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Review Article

Meta-analysis of the association between indoor environmental pollution and lung cancer risk in never-smokers

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Abstract: Objective: This review systematically evaluates the association between indoor environmental pollution and lung cancer risk in never-smokers by meta-analysis, providing evidence-based prevention strategies for lung cancer. Methods: This study was registered in PROSPERO (Registration No.: CRD420251008009) following the Preferred Reporting Items for Systematic Reviews and Meta - Analyses (PRISMA) guidelines. A systematic search was conducted in the PubMed, Web of Science, Embase, and Cochrane Library databases for relevant studies published from March 2005 to March 2025. Literature screening was conducted independently by two reviewers using a double-blind method. Study quality was assessed using the criteria recommended by the Agency for Healthcare Research and Quality (AHRQ). Meta-analysis was performed using STATA 12.0 and RevMan 5.3 software. Results: A total of 22 studies met the inclusion criteria. Analysis showed that indoor environmental pollutants, including residential radon (Odds Ratio [OR] = 1.82, 95% CI: 1.31-2.54), environmental tobacco smoke (ETS) (OR = 1.96, 95% CI: 1.36-2.82), cooking fumes (OR = 3.68, 95% CI: 2.67-5.07), cooking methods (deep-frying: OR = 1.60, 95% CI: 0.72-3.52; stir-frying: OR = 1.12, 95% CI: 1.07-1.17), and the use of solid fuels (OR = 5.54, 95% CI: 3.15-9.72) were all significantly associated with an increased risk of lung cancer in non-smoking populations. In addition, the study found that residential environmental pollution, occupational exposures, and low body mass index (BMI) were also significant factors for lung cancer in non-smoking patients. Conclusion: This study confirmed that indoor environmental pollutants, including residential radon, ETS, cooking fumes, specific cooking methods (deep-frying and stir-frying), and the solid fuel use, are significantly associated with an increased risk of lung cancer in non-smoking populations. Furthermore, exposure to outdoor pollutants in residential areas and occupational environments cannot be ignored.

Keywords: Indoor environmental pollution, non-smoking population, lung cancer, incidence risk, meta-analysis

Introduction

Lung cancer, with persistently high global incidence and mortality, remains a major threat to human health. According to GLOBOCAN 2020, approximately 2.21 million new lung cancer cases occurred worldwide and about 1.8 million deaths, with an age-standardized incidence rate of 22.4 per 100,000 and a mortality rate of 18.0 per 100,000 [1]. Smoking is widely recognized as a predominant risk factor for lung cancer, with smokers exhibiting 13-fold increased risk of developing lung cancer than non-smokers [2]. Although substantial progress has been made in the prevention and control of lung cancer among smokers, the disease burden in non-smokers has become increasingly prominent [3]. A 2023 review reported over 20,000 lung cancer-related deaths among never-smokers in the United States, ranking it as the eighth leading cause of cancer-related death in this group. Globally, lung cancer in non-smokers is currently the fifth leading cause of cancer-related death [4].

Occupational exposure is a key risk factor for lung cancer in non-smokers, such as exposure to asbestos, which is widely used in industries

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like automotive, chemical, and construction. Asbestos exposure increases the risk of lung cancer by 5 to 10 times compared to the general population [5]. Beyond occupational environments, indoor environmental pollution, due to its chronic and widespread exposure in residential settings, has become a critical health risk [6]. Major sources of indoor air pollution include tobacco products (e.g., secondhand smoke, heated tobacco products), decoration materials (e.g., radon and formaldehyde), and kitchen fumes (complex decomposition products released by high-temperature cooking) [7-10].

Despite numerous studies exploring the relationship between indoor environmental pollution and lung cancer risk in non-smokers, findings vary considerably. Discrepancies arise from differences in study design, population characteristics, pollutant measurement methods, and geographical regions. Small sample sizes and inadequate adjustment for confounders limit the reliability of some findings. Furthermore, inconsistencies in pollutant measurement standards across studies also hampers comparability, complicating efforts to quantify the true effect of indoor pollution. This meta-analysis aims to identify the indoor environmental pollution risk factors for lung cancer in non-smokers, quantify their effect size, and provide a scientific basis for early clinical intervention and the development of targeted prevention strategies to reduce disease burden in non-smokers.

