Original Article

Lung Cancer Risk Attributable to Active Smoking in China: A Systematic Review and Meta-Analysis

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Abstract

Objective No consensus exists on the relative risk (*RR*) of lung cancer (LC) attributable to active smoking in China. This study aimed to evaluate the unified *RR* of LC attributable to active smoking among the Chinese population.

Methods A systematic literature search of seven databases was conducted to identify studies reporting active smoking among smokers *versus* nonsmokers in China. Primary articles on LC providing risk estimates with their 95% confidence intervals (*CI*s) for "ever" "former" or "current" smokers from China were selected. Meta-analysis was used to estimate the pooled *RR* of active smoking.

Results Forty-four unique studies were included. Compared with that of nonsmokers, the pooled *RR* (95% *CI*) for "ever" "former" and "current" smokers were 3.26 (2.79–3.82), 2.95 (1.71–5.08), and 5.16 (2.58–10.34) among men, 3.18 (2.78–3.63), 2.70 (2.08–3.51), and 4.27 (3.61–5.06) among women, and 2.71 (2.12–3.46), 2.66 (2.45–2.88), and 4.21 (3.25–5.45) in both sexes combined, respectively.

Conclusion The *RR* of LC has remained relatively stable (range, 2–6) over the past four decades in China. Early quitting of smoking could reduce the *RR* to some extent; however, completely refraining from smoking is the best way to avoid its adverse effects.

Key words: Active smoking; Chinese population; Lung cancer; Systematic review; Meta-analysis

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INTRODUCTION

Lung cancer (LC) is one of the most prevalent and deadliest cancers worldwide, accounting for an estimated 2 million diagnoses and almost 1.8 million global deaths per year[1]. Active smoking is considered the leading cause of LC, contributing to approximately 75% of LC-related deaths in men and 37% in women across the world[2]. Over the past three decades, cigarette smoking has continued to be a major public health concern, especially in China, where the morbidity and mortality rates of LC have increased faster than the global average. Meanwhile, China has experienced an increase in deaths attributable to smoking, with 1.5 million deaths in 1990 to 2.4 million deaths in 2019[3]. Consequently, active smoking imposes a huge burden on the Chinese government, the Department of Health Management, and professional LC specialists.

Smoking-associated relative risk (*RR*), which varies across countries with different patterns of smoking, is often used to estimate the size of the effect of tobacco smoking on the risk of LC based on its ability to capture the "risk magnification" role of most risk factors[4]. Additionally, it is one of the important

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parameters used for calculating population attributable fraction (PAF) in the estimation of the disease burden attributable to tobacco use, and it has been widely used by Global Burden of Disease (GBD) studies[5]. Previous estimates indicated that active smoking significantly increased the risk of LC. However, the *RR*s reported in China (range, 2.4–6.5) were much lower than those in western countries (range, 9.4–23.2)[6]. Historically, *RR*s are usually derived from two previous studies when estimating the PAF of LC attributable to active smoking in China. One is the retrospective proportional mortality study of one million deaths, which was conducted to examine the hazards at an early phase of the growing epidemic of death from tobacco in China (*RR*: 2.6 in men and 2.0 in women)[7]. The other is a successive nationwide prospective cohort study from Chen and the China Kadoorie Biobank (CKB) collaborative group, which was conducted to assess the contrasting effects of smoking on mortality in China (*RR*: 2.5 in men and 2.3 in women)[7]. Nevertheless, there is a lag between population-level tobacco exposure and the effect on cancer rates, as studies conducted in the early stages of a tobacco epidemic may underestimate the risks of LC, and the full impact of long-term smoking in a population may not be realized.

In China, several reviews have explored the association between tobacco smoking and the *RR* of LC. However, some of them focused on the effect of passive smoking on nonsmokers, while others used earlier research data or just included literature published in English journals[8-13]. To the best of our knowledge, the magnitude of the risk of LC from active smoking varies across studies, and there have been no unified estimates of recent *RR* in China. Therefore, this systematic review aimed to estimate the unified *RR* of LC attributable to active smoking among "ever" "former" and "current" smokers in China. To do so, seven databases were searched exhaustively for observational studies up to July 2021, and subgroup techniques were used to assess whether specific associations are influenced by study characteristics. Additionally, we aimed to estimate the RR for a specific subtype of LC attributable to active smoking and discussed possible reasons for the differences observed.

METHODS

Search Strategy and Data Sources

This study was reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. We conducted a comprehensive search for relevant articles using four English (PubMed, Web of Science, Embase, and Cochrane Library) and three Chinese (CNKI, VIP, and Wan Fang Database) databases for publications in English or Chinese, respectively.

All databases were searched from inception to January 1st, 2022, with the following search terms "tobacco" "smoking" "cigarette" "smoker" "smokers" "nicotine" "cohort" "case-control" "China" and "Chinese"). Additional information was further manually identified by searching the bibliographies of the included papers and other relevant reviews.

