Attributable fraction of tobacco smoking on cancer deaths from 2010 to 2019 using mortality case-control study in Tianjin, China

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Research Article

Keywords: Risk factor, Smoking-attributed death, Lifestyle, Asia, China, Mortality Case-control Study

Posted Date: August 17th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-819145/v1>

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Abstract

Background: Smoking is by far the most important cause of cancer that can be modified at the individual level. Asia has a high incidence of cancer incidence and death, while China has the highest incidence in Asia, and accounting for 27% of the world's cancer deaths. The purpose of the current study was to perform an evidence-based assessment of the burden of tobacco smoking-related cancers death in the Tianjin, China.

Methods: A mortality case-control study to assess the risks of all-cause and major causes of cancer death attributable to smoking from 2010 to 2019.

Results: Tobacco smoking was responsible for 23,709 (28.87%) cancer deaths among adult men and 8,648 (13.37%) among adult women in 2010 to 2019 in Tianjin. Lung cancer remains the largest cause of cancer death. In men, 49.06% of lung cancer, 27.55% of upper aerodigestive cancer, 10.11% of liver, 13.56% of kidney and other urinary cancer deaths were attributable to tobacco smoking. In women the proportion of ever-smoking-attributable lung cancer was 31.56%, 10.59% of upper aerodigestive and 10.56% of bladder cancer deaths. By year, smoking-attributable cancer deaths in men increased from 1817 in 2010 to 2695 in 2019; for women, the number remained stable at just over 800 per year.

Conclusions: Approximately one in three cancer deaths in men and one in six cancer deaths in women would be potentially preventable through appropriate control of tobacco smoking in Tianjin. Effective control programs against tobacco smoking should be further implemented.

Background

Cancer has become the largest public health problem in the world [1], and the prevention and treatment of malignant tumors in China is also very serious. Asia has a high incidence of cancer incidence and death, while China has the highest incidence in Asia. The results of the survey of China's cancer death from 2004 to 2005 showed that the mortality rate of cancer in China increased by 83.1% compared with that in the mid 1970s, and 22.5% higher than that in the early 1990s. According to the statistics of the world cancer report [3], in 2012, China accounted for 20% of the world's new malignant tumor cases, 22% of the world's cancer cases and 25% of the world's deaths.

Smoking is by far the most important cause of cancer that can be modified at the individual level. More than one in four male cancer deaths (29%) and one in five female cancer deaths (20%) could be attributed to smoking in 2008 [4].

Tianjin is one of the largest and most developed cities in China. We have a more sophisticated and reliable system of death registration than most cities in China and other low- and middle-income countries. The Tianjin All Causes of Death Registration System (CDRS) was established in 1984, which now covers the entire population of approximately 10 million (as in 2013) with 40% urban and 60% rural residents [5]. The leading causes of death were cardiovascular disease, cancer, and respiratory disease in Tianjin, China. Through this system, all causes of death should be reported, and all death certificates entered into the database must be completed by physicians in hospitals or community health service centers. Each death certificate has approximately 50 data fields, including age, sex, education, and cause of death, as well as the home address for classifying area of residence as urban or rural. Starting at the end of 2009, Tianjin Centers for Disease Control and Prevention (TJCDC) has been collecting information routinely on smoking (including 3 questions) of the deceased in the death certificate. This is the first and only death registration system in China doing so. Tianjin, being the second to include smoking in death registration in the world after South Africa, collects more information on smoking than South Africa. Then Tianjin developed the mortality case-control (MCC) studies use the information collected from CDRS since 2010 [6].

The purpose of the current study was to perform an evidence-based assessment of the burden of tobacco smoking-related cancers death in the Tianjin, China.

Methods

Definition of case and control

We included deaths ≥ 35 age years old in 2010 through 2019. We excluded deaths at 34 years or younger because smoking was expected to cause very few deaths at a young age caused by smoking could be less reliable. We followed the methods of Sitas et al [7], and the definition of cases and controls were according to the American Cancer Society's A Report of the Surgeon General [8]. Cases were deaths from 9 groups of cancers that are causally or strongly associated with smoking, including lung, upper aerodigestive, stomach, liver, pancreas, bowel, kidney and other urinary, Bladder, myeloid leukemia. Controls were deaths from all other specified diseases that were not confirmed to be caused by or were not strongly associated with smoking. Ill-defined and unknown causes were also excluded. The cases were current and former smokers and controls were never smokers.