Literature search and review methods

Search strategy

This meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. The protocol was registered in PROSPERO (Registration No.: CRD42025100-8009). A comprehensive literature search was performed in English databases, including PubMed, Embase, Medline, Web of Science, and Cochrane Library. The search covered studies published from March 2005 to March 2025. A combination of Medical Subject Headings (MeSH) and free-text terms, along with a citation tracking method, was used. The search terms included: “Air Pollution, Indoor”, “Air Pollution”, “Working Conditions”, “Non-Smokers”, “Lung Neoplasms”, “Small Cell Lung Carcinoma”, and “Carcinoma, Non-Small-Cell Lung”. Detailed search strategies for each database are provided in Appendix 1.

Inclusion criteria

a. Patients with primary lung cancer; b. Cohort studies, retrospective studies, case-control studies; c. The outcome measured was the incidence of lung cancer in non-smokers; d. The study reported a risk estimate (e.g., odds ratio or relative risk) with a 95% confidence interval.

Exclusion criteria

a. Reviews, meta-analyses, case reports, animal studies; b. Inclusion of participants who smoked; c. No assessment of indoor environmental pollution factors; d. Inability to extract or calculate effect size data; e. Duplicate publications; f. Low methodological quality.

Literature screening

A double-blind method was employed for literature screening. Two researchers (Yan Hong and Haihui Xie) independently reviewed all retrieved literature according to the inclusion and exclusion criteria. This step ensured the objectivity and accuracy of the screening process. For studies meeting the inclusion criteria, key data were extracted, including first author, publication year, patient age, study design type, sample size, and indicators related to lung cancer risk factors in non-smoker. Data were conducted using a standardized, pre-designed form to ensure accuracy and completeness. Any discrepancies during the screening or extraction process were resolved through consultation with a third researcher (Jang Kwang-Sim). Ethics approval was waived as this study did not involve any human participants or animal experiments.

Literature quality assessment

The methodologic quality of the included studies was assessed using criteria recommended by the Agency for Healthcare Research and Quality (AHRQ) [11]. These criteria are applicable to various study designs, including randomized controlled trials, controlled clinical trials, cohort studies, case-control studies, case series, and cross-sectional studies. Risk of bias

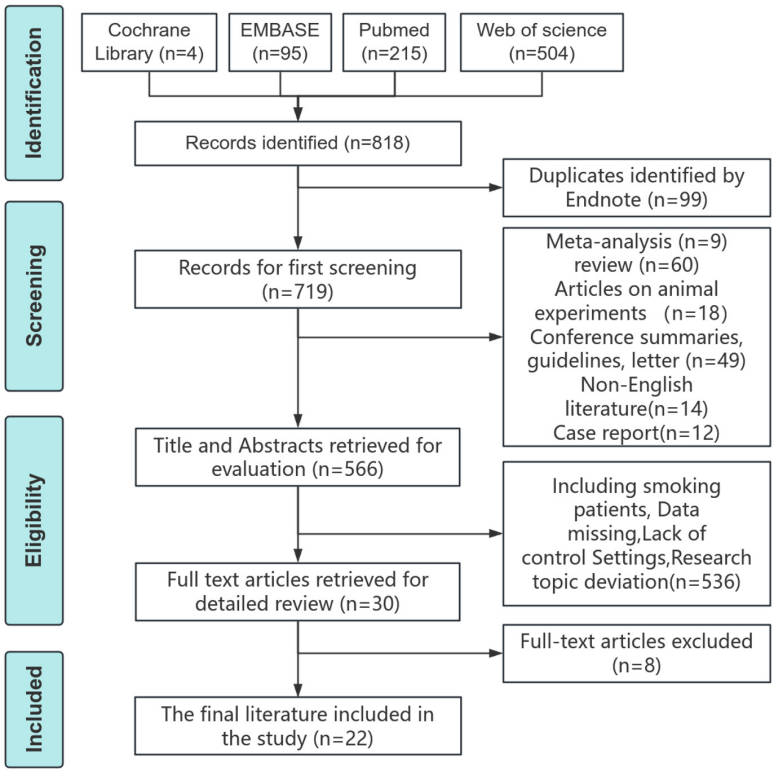

Figure 1. Flow chart of literature inclusion.