Inclusion and Exclusion Criteria

Inclusion Criteria Firstly, all article titles and abstracts were screened to identify relevant articles following the initial literature search. Secondly, eligible studies were identified according to the PECOS format: (1) Participants (P): studies were conducted on Chinese participants, and the participants were representative of the Chinese population; (2) Exposure (E): active smoking; (3) Comparison (C): Active smoking had to be reported as "ever" "former" and "current" smoking with "non-smoking" serving as the control; (4) Outcomes (O): studies that reported sufficient information on risk estimates [odds ratios (*OR*s), relative risks (*RR*s), or hazard ratios (*HR*s)] and their corresponding 95% confidence intervals (*CI*s) or cross-table data with the accessibility of the complete text were included; (5) Types of study (S): case-control and cohort studies without restriction to language and time period; (6) Based on the Newcastle Ottawa Scale (NOS) assessment, studies scoring ≥ 6, which are considered to have a low risk of bias, were included[14].

Exclusion Criteria (1) Studies analyzing diseases other than LC or studies without data specifically for LC; (2) studies in the form of conference papers, systematic reviews, meta-analyses, letters, abstracts, or comments; (3) studies not reporting effect estimates for active smoking and LC and not containing relevant data; (4) animal and *in vitro* studies; (5) studies on special groups, such as coal miners, veterans, nurses, pregnant women, newborns, patients with mental illnesses, and (6) duplicate publications or abstracts without full texts available.

Study Selection and Data Extraction

Study screening and data extraction were carried

out independently by two researchers, with verification by a third reviewer. The title, first author, year of publication, time of investigation, sampling method, location, definition of SHS, number of cases and controls, basic information about participants, and other relevant parameters were extracted. The risk of bias according to the PRISMA recommendations was assessed independently by the aforementioned two researchers.

Data extraction was performed independently by two investigators, and any disagreements were resolved by a third reviewer or group discussion. Data retrieved from the reports included the risk estimates and their 95% *CI* of LC of "ever" "former" and "current" smokers *versus* "nonsmokers" both in men and women. Additionally, data on the description of the study and population characteristics, study design and setting, the definition of LC outcomes, histopathologic subtypes, risk estimates, and their 95% *CI* were extracted. For studies that reported both crude and adjusted risk estimates, the adjusted risk estimate was selected for the analysis. The methodological quality of included studies was independently assessed by two of the authors using the NOS.

Statistical Analysis

A meta-analysis was performed using Stata software version 16.0 (TX, USA). No distinction was made among various measures of relative risk (i.e., *OR*, *RR*, or *HR*) due to the small number of cohort studies. Cochran's Q test and the I^2 statistics were conducted to evaluate the heterogeneity of effects across the studies. I^2 represents the proportion of total variation in effect estimates due to the heterogeneity between study results[15]. Significant heterogeneity was defined as Cochrane Q < 0.10 and/or I^2 > 50%. Fixed-effect or random-effect models were used based on the absence or presence of heterogeneity and/or methodological diversity among the included studies. Egger's regression test was used to statistically evaluate the presence of publication bias with a visual inspection of the funnel plots. The meta-analytic techniques were used to assess the *RR* of LC for "ever" "former" and "current" smokers, compared with "nonsmokers" separately by sex. Subgroup analyses were carried out to investigate between-study heterogeneity focusing on the initial year of the survey, study type, and outcome of disease in the "ever" smoker group. Sensitivity analyses were carried out to assess the stability of the results by using the "leave-one-out" method[16]. For each subtype of LC, we used descriptive studies because of the limited data available in the literature.

RESULTS

Selection Process

Of 12,998 potentially relevant studies identified in the initial literature search, 1,077 were removed because they were duplicates, and another 1,502 were excluded because of irrelevance after reviewing the titles and abstracts. Subsequently, a total of 10,419 studies were thoroughly reviewed for eligibility criteria, and of them, 716 were considered relevant studies that met inclusion criteria. Research on specialized populations was the most frequent reason for exclusion within the review process, followed by research without original data. Finally, 44 studies were included in the review, and the study populations ranged from 158 to 360,127. The process of identifying and assessing the eligibility of studies is shown in a flowchart in Figure 1.