Tobacco smoking status was classified as "never", "former", and "current" in this study. We used the term "ever-smoking" to mean "former" or "current" smoking.

Relative risk of tobacco smoking and estimation of population attributed fraction (PAF)

Unmatched multiple logistic regression was used to calculate risk ratios (RR) or mortality rate ratio of all-cause and cause-specific death in ever smokers versus never smokers adjusted by 5-year age group, education (none, primary, higher, do not know), marital status (never, widowed, divorced, married or living as married, do not know), and year of death (single year from 2010 through 2019).

If D is the total number of deaths (from a particular disease) in smokers, then the number of deaths attributed to smoking, D_s , can be calculated separately for men and women as $D_s = D (1 - 1 \div RR)$, where RR is risk ratio (to estimate relative risk), where D_s is positive, D_s divided by the total number deaths in the whole population gives the PAF of smoking [9]. Where D_s are negative, the fraction could be due to the "protective" effect of smoking. Attributable numbers for groups of diseases (and for overall mortality) were derived from the sum of the number of each specific disease within the group.

Men and women were analyzed separately. Statistical tests and 2-sided 95% confidence intervals (CIs) were based on changes in log-likelihood. When the 95% CI for the relative risk in men did not overlap with that in women, the sex difference was significant at P less than .05 levels. Otherwise, the interaction of sex and smoking was tested by adding an interaction term in the model. All analyses were performed with SPSS 23.0 (SPSS Inc).

Sensitivity analysis for the estimation of PAF of tobacco smoking

To account for the uncertainty in PAF estimation arising from the estimation of RRs for each cancer site, a sensitivity analysis was performed under alternative scenarios using the lower and upper limits of the 95% CIs of RR estimates.

Results

Relative risk of tobacco smoking

Among all cancer sites reviewed in this study, the total RR for ever smoking was respectively 1.861 and 2.380 in men and women (Table 1). Top three RR among ever smokers' men was lung cancer (3.061, 2.956-3.170), upper aerodigestive cancer (1.798, 1.698-1.904), kidney and other urinary cancer (1.333, 1.210-1.468) respectively. And among ever smokers' women were lung cancer (3.870, 3.703-4.045), upper aerodigestive cancer (1.708, 1.536-1.899) and bladder cancer (1.679, 1.416-1.991). The RRs for ever smokers ranged from 1.078 to 3.870 for cancer mortality, except for a few cases where the RR was estimated to be less than one with insignificant p-values (Table 1).

Table 1 Mortality Rate Ratio at Age ≥35 Years, Selected Cancer Causes, Ever Smokers Versus Never Smokers, Tianjin, China, 2010–2019

Smoking-attributable cancer deaths by age and cancer type

Tobacco smoking was responsible for 23,709 (28.87%) cancer deaths among adult men and 8,648 (17.37%) cancer deaths among adult women among 2010 to 2019 in Tianjin, China (Table 2). As expected, lung cancer comprised the greatest proportion of all smoking-related cancer deaths both in men and women. In men, nearly 50% of lung cancer deaths, 27.55% of upper aerodigestive cancer deaths, 10.11% of liver, 8.08% of stomach, 8.36% of pancreas, 13.56% of kidney and 12.35% of bladder cancer deaths were attributable to tobacco smoking. In women, however, ever-smoking-attributable lung cancer deaths were 31.56% of the total lung cancer deaths. 10.59% of upper aerodigestive cancer deaths, 10.11% of liver, 8.08% of stomach, 10.56% of bladder cancer deaths were attributable to tobacco smoking. In women, the ever-smoking attributable death in 2010, 2014 and 2019 was respectively 20.62%, 16.72% and 16.30%, taking on a decreasing change. But could not found a same trend in men, the ever-smoking attributable death was 27.31%, 30.59% and 29.22% in the above three years (Table 2).