was evaluated across five domains: selection bias, performance bias, attrition bias, detection bias, and reporting bias. Each domain contains specific assessment items tailored to relevant study designs. Studies were scored as follows: 1-3 points indicated low quality; 4-7 points indicated moderate quality; and 8-11 points indicated high quality.

Statistical methods

Meta-analysis was performed using STATA 12.0 and RevMan 5.3 software. When more than two studies reported on the same risk factor, relevant data were extracted and pooled. For binary categorical variables, odds ratios (OR) and their 95% confidence intervals (CI) were used to estimate the association between indoor environmental pollutants and lung cancer risk in non-smokers. Statistical significance was defined as $P < 0.05$. Heterogeneity among studies was assessed using the Q test and I^2 statistic. I^2 value > 50% and $P < 0.1$ indicated substantial heterogeneity, in which case a random-effects model was applied. If heterogeneity was not significant ($P \geq 0.1$ and $I^2 \leq 50\%$), a fixed-effects model was used.

Results

Characteristics of included studies

A preliminary search of the literature in Cochrane, PubMed, Web of Science, and EMBASE identified 818 potentially eligible studies. Ultimately, 22 studies were included in the analysis [12-33]. The literature selection process is shown in **Figure 1**. The 22 included studies were conducted in multiple countries (India, China, Singapore, South Korea, Spain, Denmark, France, and several other European countries). After data extraction, more than two studies reported the same indoor environmental pollution factors associated with lung cancer risk in never-smokers, specifically: residential radon exposure, environmental tobacco smoke (ETS), cooking fumes exposure, cooking methods, and use of solid fuels (**Table 1**).

Literature quality assessment

Among the 22 included studies, 8 were rated as high quality [13, 14, 17, 20, 23, 24, 28, 29] and 14 as moderate [12, 15, 16, 18, 19, 21, 22, 25-27, 30-33], with no low-quality studies (**Figure 2**). The quality assessment results are presented in **Figure 3**.

Analysis of indoor environmental pollution factors

Residential radon exposure: A total of 7 studies [13, 20, 23-26, 30] concluded that residential radon exposure is a risk factor for lung cancer in non-smokers. Substantial heterogeneity was observed ($I^2 = 75.4\%$, $P < 0.001$, $Q = 24.32$), thus a random-effects model was applied. The pooled analysis demonstrated that radon exposure significantly increased lung cancer risk in non-smokers (OR = 1.82, 95% CI: 1.31-2.54, $Z = 3.549$, $P < 0.001$), as shown in **Figure 4A**. Sensitivity analysis showed that exclusion of any single study did not significantly affect the

