% in 2002 [36]. The adolescent smokers have decreased in both areas and gender, which was also possibly related to the decreasing cohort trends. All of the changes may explain the decreasing cohort trends. Thus, improvement remains should be conducted for earlier birth cohort to face higher risk.

Period effect is usually influenced by a complex set of historical events and environmental factors. Increasing economy was positively correlated with bladder cancer [16], and there was a rapid economy transformation and urbanization from 1989 to 2004 [37]. Thus, economy development was one of probable influential factors for those increasing period trends in bladder cancer incidence and mortality. The main risk factors for bladder cancer are exposure to occupational carcinogen and tobacco smoking. Previous study did not evaluate the reasons of rate increases observed in the present study after 2007 in China [1,2,16]. Some studies reported occupational exposure to benzidine, trichloroethylene, perchloroethylene, aromatic hydrocarbon solvents, benzene, toluene, diesel and gasoline engine emissions have a higher risk for bladder cancer [6–8,38,39]. Workers with aromatic amine exposure have the highest incidence of bladder cancer, while those exposed to polycyclic aromatic hydrocarbons and heavy metals have the greatest mortality [5]. According to the IARC Monograph evaluations for chemicals/exposures, for 30 chemicals or mixtures of chemicals, and nine industrial processes, there was sufficient evidence of carcinogenicity in humans [40], and the type of exposure to the 17 chemicals found carcinogenic to man was occupational for fourteen, and the 4 chemicals including 4-Aminobiphenyl, Auramine, Benzidine and 2-Naphthylamine could lead to bladder cancer [41]. With the rapid industrialization of China [42], the distribution of risk factors between men and women may be expected that exposure to occupational carcinogens would substantially increase in males from 1990 to 2017. According to GBD 2017, the ASMR for cancer attributable to occupational carcinogens shows a obviously increasing trend in men and no material changes in women from 1990 to 2017 in China, while ASMR for cancer attributable to occupational carcinogens decreased in men and remains stable in women in global [4]. The trend of ASMR for cancer attributable to occupational carcinogens from 1990 to 2017 was also plotted in the present study [see Appendix B Fig. B1]. Thus, the increasing period trend of incidence and mortality in men might be explained by the changing proportion of cancer caused by occupational carcinogens in China. Tobacco smoking is also the main risk factor and is closely related to bladder cancer [43,44]. In China, there are four national tobacco surveys among people aged 15 and above during 1984–2010 (Smoking prevalence among Male: 62.0% in 1984, 63.0% in

1996, 57.4% in 2002, 52.9 in 2010; Female: 7.0% in 1984, 3.8% in 1996, 2.6% in 2002, 2.4% in 2010) [24]. The survey showed tobacco smoking rates gradually decreased in both males and females over the last two decades, while the period trend in our study showed increasing trends in men through 1992 to 2017 and a substantial increase in women after 2007, thus the change of smoking prevalence wasn't probably the reasons. The potential reason was related to alcohol consumption in China [45]. As reported, global alcohol consumption continuously increased from 2006 to 2010, mainly in China and India [46]. In China, the prevalence of alcohol drinking was 2.58% for women, and the prevalence of that in 2002 was 4.5% for women [46]; while the prevalence of drinking in women was 13.9% in urban area and 13.3% in rural area in 2010–2012, which was much higher than in 1991 and 2002 [47]. But the association between alcohol intake and bladder cancer risk is still controversial. Application of Chinese guidelines may have improved treatment for bladder cancer patients over the last decades [15,48], and bladder cancer is usually regarded as an index cancer for changing occupational exposures. Additionally, the GBD study showed cancer deaths and disability adjusted life years (DALYs) attributable to occupational risks began to increase around 2007 which indicated the occupation exposures increased after 2007 [4], and the cases of occupational diseases increased substantially in China since 2007 [49], thus exposures to occupational carcinogens may be one of the main urgent measures to be reduced for bladder cancer burden.

In summary, the overall incidence rates of bladder cancer in increasing in men and no material changes are observed in women through 1990 to 2017. Mortality rates slightly decreased in both men and women. Despite mortality rates of bladder cancer significantly declined in all age groups, the age and period effects on both incidence and mortality showed remarkable increasing trends in men over the last three decades, which may be associated with the increased exposure to occupational carcinogens. Thus, it might need to reduce the exposure to the occupational carcinogens, especially in men.