Basic Characteristics of the Included Studies

Table 1 provides the characteristics of the included studies, including smoking status, sex, year of study, age, disease outcome, and specific subtype of LC. Of the 44 unique publications[17-60] included in the meta-analysis, 41 were on "ever" smokers[17-31,33-53,55,57-60], 10 on "former" smokers[17,32,44,46-49,54,56,59], and 11 on "current" smokers[17,32,44,46-50,54,56,59], with some of these studies reporting on more than one smoking status. Meanwhile, 18[17-18,23,34-35,37-39,45-47,49-51,55-56,58-59], 14[17,23,33-34,40,43-45,49,52,55-56,58], and 25[17,19-32,36,41-42,47-49,53-54,58,60] of the 44 studies were conducted in men, women, and both genders, respectively. As for study design, 31 were case-control[17-36,40-47,57-59] and 13 were cohort studies[37-39,48-56,60]. For the initial year of study, 20 were published before 2000[19,23,26,29,31,36,38-40,45-47,49-52,54-57], 16 were published between 2000 and 2009[17-18,20-22,24,27-28,30,37,43-44,48,55,59-60], and 8 studies were conducted after 2009[25,32-35,41-42,53,58]. For the outcome of LC, 27 reported incidences[17,19-23,25,27-31,37,39-47,57,59-60] and 17 reported mortalities of LC[24,32-36,38,48-56,58]. As for the different LC subtypes, six reported lung squamous cell carcinomas (SCC)[17,19,21,26,40,59], seven reported lung adenocarcinomas (AD)[17-19,21,40,44,59], and three reported small cell carcinomas (SCLC)[21,40,59]. The full list of the 44 included articles with their detailed characteristics is provided in Supplementary Table S1, available in www.besjournal.com.

Synthesized Results

LC risk for "ever" "former" and "current" smokers

Nine separate meta-analyses were conducted to compare "ever" "former" or "current" smokers with "nonsmokers" stratified by sex. The pooled *RR*s (95% *CI*s) are summarized in Table 2. Forest plots for "ever" "former" and "current" active smoking in all the studies are displayed in Figure 2 and Supplementary Figures S1 and S2, available in www.besjournal.com.

There was a significant positive association between active smoking and the risk of LC, regardless of smoking status and sex. Compared with a "nonsmoker" the pooled *RR*s (95% *CI*s) for "ever" smokers were 3.26 (2.79–3.82), 3.18 (2.78–3.63), and 2.71 (2.12–3.46) for men, women, and sexes combined, respectively. There was evidence of statistical heterogeneity of *RR*s across studies for the overall population (I^2_{men} = 92.9, I^2_{women} = 83.6, and $I^2_{sexes\ combined}$ = 95.3, P_{all} < 0.001). The pooled *RR*s of former smokers were also consistently significantly higher than those of "nonsmokers" and lower than those of "current" smokers, regardless of sex. Specifically, the pooled *RR*s (95% *CI*) for "former" smokers were 2.95 (1.71–5.08), 2.70 (2.08–3.51), and 2.66 (2.45–2.88) for men, women, and sexes combined, respectively. But significant heterogeneity was observed among studies (I^2_{men} = 94.9, P < 0.001) just for men. The pooled *RR*s (95% *CI*s) for "current" smokers were 5.16 (2.58–10.34), 4.27 (3.61–5.06), and 4.21 (3.25–5.45) for men, women, and sexes combined, respectively. Significant heterogeneity existed among the studies of men and both sexes (I^2_{men} = 98.1 and $I^2_{sexes\ combined}$ = 89.0, P_{all} < 0.001). Sensitivity analysis suggested