Table 1. Includes specific characteristics of the study

Num	Author	Years	Country of publication	Study type	Age	Total sample size	Non-smoking population	Influencing factors
1	Behera D, et al. [12]	2005	India	Case - control study	Cases: 30-80 years old (52.5±11.1), Controls: 31-70 years old (43.5±15.5)	67 cases, 46 controls	50 cases, 43 controls	①, ②, ③
2	Darby S, et al. [13]	2005	Multiple European countries (Austria, Czech Republic, Finland, France, Germany, Italy, Spain, Sweden, UK, etc.)	Case - control study	/	7148 cases, 14208 controls	/	④
3	Yu IT, et al. [14]	2006	Hong Kong, China	Population - based case - control study	Case group: 63.3 (30-79) years old; Control group: 64.1 years (30-79 years)	485 cases	200 cases	⑨, ⑱
4	Vineis P, et al. [15]	2007	Multiple European countries (Sweden, Denmark, Norway, Netherlands, UK, France, Germany, Spain, Italy, Greece)	Prospective study	35-74 years old	Over 520,000 cases	/	③, ⑥, ⑦
5	Sapkota A, et al. [16]	2008	India	Multicentric case - control study	Age less than 80 years for both cases and controls	799 cases, 718 controls	177 cases, 149 controls	⑧
6	Wang XR, et al. [17]	2009	Hong Kong, China	Case - control study	Case group: SD: (65.4±10.6) years old, 30-79 years old Control group: SD: (64.8±10.6) years old, 30-79 years old	601 cases	Control group: 213 cases; Study group: 292 cases	③, ⑤, ⑨, ⑩
7	Clément-Duchêne C, et al. [18]	2009	France	Prospective descriptive study	Never smokers 33-84 years old; former smokers 39-91 years old; current smokers 34-89 years old	1493 cases	67 cases	③, ⑦
8	Tang L, et al. [19]	2010	Singapore	Case - control study	Case group: 65.9±11.9 years old; Control group: 64.1±12.3 years old	2281 cases	Control group: 1375 cases; Study group: 434 cases	⑨, ⑪
9	Bräuner EV, et al. [20]	2012	Denmark	Prospective cohort study	Enrolled at 50-64 years old (Median age 56.1 years old, Interquartile range 50.7-64.1 years old)	52692	/	④
10	Mu L, et al. [21]	2013	China	Case - control study	Age ≥ 20 years old	865 cases	Control group: 218 cases; Study group: 164 cases	②, ③, ⑤, ⑫, ⑬
11	Xue X, et al. [22]	2013	China	Hospital - based case - control study	Case group: 53.05±4.48 years old; Control group: 53.61±4.13 years old	820 cases	410 cases	⑤, ⑭
12	Ruano-Ravina A, et al. [23]	2014	Spain	Hospital - based case - control study	Age range > 30 years old	792 cases	33 cases	④, ⑭
13	Torres-Durán M, et al. [24]	2014	Spain	Multicenter hospital - based case - control study	Case group 34-87 years old, Control group 43-90 years old	580 cases	Control group: 329 cases; Study group: 192 cases	③, ④
14	Tse LA, et al. [25]	2014	Hong Kong, China	Case - control study	Male cases and controls: 30-79 years old; Female cases and controls: 30-79 years old	1173 cases	345 cases	③, ④, ⑤, ⑨, ⑩, ⑮
15	Lorenzo-González M, et al. [26]	2019	Spain	Case - control study	Cases: Median age 71 years old (Interquartile range 62-78), Controls: Median age 65 years old (Interquartile range 57-74)	523 cases, 892 controls	1415 cases	④
16	Wong JYY, et al. [27]	2019	China	Population - based case - control study	Mean age: 54.7 years old	1524 cases	1031 cases	②, ⑯
17	Chen TY, et al. [28]	2020	Taiwan, China	Case - control study	Case group: 58.55 years old; Control group: 58.62 years old	2604 cases	1302 cases	⑤, ⑱

18	Li J, et al. [29]	2020	China	Prospective cohort study	Enrolled at 23-79 years old (56.5±9.5 years old)	23415 cases	1046 cases	③
19	Park EJ, et al. [30]	2020	Korea	Multi - center matched case - control study	Median age: 64 years old	1038 cases	519 cases	③, ④
20	Zheng Lingling, et al. [31]	2011	China	Case-control study	Cases and controls were frequency-matched by age (±3 years)	612 cases	306 cases	③, ⑥, ⑩, ⑲, ⑳, ㉑, ㉒, ㉓
21	Daojuan Li, et al. [32]	2022	China	Retrospective observational study	68.91±11.21 years old (65-69 years old)	23,674 cases	10,913 cases	㉓, ㉔, ㉕, ㉖
22	Rohit Shirgaonkar, et al. [33]	2024	India	Case-control study	21-80 years old	442 cases	145 cases	①, ⑥, ⑩, ⑲, ㉕, ㉖