5. Conclusions

During the period 1990–2017, the overall incidence of bladder cancer is increasing in men, but not in women. The incidence and mortality in men substantially increase with age and period in China. The period effect may indicate the increased exposure to occupational carcinogens. Although cohort effect showed a decreasing trend, the period effect may be the key factor affecting trends of bladder cancer incidence and mortality, mainly reflecting the immediate effects of effective prevention and treatments. Measures are need for men and earlier birth cohort at high risk.

6. Limitations

These findings provided epidemiology evidences for understand on reasons of increasing bladder cancer burden. However, this study has some limitations. First, APC analysis considers a community as the observed and analysed unit, which might result in ecological fallacies. Moreover, we only tried to bring forth scientific hypotheses regarding the causality of these trends in bladder cancer incidence and mortality, based on the available data and existing literatures. Second, despite many methods in GBD study estimations were used to reduce bias, including misclassification corrections, incompleteness and redistribution of garbage codes, there might be difficult to thoroughly avoid inaccuracy of data. Therefore, our results in the present study on epidemiology of bladder cancer should be treated carefully.

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Conflict of interest statement

None.

Authorship contribution statement

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All authors were involved in the conception and design of this study. Z.J.Z contributed to acquisition of data. YB contributed to interpretation of data for the work. ZJZ and XL analysed the data and drafted the manuscript. JJ, YL, YW, YS, JT, and TC revised it critically for important intellectual content. All authors read and approved the final manuscript.

Appendix A

Table A1

Bladder cancer incidence and mortality rates estimated coefficients for the age, period and cohort effects.

Factor	Incidence (Coef.)		Mortality (Coef.)	
	Men	Women	Men	Women
Age				
20-24	-2.194034	-1.804043	-2.608553	-2.213329
25-29	-1.734121	-1.047789	-2.383532	-1.667753
30-34	-1.069083	-0.9146239	-1.69882	-1.512219
35-39	-0.8297134	-0.8147707	-1.427707	-1.388809
40-44	-0.7584046	-0.7326098	-0.9664543	-0.9282748
45-49	-0.5113622	-0.4333141	-0.6057798	-0.5116368
50-54	-0.1082164	-0.1170573	-0.155185	-0.1939964
55-59	0.2488187	0.059796	0.307046	0.0898442
60-64	0.7832528	0.4995369	0.9254858	0.6498744
65-69	1.141192	0.8603596	1.415922	1.138844
70-74	1.53506	1.2522	1.996021	1.710212
75-79	1.705113	1.576563	2.374157	2.218786
80-84	1.791498	1.615752	2.827399	2.608458
Period				
1992	-0.3301455	0.0259016	-0.1386619	0.2096376
1997	-0.1962634	0.0136872	-0.0857127	0.1093075
2002	-0.0753681	-0.0618306	-0.0307863	-0.0308202
2007	0.0253461	-0.1233472	-0.0212886	-0.1677926
2012	0.1921959	0.0118278	0.0618623	-0.1005565
2017	0.3842349	0.1337611	0.2145872	-0.0197758
Cohort				
1912-1916	0.9677215	0.6202624	1.170715	0.7621027
1917-1921	0.7983068	0.5561224	1.041584	0.7628922
1922-1926	0.7117674	0.5339067	0.9609993	0.7680374
1927-1931	0.6326713	0.506836	0.8814239	0.7589486
1932-1936	0.5117669	0.4777625	0.7516986	0.7320443
1937-1941	0.4008041	0.4130758	0.6258681	0.657709
1942-1946	0.3017833	0.3389834	0.4951027	0.5600852
1947-1951	0.2715485	0.3210622	0.4245673	0.4972627
1952-1956	0.3023579	0.3663876	0.4212967	0.4945513
1957-1961	0.1830001	0.243815	0.2457339	0.3191321
1962-1966	-0.001783	0.0649421	-0.0074746	0.0715185
1967-1971	-0.0493289	0.0062872	-0.0911264	-0.0351159
1972-1976	-0.300999	-0.2114951	-0.3934965	-0.3124066
1977-1981	-0.5781921	-0.5035697	-0.7398427	-0.6611081
1982-1986	-0.7374248	-0.7159294	-1.021721	-1.002715
1987-1991	-0.8798751	-0.8668616	-1.258764	-1.251291
1992-1996	-1.102937	-1.005581	-1.564547	-1.460965
1997-2001	-1.431188	-1.146007	-1.942019	-1.660683

Coef.: Coefficient.

Table A2
Bladder cancer incidence and mortality rates estimated coefficients of 95% confidence interval (CI) for the age, period and cohort effects.