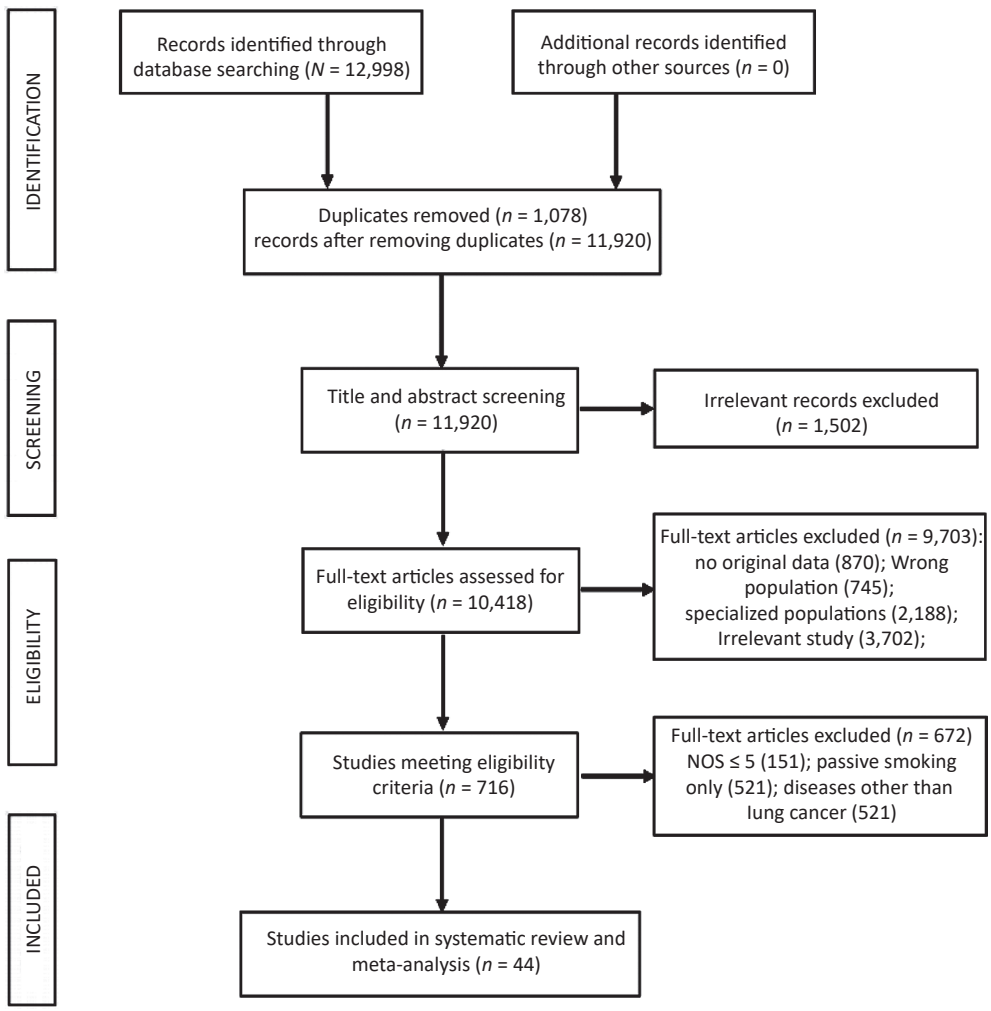

Figure 1. Study selection process.

that the pooled *RR*s were substantially unchanged after excluding one study at a time (data not shown). There was no statistically significant evidence of publication bias, and funnel plots are presented in Figure 3.

Variation in "ever" Smoking Effects on LC between Subgroups

Despite the high heterogeneity across all the smoking statuses, we performed stratified analyses

Table 1. Characteristics of included studies

Characteristic	Groups	No. of studies			NOS Score[1,2]
		Chinese	English	All	
Smoking status	Ever smoker	23	18	41	7.02 ± 1.17
	Former smoker	2	8	10	7.50 ± 1.43
	Current smoker	2	9	11	7.64 ± 1.43
Sex	Men	7	11	18	7.47 ± 1.18
	Women	4	10	14	7.07 ± 1.21
	Sexes combined	18	7	25	7.04 ± 1.24
Study type	Case-control	23	8	31	6.48 ± 0.63
	Cohort	3	10	13	8.23 ± 1.17
Study begin[2]	–1999	9	11	20	7.00 ± 1.26
	2000–2009	11	5	16	7.06 ± 1.12
	2010–	6	2	8	6.88 ± 0.99
LC outcome	Morbidity	19	8	27	6.63 ± 0.93
	Mortality	7	10	17	7.59 ± 1.23
Age	≥ 18 years	19	10	29	7.10 ± 1.11
	None	7	8	15	6.80 ± 1.21
Histopathologic subtype	LC	24	18	42	7.02 ± 1.16
	SCC	5	1	6	6.71 ± 0.76
	AD	4	3	7	6.75 ± 0.71
	SCLC	2	2	3	7.00 ± 0.82

Note. [1]The quality of selected articles was assessed by The Newcastle-Ottawa Scale (NOS). [2]The NOS variable are expressed as the mean ± standard deviation and analyzed by mean difference (MD).

Table 2. Summary of meta-analyses results, stratified by sex and smoking status[1]

Smoking status	Sex	No. of studies	Pooled *RR* (95% *CI*)	I^2 (%)	Model
Ever smokers	Men	16	3.26 (2.79–3.82)	92.9	Random
	Women	13	3.18 (2.78–3.63)	83.6	Random
	Sexes combined	23	2.71 (2.12–3.46)	95.5	Random
Former smokers	Men	6	2.95 (1.71–5.08)	94.9	Random
	Women	3	2.70 (2.08–3.51)	44.9	Fixed
	Sexes combined	4	2.66 (2.45–2.88)	7.7	Fixed
Current smokers	Men	6	5.16 (2.58–10.34)	98.1	Random
	Women	3	4.27 (3.61–5.06)	0.0	Fixed
	Sexes combined	6	4.21 (3.25–5.45)	89.0	Random

Note. [1]Never smokers were used as the reference group for each analysis.