Note: ① Biomass fuel exposure; ② Solid fuel exposure; ③ Indoor environmental tobacco exposure; ④ Indoor radon exposure; ⑤ Cooking fume exposure; ⑥ Residence proximity to busy traffic streets; ⑦ Asbestos exposure; ⑧ Indoor solid fuel use; ⑨ Dietary factors; ⑩ Family history of cancer; ⑪ Indoor incense use; ⑫ Housing ventilation; ⑬ PM concentration; ⑭ Gene polymorphism; ⑮ Occupational exposure; ⑯ Geological strata; ⑰ No use of range hood; ⑱ Cooking method; ⑲ BMI; ⑳ Decoration-related irritant odor; ㉑ Pesticide use; ㉒ Fried food consumption; ㉓ Gender; ㉔ Age; ㉕ Residential pollution level; ㉖ History of lung-related diseases.

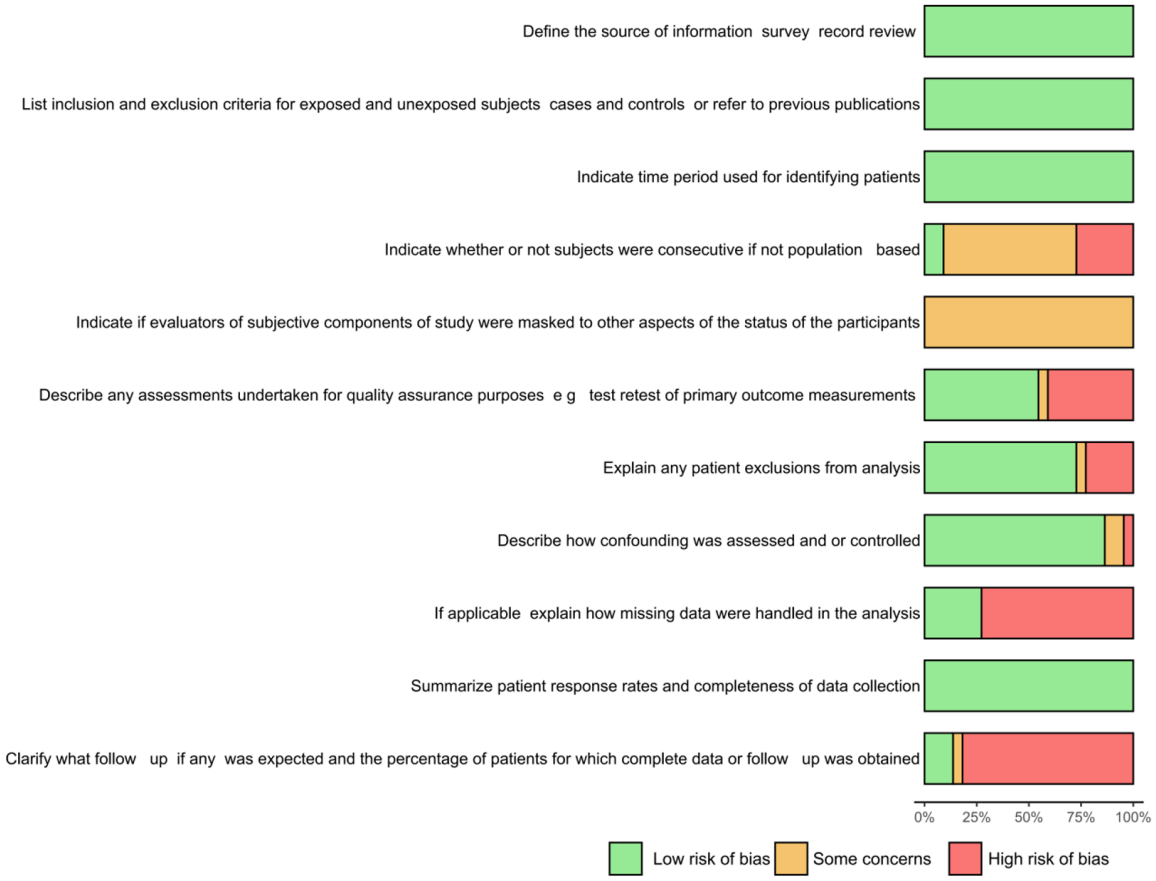

Figure 2. AHRQ literature quality assessment. AHRQ: Agency for Healthcare Research and Quality.

overall effect size, confirming the robustness of the meta-analysis results (**Figure 4B**). Begg's test indicated no significant risk of publication bias (P = 0.764) (**Figure 4C**).