Factor	Incidence (95% CI)				Mortality (95% CI)			
	Men		Women		Men		Women	
	Lower	Upper	Lower	Upper	Lower	Upper	Lower	Upper
Age								
20-24	-3.724208	-0.6638594	-3.721026	0.1129403	-6.612753	1.395647	-6.964377	2.537718
25-29	-2.794175	-0.6740674	-2.232665	0.1370861	-5.431221	0.6641577	-4.842739	1.507234
30-34	-1.840278	-0.2978877	-1.993712	0.1644642	-3.845484	0.4478445	-4.316268	1.291829
35-39	-1.494275	-0.1651519	-1.788841	0.1593001	-3.209651	0.3542366	-3.828882	1.051265
40-44	-1.358507	-0.158302	-1.608441	0.1432216	-2.353823	0.4209145	-2.796249	0.9396998
45-49	-1.021153	-0.0015714	-1.166756	0.3001281	-1.72771	0.5161507	-1.992546	0.9692727
50-54	-0.5233541	0.3069214	-0.7356373	0.5015227	-1.043978	0.7336078	-1.413185	1.025192
55-59	-0.0927513	0.5903887	-0.4844772	0.6040693	-0.3940831	1.008175	-0.9211514	1.10084
60-64	0.5161229	1.050383	0.0617006	0.9373731	0.3649747	1.485997	-0.1592224	1.458971
65-69	0.9103195	1.372065	0.4805277	1.240192	0.8797211	1.952123	0.3774318	1.900255
70-74	1.311011	1.759108	0.8924563	1.611944	1.386079	2.605964	0.8700555	2.550368
75-79	1.452102	1.958124	1.191802	1.961324	1.620291	3.128022	1.204111	3.233461
80-84	1.485541	2.097455	1.157813	2.073692	1.895163	3.759635	1.365021	3.851894
Period								
1992	-0.5741253	-0.0861656	-0.3256464	0.3774497	-0.7225024	0.4451786	-0.5602411	0.9795163
1997	-0.3730273	-0.0194995	-0.263471	0.2908455	-0.4570213	0.2855959	-0.4044305	0.6230456
2002	-0.2139298	0.0631937	-0.3114957	0.1878346	-0.2351791	0.1736065	-0.3746204	0.31298
2007	-0.1148379	0.1655301	-0.3848752	0.1381808	-0.2342559	0.1916787	-0.534674	0.1990888
2012	0.0202264	0.3641654	-0.2749231	0.2985787	-0.3141584	0.4378831	-0.6364979	0.4353849
2017	0.1631157	0.6053541	-0.2052785	0.4728007	-0.3581804	0.7873548	-0.7895929	0.7500413
Cohort								
1912-1916	0.4755041	1.459939	-0.1021419	1.342667	-0.0754227	2.416853	-0.8379848	2.36219
1917-1921	0.399591	1.197023	-0.0118778	1.124123	-0.0330097	2.116179	-0.6040643	2.129849
1922-1926	0.3732637	1.050271	0.0451619	1.022652	0.019787	1.902212	-0.4332412	1.969316
1927-1931	0.3310542	0.9342884	0.0593949	0.9542771	0.0294752	1.733373	-0.3403047	1.858202
1932-1936	0.2260233	0.7975104	0.047911	0.9076141	-0.0639058	1.567303	-0.3322757	1.796364
1937-1941	0.1137497	0.6878585	-0.019348	0.8454997	-0.2078269	1.459563	-0.4386635	1.754082
1942-1946	-0.0265297	0.6300962	-0.16151	0.8394769	-0.4298527	1.420058	-0.676951	1.797121
1947-1951	-0.112381	0.655478	-0.2692329	0.9113572	-0.635633	1.484768	-0.9394334	1.933959
1952-1956	-0.1466743	0.75139	-0.3174606	1.050236	-0.8056821	1.648276	-1.176027	2.165129
1957-1961	-0.3434347	0.7094349	-0.5549835	1.042613	-1.183244	1.674712	-1.643789	2.282053
1962-1966	-0.6192303	0.6156642	-0.8579165	0.9878007	-1.680573	1.665624	-2.235519	2.378556
1967-1971	-0.7391018	0.6404441	-0.9871561	0.9997305	-1.992316	1.810063	-2.604324	2.534092
1972-1976	-1.097221	0.4952231	-1.34259	0.9196	-2.601214	1.814221	-3.271554	2.646741
1977-1981	-1.535741	0.3793566	-1.913684	0.9065445	-3.501582	2.021896	-4.503803	3.181587
1982-1986	-1.864963	0.3901132	-2.433162	1.001303	-4.605862	2.56242	-6.171935	4.166505
1987-1991	-2.304496	0.5447455	-2.973544	1.239821	-6.019264	3.501736	-7.944456	5.441874
1992-1996	-3.264785	1.058911	-3.79572	1.784558	-8.973442	5.844349	-10.58885	7.666917
1997-2001	-5.843645	2.981269	-6.972168	4.680155	-16.42614	12.5421	-19.97824	16.65688