Table 2 Number of smoking-attributable cancer deaths and attributable fraction by site, Tianjin, China, 2010–2019

The smoking rate of men in the study remained stable for 10 years (average: 62.39%), while women showed a downward trend (from 35.33% to 27.58%). The annual number of smoking-attributable cancer deaths among women has remained relatively constant at around 800 each year since the 2010s (Figure 1), despite the population growth and ageing during this time. The number of smoking-attributable cancer deaths in 55-74 year old women decreased by 31.81% and in ≥75 year old increase by 20.77%, between 2010 and 2019 (Table 3). The annual number of smoking-attributable cancer deaths among men has gradual growth from 1822 to 2684 (increase by 47.3%) between 2010 and 2019 (Figure 1 and Table 3). The number of smoking-attributable cancer deaths in 35-54, 55-74, ≥75 years old men increased by 27.40%, 82.31% and 11.56% respectively between 2010 and 2019 (Table 3). The greatest increase in the annual number of smoking attributable cancer deaths was in men 55-74 years of age with a more the one fold increase between 2010 (n=978) and 2019 (n=1786).

Figure 1 Smoking-attributable cancer deaths by age group, males and females, Tianjin, China, 2010-2019

Table 3 Number of smoking-attributable cancer deaths and attributable fraction by age, 2010, 2014, 2019

Sensitivity analysis for the estimation of PAF of tobacco smoking

Sensitivity analysis showed that the PAF estimates were more sensitive to the variation in RR in women than in men when the upper and lower limits of the 95% CI of RR was used, due to the larger uncertainty in the estimation of RRs for women, particularly for stomach and pancreas (Figure 2).

Figure 2 Sensitivity analysis of the PAF for ever-smoking using the lower and upper limits of 95% confidence interval for relative risks

Discussion

Our study provides a systematic assessment of the burden of smoking-related cancer in Tianjin, China among 2010 to 2019. RR for eve-smokers death from lung cancer in men was 3.061 (2.956–3.170), was similar with the nationwide prospective cohort studies result (2.98, 2.66–3.33). But the RR for women was higher in our study (3.870, 3.703–4.045 vs. 2.56, 2.02–3.26) [10]. The RR for women death from lung cancer in Tianjin was similar with Japan and Korea which was 3.6 and 3.2 respectively [11]. But the results were much lower than France and United Kingdom.

Overall, 32,357 of 131,919 (24.53%) cancer deaths were attributable to tobacco smoking in Tianjin. There was a large discrepancy between men and women in the PAF estimates of cancer mortality (28.87% vs. 17.37%), which was a little lower to previous reports in men in Korea (32.9%), Japan (34.4%), France (33.4%) and much higher to above country, Korea (5.2%), Japan (6.2%), France (9.6%) [11–13]. It much similar to United Kingdom, that PAF was 23.0% and 15.6% in men and women respectively. Our results suggest that Tianjin women have the highest percentage of all-cause and lung cancer deaths attributable to

smoking in China, probably because of their high smoking prevalence. The First National Smoking Prevalence Survey in 1984 showed that the smoking prevalence was 7.04% in women in China, while the prevalence of 27.4% in Tianjin women was the highest [14]. Also we found that the number of smoking-attributable cancer deaths in ≥ 75 year old increase from 467 to 564 between 2010 and 2019. That was also because the smoking prevalence of the women born before year 1935 was higher than the women born after 1935.

These results of comparison support the necessity of ethnic- or country-specific evaluation of the PAF because even though the overall PAF appear to be same, the exposure prevalence and the RRs can be different across countries or districts, therefore, the prevention strategy in each country or district should be different. It is very important to monitor and calculate RR and PAF in country and region level for formulating targeted prevention and control strategies.

Due to the significant decrease of smoking rate in women [15–17], it can be observed that the smoking attributable lung cancer death in women decreased from 36.6% in 2010 to 29.6% in 2019, but it remained stable in men. Since the majority of lung cancers are attributable to smoking, changes in smoking prevalence are the key driver of lung cancer mortality trends. In particular, 49.06% of all lung cancer deaths in Tianjin among more than 35 years old men could have been prevented if no man had smoked in Tianjin, and the percentage was 31.56% in women.

The MCC study which developed in the Tianjin design can be a quick, efficient, and reliable method to assess and monitor mortality risks of smoking, and it can be promoted in other cities or countries with a reliable system of death certification and good quality control measures like the Tianjin CDRS. Use of RRs from the MCC study in Tianjin can measure the data of more accurately smoking-attributable death than the general RRs from the global study, such as GBD and et al.