for "ever" smokers only (Table 3). The results were stable across the different subgroup analyses, especially for the year of study and the study type in men and sexes combined. In the year of study subgroup, *RR*s (95% *CI*) ranged from 3.17 (95% *CI*: 2.82–3.56) to 3.30 (95% *CI*: 2.43–4.48) for men and from 2.39 (95% *CI*: 1.30–3.46) to 3.12 (95% *CI*: 2.30–4.22) for sexes combined. Despite fluctuations in the above *RR*s, no significant differences were observed in the studies with men only and sexes combined. However, the *RR*s for women varied across survey periods, with a higher *RR* for women investigated after 2010 than those in other time periods, probably due to a limited number of included literature. Additionally, there was a significant sex difference in the risk of LC morbidity or mortality due to active smoking, as the *RR* (95% *CI*) of incidence (*RR* = 4.47, 95% *CI*: 3.50–5.71) was higher than that of mortality (*RR* = 2.77, 95% *CI*: 2.33–3.28) in men, but lower (*RR* = 3.74, 95% *CI*: 3.39–4.12) than that of incidence (*RR* = 2.56, 95% *CI*: 2.23–2.93) in women. Furthermore, smoking increased the risk of LC both in case-control and cohort studies, and the risk of LC did not vary significantly according to the type of research, regardless of sex. There was no obvious evidence of publication bias for any of the outcomes, as indicated by the results of heterogeneity tests and visual inspection of funnel plots.

Risk of LC Subtypes for "ever" Smokers

Generally, the associations of the LC subtypes were stronger for SCC and SCLC than for AD in the sexes combined. Based on the literature description,

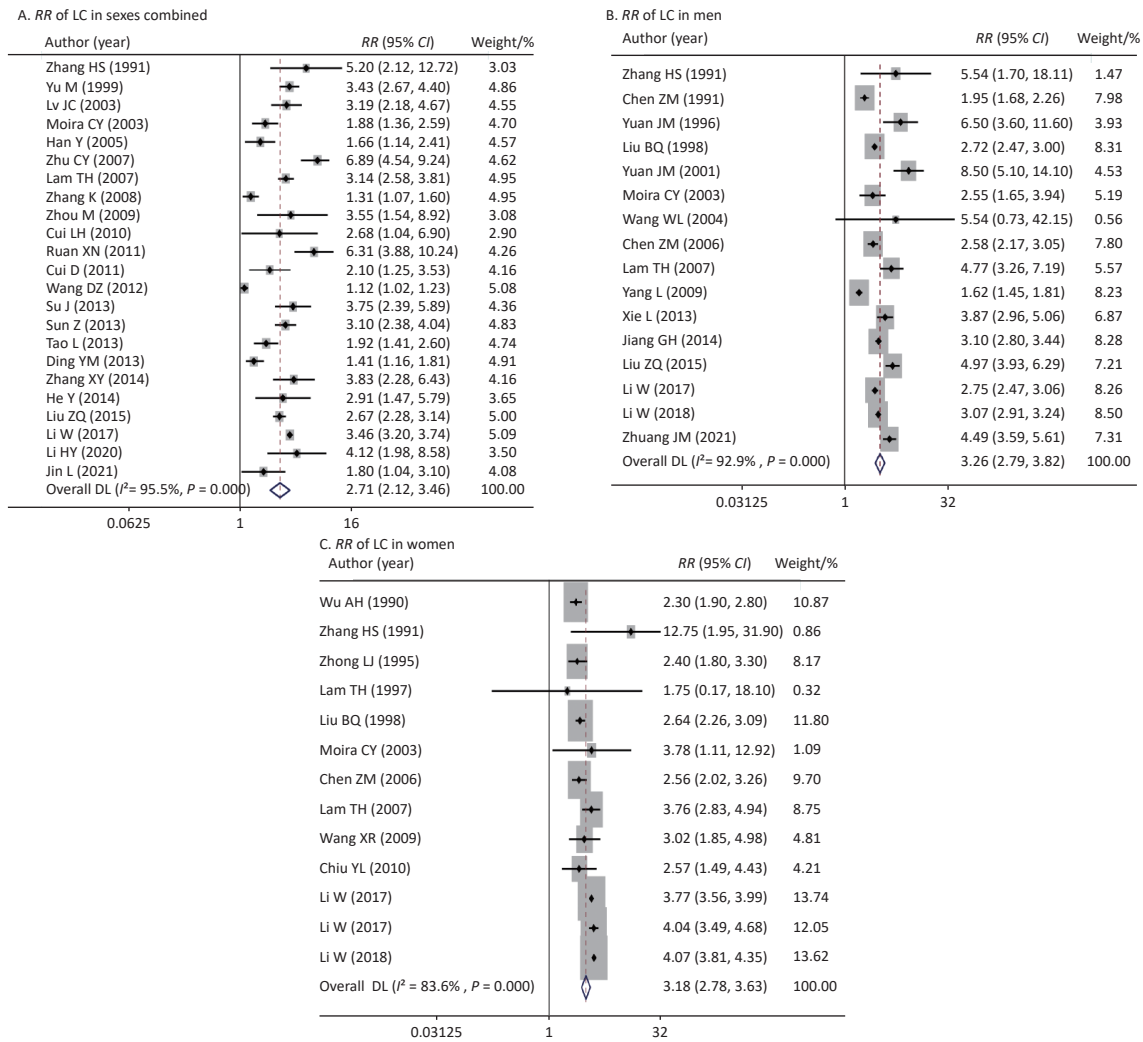

Figure 2. Forest plots showing pooled *RR* values of LC caused by "ever" smoking compared with non-smoking in different sexes (A) *RR* of LC in sexes combined (B) *RR* of LC in men (C) *RR* of LC in women.