Table A3
Bladder cancer incidence and mortality relative risks (RR) due to age, period, and cohort effects.

Factor	Incidence (RR 95% CI)		Mortality (RR 95% CI)	
	Men	Women	Men	Women
Age				
20-24	0.11 (0.02, 0.51)	0.16 (0.02, 1.12)	0.07 (0.00, 4.04)	0.11 (0.00, 12.65)
25-29	0.18 (0.06, 0.51)	0.35 (0.11, 1.15)	0.09 (0.00, 1.94)	0.19 (0.01, 4.51)
30-34	0.34 (0.16, 0.74)	0.40 (0.14, 1.18)	0.18 (0.02, 1.56)	0.22 (0.01, 3.64)
35-39	0.44 (0.22, 0.85)	0.44 (0.17, 1.17)	0.24 (0.04, 1.43)	0.25 (0.02, 2.86)
40-44	0.47 (0.26, 0.85)	0.48 (0.20, 1.15)	0.38 (0.10, 1.52)	0.40 (0.06, 2.56)
45-49	0.60 (0.36, 1.00)	0.65 (0.31, 1.35)	0.55 (0.18, 1.68)	0.60 (0.14, 2.64)
50-54	0.90 (0.59, 1.36)	0.89 (0.48, 1.65)	0.86 (0.35, 2.08)	0.82 (0.24, 2.79)
55-59	1.28 (0.91, 1.80)	1.06 (0.62, 1.83)	1.36 (0.67, 2.74)	1.09 (0.40, 3.01)
60-64	2.19 (1.68, 2.86)	1.65 (1.06, 2.55)	2.52 (1.44, 4.42)	1.92 (0.85, 4.30)
65-69	3.13 (2.49, 3.94)	2.36 (1.62, 3.46)	4.12 (2.41, 7.04)	3.12 ((1.46, 6.69)
70-74	4.64 (3.71, 5.81)	3.50 (2.44, 5.01)	7.36 (4.00, 13.54)	5.53 (2.39, 12.81)
75-79	5.50 (4.27, 7.09)	4.84 (3.29, 7.11)	10.74 (5.05, 22.83)	9.20 (3.33, 25.37)
80-84	6.00 (4.42, 8.15)	5.03 (3.18, 7.95)	16.90 (6.65, 42.93)	13.58 (3.92, 47.08)
Period				
1992	0.72 (0.56, 0.92)	1.03 (0.72, 1.46)	0.87 (0.49, 1.56)	1.23 (0.57, 2.66)
1997	0.82 (0.69, 0.98)	1.01 (0.77, 1.34)	0.92 (0.63, 1.33)	1.12 (0.67, 1.86)
2002	0.93 (0.81, 1.07)	0.94 (0.73, 1.21)	0.97 (0.79, 1.19)	0.97 (0.69, 1.37)
2007	1.03 (0.89, 1.18)	0.88 (0.68, 1.15)	0.98 (0.79, 1.21)	0.85 (0.59, 1.22)
2012	1.21 (1.02, 1.44)	1.01 (0.76, 1.35)	1.06 (0.73, 1.55)	0.90 (0.53, 1.55)
2017	1.47 (1.18, 1.83)	1.14 (0.81, 1.60)	1.24 (0.70, 2.20)	0.98 (0.45, 2.12)

(continued on next page)

Table A3 (continued)