Our findings highlight the high risks of cancer deaths, mainly from lung cancer and upper aerodigestive cancer, in men and women ever smokers and particularly the high proportion of deaths attributable to smoking in women in Tianjin, which had the highest smoking prevalence among women around the 1980s in China. Strong tobacco control measures are needed to motivate a large proportion of smokers, including female smokers, to stop smoking. Special and urgent warnings and tobacco control campaigns are needed to prevent the increase in smoking in young women. In countries, regions, or cities with a reliable system of death certification, the mortality case-control study design using routinely collected smoking data from death certificates can be used to rapidly and periodically assess the mortality risks of smoking and evaluate the effects of tobacco control measures at different stages of the tobacco use epidemic.

This Tianjin study is China's first mortality case-control study based on smoking data from death registration. Lung cancer was the main cause (half in men and two-thirds in women) of smoking-induced deaths. The smoking-attributed fractions of all-cause and lung cancer deaths in women were the greatest probably because of the high smoking prevalence among woman in the city around the 1980s. The mortality case-control study design can be used to rapidly and periodically assess the mortality risks of smoking and evaluate the effects of tobacco control measures.

Conclusions

While the smoking prevalence in male adults has been decreasing in Tianjin, China, it remains high (more than 25% in people aged 15 and above). Because Tianjin is quickly approaching the status of an aged society, the number of cancer cases and deaths are expected to increase in the future. Approximately one in three cancer deaths in men and one in six cancer deaths in women would be potentially preventable through appropriate control of tobacco smoking in Tianjin. Effective tobacco control programs should be further developed and implemented in Tianjin to reduce the smoking-related cancer burden.

Implications

Our study provides a systematic assessment of the burden of smoking-related cancer by mortality case-control study in Tianjin, China among 2010 to 2019. RR for eve-smokers death from lung cancer in men was 3.061 (2.956-3.170), was similar with the nationwide prospective cohort studies result (2.98, 2.66-3.33). But the RR for women was higher in our study (3.870, 3.703-4.045 vs. 2.56, 2.02-3.26) than the whole China, but similar with Japan and Korea. Overall, 32,357 of 131,919 (24.53%) cancer deaths were attributable to tobacco smoking in Tianjin. There was a large discrepancy between men and women in the PAF estimates of cancer mortality (28.87% vs. 17.37%). These results of comparison support that it is very important to monitor and calculate RR and PAF in country and region level for formulating targeted prevention and control strategies. Because Tianjin is quickly approaching the status of an aged society, the number of cancer cases and deaths are expected to increase in the future. Approximately one in three cancer deaths in men and one in six cancer deaths in women would be potentially preventable through appropriate control of tobacco smoking in Tianjin. Effective tobacco control programs should be further developed and implemented in Tianjin to reduce the smoking-related cancer burden.

Declarations

Competing interests

The authors declare that they have no competing interests.

Author's contributions

LI Wei and XUE Xiaodan wrote the main manuscript text, tables and figures; LI Dandan, ZHANG Ying and SHEN Wenda cleaned up the data; JIANG Guohong gave the guidance to analyses. All authors reviewed the manuscript.

Acknowledgements

We thank all staff who are involved in the Tianjin CDRS, local CDCs, hospitals, and community health service centers. We do not use copyrighted material and copyrighted surveys, instruments, or tools in our study.

This study was implemented as a register-based study based on anonymous data at TJCDC CDC and was approved by the TJCDC Ethics Committee. Register-based studies on anonymous data do not require written consent in Tianjin. There was no funding for this study.