Environmental Tobacco Smoke (ETS) exposure: A total of 9 studies [12, 15, 17, 18, 21, 24, 25, 29, 30] identified indoor ETS as a risk factor for lung cancer in non-smoking patients. Substantial heterogeneity was observed (I^2 = 72.6%, P < 0.001, Q = 27.48), and a random effects model was used for the analysis. Among the included studies, two studies focused exclusively on female patients [12, 18], while the remaining 8 studies did not specify gender restrictions. Subgroup analysis revealed that the pooled odds ratio (OR) for female non-smokers exposed to ETS was 5.30 (95% CI: 1.47-19.10, z = 2.550, P = 0.011). For studies without gender limitation, the pooled OR was 1.63 (95% CI: 1.19-2.25, z = 2.597, P < 0.001). Overall, the combined analysis indicated a significant association between ETS exposure and lung cancer risk in non-smokers (OR = 1.96, 95% CI: 1.36-2.25, Z = 4.128, P < 0.001), as shown in **Figure 5A**. Sensitivity analysis showed that exclusion of any single study did not significantly affect the overall effect size, with all results remaining statistically significant, suggesting good robustness of the model (**Figure 5B**). Begg's test (P = 0.754) and Egger's test (P = 0.290) showed no significant evidence of publication bias (**Figure 5C**).

Cooking fumes exposure: Six studies [14, 17, 21, 22, 25, 28] reported that indoor cooking fumes exposure is a risk factor for lung cancer in non-smokers. No heterogeneity was observed across the studies (I^2 = 0.0%, P = 0.817, Q = 2.11), as shown in (**Figure 6A**). Meta-analysis yielded a pooled OR of 3.68 (95% CI: 2.67-5.07, Z = 7.953, P < 0.001), indicating a significant association. Sensitivity analysis confirmed the stability of the results, as exclusion of any individual study did not significantly alter the overall findings (**Figure 6B**). Publication bias was not detected by Begg's test (P = 0.260) or Egger's test (P = 0.239), supporting the reliability of the results, the funnel plot