the *RR*s (95% *CI*) ranged from 2.73 (95% *CI*: 3.16–5.31) to 3.00 (95% *CI*: 1.74–5.17) for AD, from 3.14 (95% *CI*: 1.75–5.73) to 8.10 (95% *CI*: 9.26–36.4) for SCC, and 5.06 (95% *CI*: 2.10–12.18) for SCLC. A sex comparison revealed that the *RR* of each subtype of LC from the present study was generally higher in men than in women. Specifically, in men, the *RR*s (95% *CI*) ranged from 7.24 (95% *CI*: 4.84–10.84) to 8.38 (95% *CI*: 5.40–12.88) for SCC, from 3.00 (95% *CI*: 2.24–4.02) to 3.04 (2.30–4.01) for AD, and 15.08 (95% *CI*: 6.00–37.92) for SCLC. Meanwhile, in women, the *RR*s (95% *CI*) for SCC, AD, and SCLC ranged from 4.20 (95% *CI*: 3.00–5.90) to 5.60 (95 *CI*: 3.30–9.60), 1.10 (95% *CI*: 0.70–1.70) to 1.86 (95% *CI*: 0.98–3.50), and 2.20 (95% *CI*: 1.40–3.20) to 9.90 (95% *CI*: 3.20–30.1), respectively. The association between smoking and the LC subtypes of interest is reported in Table 4.

DISCUSSION

This study demonstrated that the *RR* of LC attributable to active smoking in China remained relatively stable (range, 2.66–5.16) over the past four decades. Compared with nonsmokers, the *RR* (ranges, 4.21–5.16) of LC attributed to active smoking was larger than that from former smoking (range, 2.66–2.95), which also corroborates prior findings[61-64]. All epidemiological evidence indicates that long-term smoking can cause future health harm while quitting tobacco use reduces the risk. Generally, the RR of LC due to active smoking among men was larger than that among women in China. Meanwhile, active smoking increased the *RR* of each subtype of LC, regardless of sex. There is no safe threshold for smoking, and early smoking cessation could reduce the risk of LC caused by smoking to some extent; however, not smoking at all is always the best way to avoid the adverse effects attributed to active smoking.

The results of the meta-analysis of *RR* for LC (range, 2.2–5.1) align with the findings from Japan (ranges, 3.5–5.1) and Korea (ranges, 4.0–4.6) and substantially less than that in western populations[65]. A recent population-based cohort study in Australia reported that the *RR* for LC was 17.7, which was similar to that observed in the National Institute of Health-AAPP cohort in the US