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Tables

Table 1 Mortality Rate Ratio at Age ≥35 Years, Selected Cancer Causes, Ever Smokers Versus Never Smokers, Tianjin, China, 2010–2019

Sex	Site (ICD-10 Code)	2010	95% CI			2014	95% CI			2019	95% CI			Total
Male	Lung (C33-4)	3.013	2.644	,	3.434	3.166	2.833	,	3.537	3.162	2.852	,	3.505	3.06
	Upper aerodigestive (C00-15,C32)	1.365	1.111	,	1.677	1.905	1.589	,	2.284	1.904	1.604	,	2.259	1.79
	Stomach(C16)	1.070	0.895	,	1.280	1.202	1.024	,	1.412	1.131	0.966	,	1.324	1.18
	Liver(C22)	1.165	0.996	,	1.363	1.339	1.157	,	1.549	1.214	1.053	,	1.400	1.22
	Pancreas(C25)	1.036	0.806	,	1.332	1.436	1.158	,	1.780	1.120	0.926	,	1.354	1.18
	Bowel(C18-21)	0.987	0.801	,	1.217	1.213	1.021	,	1.440	1.023	0.879	,	1.191	1.07
	Kidney and other urinary(C64-6,C68)	1.112	0.762	,	1.624	1.755	1.288	,	2.392	1.237	0.950	,	1.611	1.33
	Bladder(C67)	1.580	1.134	,	2.201	1.309	0.998	,	1.718	1.419	1.112	,	1.810	1.32
	Myeloid leukemia(C92,C93.0,C94.0,C94.2,C94.4-5)	1.062	0.466	,	2.422	0.821	0.416	,	1.618	0.794	0.431	,	1.462	1.01
Total		1.745	1.563	,	1.948	1.987	1.806	,	2.186	1.846	1.693	,	2.013	1.86
Female	Lung (C33-4)	4.046	3.483	,	4.700	3.699	3.200	,	4.276	3.964	3.471	,	4.529	3.87
	Upper aerodigestive (C00-15,C32)	1.890	1.359	,	2.630	1.464	1.033	,	2.076	2.032	1.458	,	2.831	1.70
	Stomach(C16)	1.135	0.842	,	1.528	1.048	0.770	,	1.425	1.161	0.861	,	1.566	1.09
	Liver(C22)	1.257	0.991	,	1.595	1.001	0.759	,	1.319	1.422	1.095	,	1.846	1.21
	Pancreas(C25)	1.475	1.084	,	2.007	1.218	0.890	,	1.668	1.343	1.018	,	1.771	1.16
	Bowel(C18-21)	0.970	0.717	,	1.312	0.899	0.677	,	1.194	1.138	0.892	,	1.451	0.97
	Kidney and other urinary(C64-6,C68)	0.680	0.327	,	1.415	1.196	0.688	,	2.078	1.028	0.619	,	1.706	1.12
	Bladder(C67)	1.513	0.810	,	2.823	1.881	1.085	,	3.261	1.647	0.997	,	2.719	1.67
	Myeloid leukemia(C92,C93.0,C94.0,C94.2,C94.4-5)	0.333	0.042	,	2.659	-	-	,	-	0.797	0.187	,	3.396	0.78
Cervix(C53)		1.009	0.503	,	2.024	1.049	0.611	,	1.802	1.192	0.725	,	1.960	1.10
Total		2.402	2.096	,	2.752	2.296	2.007	,	2.626	2.445	2.168	,	2.757	2.38

Table 2 Number of smoking-attributable cancer deaths and attributable fraction by site, Tianjin, China, 2010–2019