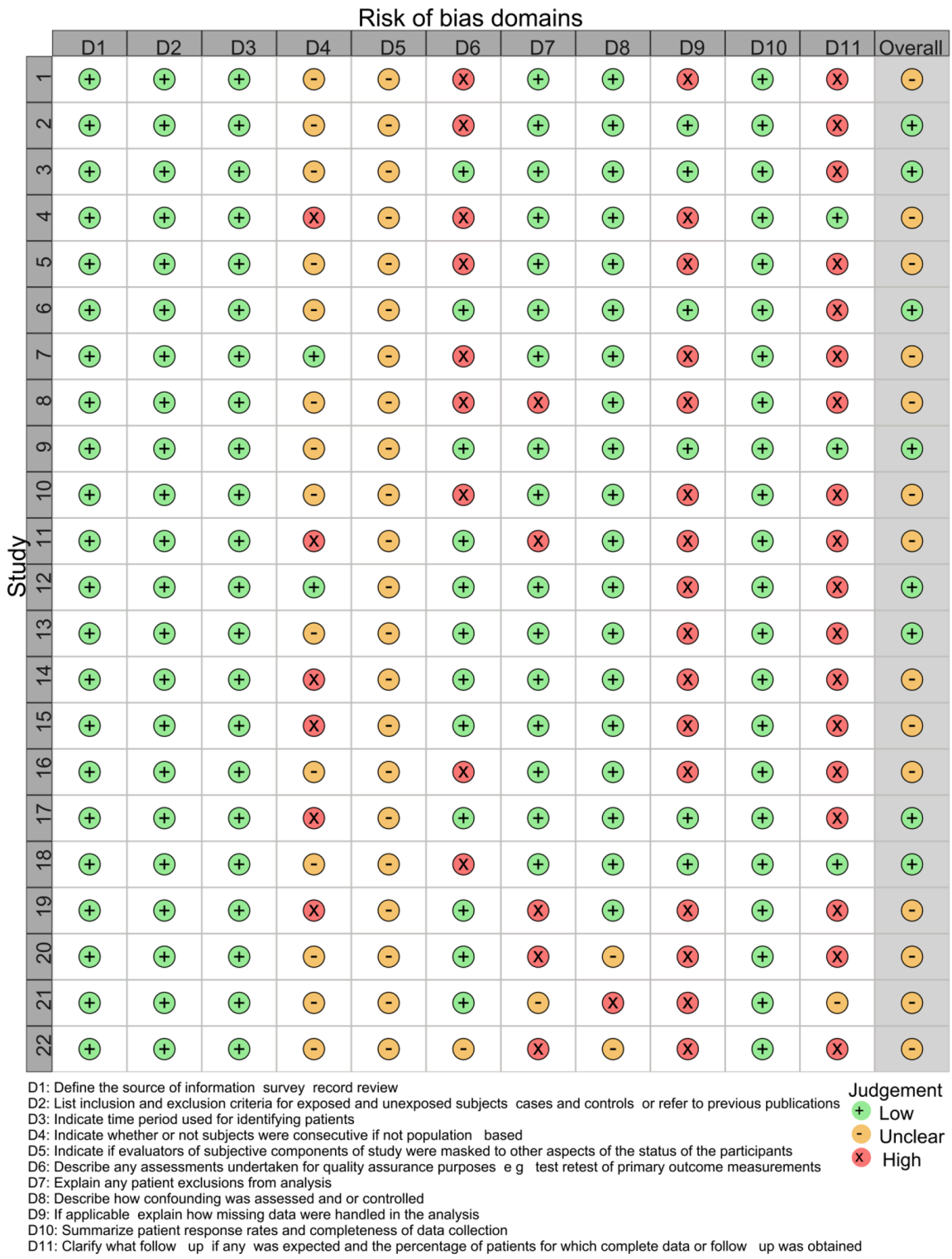

Figure 3. Specific quality evaluation results of the 22 included studies. Study1-22 corresponds to literature [12-33] in turn, and D1 to D11 are 11 evaluation items.

results show some degree of symmetry, as shown in (**Figure 6C**).

Cooking method: Two studies [14, 21] reported the effect of cooking methods on the incidence