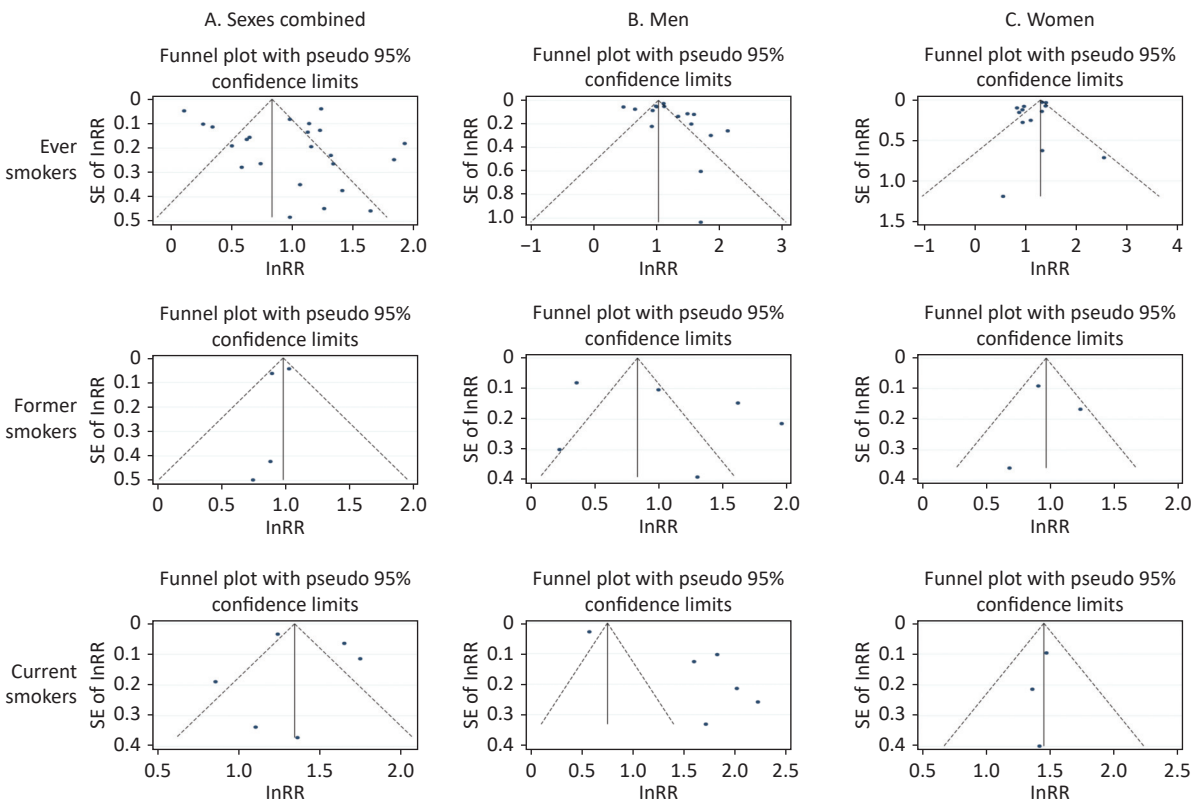

Figure 3. Funnel plots for smoking status, compared with non-smoking in different sexes (A) *RR* of LC in sexes combined (B) *RR* of LC in men (C) *RR* of LC in women.

(19.5 for women and 29.4 for men). Additionally, findings from a prospective investigation reported that the *RR* of LC was 13.6 in a European population[66-67]. The discrepancy between our findings and the results for the West could be explained by several reasons, including mainly the differences in smoking patterns. It is well known that widespread smoking occurred in China decades later than in the West; hence, China is still in the early stages of the tobacco epidemic relative to Western countries. Another possible explanation is the competing effects of smoky coal pollution and

Table 3. Subgroup analysis investigating the association between "ever" smoking and LC risk

Sex	Group	Subgroup	No. of Studies	I^2 (%)	*RR* (95% *CI*)
Men	Year of study	–1999	9	92.5	3.30 (2.43–4.48)
		2000–2009	3	90.5	3.65 (2.41–5.53)
		2010–	4	80.1	3.17 (2.82–3.56)
	Disease outcome	Incidence	6	65.7	4.47 (3.50–5.71)
		Mortality	10	93.8	2.77 (2.33–3.28)
	Study type	Case-control	9	85.3	3.42 (3.00–3.91)
		Cohort	7	92.4	2.99 (2.16–4.14)
Women	Year of study	–1999	8	49.3	2.76 (2.30–3.31)
		2000–2009	2	0	2.64 (2.13–3.28)
		2010–	3	36.8	3.92 (3.71–4.15)
	Disease outcome	Incidence	7	18.5	2.56 (2.23–2.93)
		Mortality	6	67.3	3.74 (3.39–4.12)
	Study type	Case-control	10	85.9	3.21 (2.77–3.72)
		Cohort	3	54.5	3.04 (2.18–4.24)
Sexes combined	Year of study	–1999	8	83.1	3.12 (2.30–4.22)
		2000–2009	9	89.7	2.58 (1.85–3.60)
		2010–	6	98.5	2.39 (1.30–3.46)
	Disease outcome	Incidence	16	84.1	2.96 (2.31–3.78)
		Mortality	7	98.4	2.25 (1.38–.64)
	Study type	Case-control	18	96.4	2.75 (2.06–3.07)
		Cohort	5	61.7	2.56 (1.89–3.47)

Table 4. Association between "ever" smoking and risk of LC subtypes

Histological type	Sex	No. of studies	*RR* ranges	
			Minimum (95% *CI*)	Maximum (95% *CI*)
SCC	Men	2	7.24 (4.84–10.84)	8.38 (5.40–12.88)
	Women	2	4.20 (3.00–5.90)	5.60 (3.30–9.60)
	Sexescombined	3	3.14 (1.75–5.73)	8.10 (2.40–27.35)
AD	Men	3	3.00 (2.24–4.02)	3.04 (2.30–4.01)
	Women	3	1.10 (0.70–1.70)	1.86 (0.98–3.50)
	Sexescombined	2	2.73 (1.42–5.26)	3.00 (1.74–5.17)
SCLC	Men	1	15.08 (6.00–37.92)	
	Women	2	2.20 (1.40–3.20)	9.90 (3.20–30.1)
	Sexescombined	2	5.06 (2.10–12.18)	

tobacco smoking[9]. A meta-analysis of studies published up to 2008 indicated that the health hazard of smoking for LC has been underestimated in China[12]. Extensive passive exposure to environmental smoke may have led to an underestimation of the true *RR* of smoking since such individuals were classified as "nonsmokers" in most studies, while their exposure to environmental tobacco smoke was neglected. Environmental air pollutants, such as combustion products, are of particular concern in developing regions where wood and charcoal are commonly used for cooking and heating, and they may increase the risk of LC. Lee et al. reported a stronger association between smoking and LC risk after chimney installation[68]. With the decline in coal use and the improvement of indoor air quality, the adverse effects of tobacco use on LC may be more apparent[69]. China's population has continued to switch to cleaner fuels for homes, highlighting the urgent need for smoking cessation in China and other parts of the world.