Sex	Site (ICD-10 Code)	2010			2014			2019			Total		
		Current and ever (%)	No. Attributed to Smoking	(%)	Current and ever (%)	No. Attributed to Smoking	(%)	Current and ever (%)	No. Attributed to Smoking	(%)	Current and ever (%)	No. Attributed to Smoking	(%)
Male	Lung (C33-4)	75.32%	1549	50.32%	77.82%	1886	48.91%	74.46%	2183	50.91%	72.87%	18705	49.06%
	Upper aerodigestive (C00-15,C32)	58.43%	80	15.62%	60.86%	189	29.00%	65.94%	243	31.31%	62.07%	1802	27.55%
	Stomach(C16)	51.07%	25	3.34%	48.78%	71	8.20%	51.46%	51	5.96%	50.82%	674	8.08%
	Liver(C22)	56.99%	96	8.07%	54.09%	169	13.69%	56.03%	120	9.88%	54.65%	1282	10.11%
	Pancreas(C25)	51.27%	6	1.78%	53.70%	68	16.30%	52.37%	31	5.61%	52.60%	380	8.36%
	Bowel(C18-21)	48.78%	-3	-0.64%	48.02%	60	8.43%	48.03%	10	1.08%	47.64%	250	3.45%
	Kidney and other urinary(C64-6,C68)	53.17%	7	5.36%	58.38%	46	25.11%	53.91%	26	10.33%	54.26%	253	13.56%
	Bladder(C67)	58.33%	36	21.41%	47.92%	27	11.31%	53.29%	48	15.74%	49.90%	302	12.35%
	Myeloid leukemia(C92,C93.0,C94.0,C94.2,C94.4-5)	45.83%	1	2.68%	40.54%	-3	-8.84%	43.18%	-5	-11.20%	46.70%	2	0.51%
Total		63.96%	1817	27.31%	61.58%	2506	30.59%	63.77%	2695	29.22%	62.39%	23709	28.87%
Female	Lung (C33-4)	48.62%	807	36.60%	41.74%	804	30.46%	39.58%	754	29.60%	42.56%	8035	31.56%
	Upper aerodigestive (C00-15,C32)	31.55%	31	14.86%	22.73%	16	7.20%	26.05%	28	13.23%	25.54%	229	10.59%
	Stomach(C16)	19.55%	8	2.33%	15.31%	3	0.70%	14.15%	8	1.96%	15.33%	50	1.27%
	Liver(C22)	21.33%	26	4.36%	14.95%	0	0.01%	17.10%	25	5.08%	17.60%	171	3.11%
	Pancreas(C25)	23.71%	22	7.64%	16.71%	11	2.99%	16.13%	19	4.12%	16.15%	84	2.24%
	Bowel(C18-21)	16.41%	-2	-0.51%	14.00%	-8	-1.57%	14.67%	12	1.78%	14.63%	-20	-0.38%
	Kidney and other urinary(C64-6,C68)	14.29%	-4	-6.72%	16.50%	3	2.70%	14.29%	1	0.39%	16.52%	18	1.78%
	Bladder(C67)	27.27%	5	9.25%	26.32%	9	12.33%	25.00%	9	9.82%	26.12%	80	10.56%
	Myeloid leukemia(C92,C93.0,C94.0,C94.2,C94.4-5)	5.88%	-2	-11.78%	0.00%	0	0.00%	5.00%	0	0.00%	8.76%	0	0.00%
Total	Cervix(C53)	14.29%	0	0.13%	11.04%	1	0.52%	10.50%	3	1.69%	11.09%	17	1.07%
		35.33%	876	20.62%	29.61%	831	16.72%	27.58%	853	16.30%	29.96%	8648	17.37%

Table 3 Number of smoking-attributable cancer deaths and attributable fraction by age, 2010, 2014, 2019

Sex	Age group	2010			2014			2019			Total		
		Current and ever (%)	No. Attributed to Smoking	(%)	Current and ever (%)	No. Attributed to Smoking	(%)	Current and ever (%)	No. Attributed to Smoking	(%)	Current and ever (%)	No. Attributed to Smoking	(%)
Male	35-54	68.94%	146	17.41%	67.31%	296	35.75%	66.18%	186	30.08%	66.22%	2331	28.55%
	55-74	67.03%	978	29.54%	66.17%	1591	36.59%	69.83%	1786	33.69%	67.09%	13941	31.80%
	75+	58.24%	675	26.93%	53.40%	689	22.85%	53.58%	753	22.82%	54.52%	7580	25.16%
	total	63.96%	1822	27.39%	61.58%	2514	30.68%	63.77%	2684	29.11%	62.39%	23783	28.96%
Female	35-54	9.77%	19	4.65%	6.88%	15	3.76%	8.22%	16	5.29%	8.42%	146	3.65%
	55-74	34.92%	396	20.71%	24.90%	292	13.53%	20.86%	270	11.57%	25.51%	3214	14.77%
	75+	41.01%	467	24.11%	37.68%	527	21.85%	35.86%	564	21.71%	37.56%	5306	22.07%
	total	35.33%	877	20.65%	29.61%	835	16.78%	27.58%	852	16.28%	29.96%	8648	17.37%

Figures

Figure 1

Smoking-attributable cancer deaths by age group, males and females, Tianjin, China, 2010-2019

Figure 2

Sensitivity analysis of the PAF for ever-smoking using the lower and upper limits of 95% confidence interval for relative risks