Factor	Incidence (RR 95% CI)		Mortality (RR 95% CI)	
	Men	Women	Men	Women
Cohort				
1912-1916	2.63 (1.61, 4.31)	1.86 (0.90, 3.83)	3.22 (0.93, 11.21)	2.14 (0.43, 10.61)
1917-1921	2.22 (1.49, 3.31)	1.74 (0.99, 3.08)	2.83 (0.97, 8.30)	2.14 (0.55, 8.41)
1922-1926	2.04 (1.45, 2.86)	1.71 (1.05, 2.78)	2.61 (1.02, 6.70)	2.16 (0.65, 7.17)
1927-1931	1.88 (1.39, 2.55)	1.66 (1.06, 2.60)	2.41 (1.03, 5.66)	2.14 (0.71, 6.41)
1932-1936	1.67 (1.25, 2.22)	1.61 (1.05, 2.48)	2.12 (0.94, 4.79)	2.08 (0.72, 6.03)
1937-1941	1.49 (1.12, 1.99)	1.51 (0.98, 2.33)	1.87 (0.81, 4.30)	1.93 (0.64, 5.78)
1942-1946	1.35 (0.97, 1.88)	1.40 (0.85, 2.32)	1.64 (0.65, 4.14)	1.75 (0.51, 6.03)
1947-1951	1.31 (0.89, 1.93)	1.38 (0.76, 2.49)	1.53 (0.53, 4.41)	1.64 (0.39, 6.92)
1952-1956	1.35 (0.86, 2.12)	1.44 (0.73, 2.86)	1.52 (0.45, 5.20)	1.64 (0.31, 8.72)
1957-1961	1.20 (0.71, 2.03)	1.28 (0.57, 2.84)	1.28 (0.31, 5.34)	1.38 (0.19, 9.80)
1962-1966	1.00 (0.54, 1.85)	1.07 (0.42, 2.69)	0.99 (0.19, 5.29)	1.07 (0.11, 10.79)
1967-1971	0.95 (0.48, 1.90)	1.01 (0.37, 2.72)	0.91 (0.14, 6.11)	0.97 (0.07, 12.60)
1972-1976	0.74 (0.33, 1.64)	0.81 (0.26, 2.51)	0.67 (0.07, 6.14)	0.73 (0.04, 14.11)
1977-1981	0.56 (0.22, 1.46)	0.60 (0.15, 2.48)	0.48 (0.03, 7.55)	0.52 (0.01, 24.08)
1982-1986	0.48 (0.15, 1.48)	0.49 (0.09, 2.72)	0.36 (0.01, 12.97)	0.37 (0.00, 64.49)
1987-1991	0.41 (0.10, 1.72)	0.42 (0.05, 3.45)	0.28 (0.00, 33.17)	0.29 (0.00, 230.87)
1992-1996	0.33 (0.04, 2.88)	0.37 (0.02, 5.96)	0.21 (0.00, 345.28)	0.23 (0.00, 2136.48)
1997-2001	0.24 (0.00, 19.71)	0.32 (0.00, 107.79)	0.14 (0.00, 279,875.46)	0.19 (0.00, 17,139,220.64)
Deviance	1.81	0.51	0.48	0.13
AIC	4.50	3.59	3.52	2.81
BIC	-189.89	-191.19	-191.22	-191.56

RR: Relative risk [RR = exp(coefficients)]; CI: Confidence interval; AIC: Akaike Information Criteria; BIC: Bayesian Information Criteria.

Appendix B

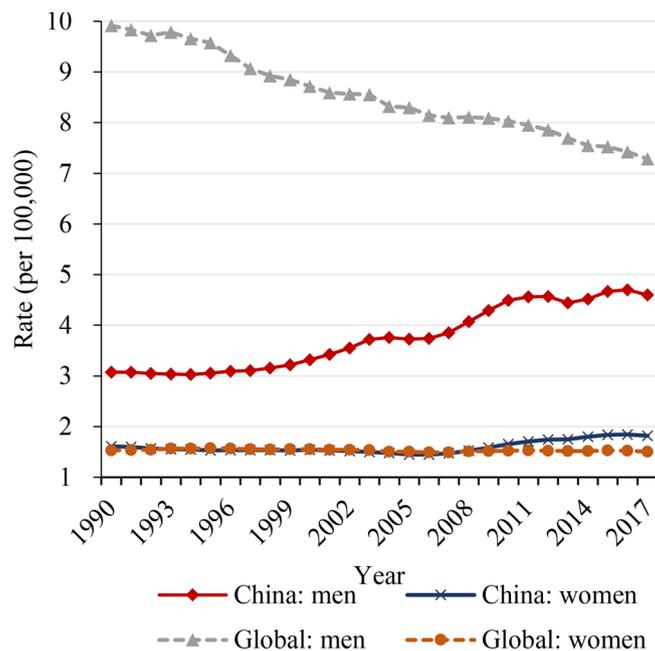


Fig. B1. The trend of ASMR for cancer attributable to occupational carcinogens from 1990 to 2017.

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