Although the incidence of smoking has been moderately decreasing or leveling off among men but rising among women in China, the results of this study were consistent with those of a previous meta-analysis, which reported that smoking yields similar risks of LC in women and men. However, there is currently inconsistent epidemiological evidence on sex-induced differences in the risk of LC induced by smoking[10]. Several studies have reported a higher risk of smoking-induced LC in men compared with that in women; however, population-based case-control research found a two to four-fold higher risk of LC in women compared with that in men, irrespective of the level of smoking. The sex-specific associations between smoking and LC varied across studies, and this may be attributed to the differences in study design, the definition of smoking status, and adjustment for confounders. In addition, the present analysis showed that some observations among women were different from those in the other groups; for example, smoking led to a significantly greater risk of LC than the risk of death, which was inconsistent with the results in men and sexes combined. In contrast, a previous study conducted in North America reported that women tend to have a higher susceptibility to smoking but a lower rate of fatal outcomes of LC than men. However, the mechanism associated with the susceptibility of men to tobacco carcinogenicity is not fully understood. Moreover, our study reported that active cigarette smoking increased the risk of all subtypes of LC. Overall, the pattern of *RR*s in relation to the subtypes of LC in the present study was similar to that previously reported, with "ever" *versus* nonsmoker risks that were higher in SCC and SCLC than in AD[70]. Previous studies in the US reported that the incidence of SSC and SCLC has decreased, whereas the incidence of AD has moderately increased, and the combined *OR* for heaviest smoking intensity ranged from 4.10 for AD to 18.3 for SCLC.

China is going through a transition period of rapid economic growth and environmental variation. Lifestyle changes, as well as an aging population, are shifting the disease burden towards Non-Communicable Chronic Diseases (NCDs). Effective LC interventions are critical to achieving NCD control goals in China and worldwide. Given the high smoking rate and psychological and financial burdens, the Chinese government launched a national strategy-Health China 2030, which aims to reduce the prevalence of smoking to < 20%. China is the largest producer and consumer of cigarettes among all countries. According to the 2018 national smoking surveys, more than 50% of men above the age of 30 are smokers, and the total smoking population exceeds 350 million. China is faced with the heaviest burden caused by LC, representing 23.8% of all cancer deaths and 17.9% of all new cancer cases in 2020. LC mortality in China may increase by approximately 6.2% for men and 9.0% for women from 2020–2030[71]. Unlike the western population, who have witnessed a steady decline in the prevalence of smoking over the last few decades owing in part to the widespread awareness of the harms of smoking, many tens of millions of smokers in China remain oblivious to the hazards of cigarette smoking[72]. Furthermore, while direct marketing and advertisement of tobacco products are restricted, indirect marketing still exists under the guise of sponsorship and corporate social responsibility. Therefore, it is important to emphasize LC prevention through tobacco control in China[73]. Moreover, the smoking rate has increased in China, and the initiation age of adolescents has recently decreased; hence, the damage from smoking may increase in the future. Therefore, tobacco control programs should be extensively advocated in order to lessen the morbidity and mortality associated with smoke-related diseases[74].

Our study had some advantages, including the longest time range of Chinese and English Studies on the *RR* value of LC caused by active smoking in the Chinese population. We also performed several subgroup analyses, which were not performed in the

previous meta-analysis. However, the study had some limitations. First, smoking status was crudely defined in the present study; for example, the definition did not include the number of years of smoking or average amounts smoked, but the broad categorization increased the number of studies available for inclusion and controlled variability. Second, there was heterogeneity across the studies in terms of study design and study population, and the verification of smoking status differed across studies.

CONCLUSION

This meta-analysis summarized all the relevant literature data and supported a consistent and statistically significant association between active smoking and increased LC risk, regardless of smoking status and sex. Moreover, this review provides data on the effect of active smoking on LC, specifically in China, and convincing evidence on the likely benefits of quitting smoking. It is essential to develop effective public health campaigns that aim to convince smokers in China to quit and dissuade others from taking up the habit towards the prevention of smoking-related LC deaths. Moreover, the present study provides data on the disease burden imposed by active smoking in the Chinese population.

AUTHOR CONTRIBUTIONS

ZHAO Jian: Identified the studies; checked and analyzed the data; wrote the initial draft of the manuscript. SHI Yu Lin, WANG Yu Tong, AI Fei Ling, WANG Xue Wei, AI Li Mei, YANG Wen Yi, WANG Jing Xin, and HU Kui Ru: Identified the studies; extracted and checked the data. WAN Xia: Conceived and designed the study; checked and verified the data; contributed to the revision and finalization of the paper; was responsible for submitting the article for publication.

DECLARATION OF COMPETING INTEREST

The authors do not have any possible conflicts of interest.

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