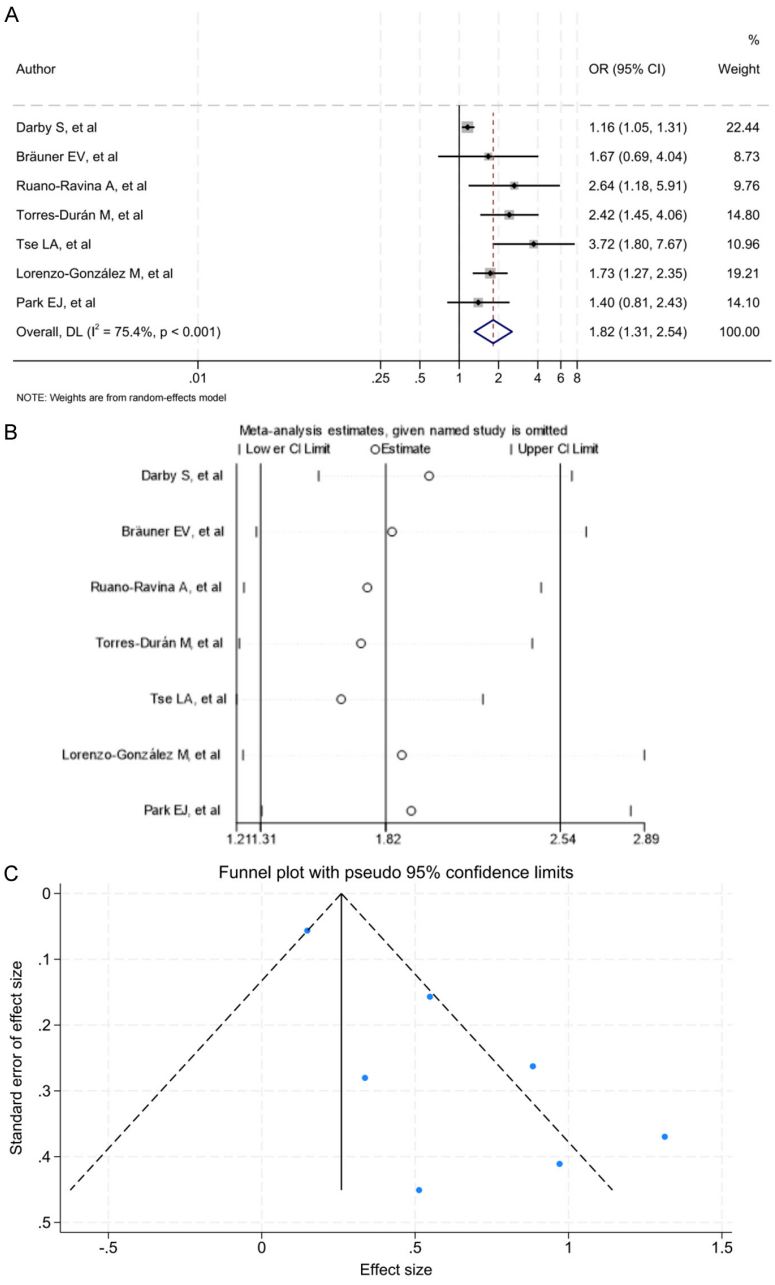

Figure 4. Meta-analysis results for residential radon exposure and lung cancer risk in never-smokers. A. Forest map for meta-analysis of residential radon exposure factors; B. Sensitivity analysis of residential radon exposure; C. Funnel plot of factors of residential radon exposure. Note: OR: Odds Ratio; CI: Confidence Interval; DL: DerSimonian and Laird method; I^2: I-squared statistic.

of lung cancer. Both studies reported that deep-frying and stir-frying cooking methods were associated with lung cancer risk in non-smoking patients. Subgroup analysis was conducted on cooking methods. The combined risk of deep-frying was 1.60 (95% CI: 0.72-3.52), with significant heterogeneity (I^2 = 80.8%, P = 0.023, Q = 10.32). The combined OR of stir-frying was 1.12 (95% CI: 1.07-1.17), with no significant heterogeneity (I^2 = 0.0%, P = 0.884, Q = 0.22), as shown in (**Figure 7A**). Egger's test (P = 0.434) indicated no evidence of publication bias, suggesting that the results are statistically robust. Sensitivity analysis showed that excluding one of the studies did not affect the stability of the combined results, as shown in (**Figure 7B**).

Use of solid fuels: Five studies [12, 16, 21, 27, 33] reported that the use of solid fuels was a significant risk factor for lung cancer in non-smokers. Two of these studies [12, 27] focused specifically on female patients. Subgroup analysis revealed that the pooled OR for female patients was 6.30 (95% CI: 1.46-27.13, z = 2.469, P = 0.014). For studies without gender restriction, the pooled OR was 4.60 (95% CI: 2.95-7.19, z = 6.71, P < 0.001). The overall combined risk across all studies was 5.54 (95% CI: 3.15-9.72, z = 5.96, P < 0.001). Significant heterogeneity was observed among the included studies (I^2 = 59.5%, P = 0.043), and a random effects model was used (**Figure 8A**). Sensitivity analysis confirmed the stability and reliability of the findings, with results remaining significant upon exclusion of individual studies (**Figure 8B**). No publication bias was detected based on Begg's test (P = 0.806) and Egger's test (P = 0.561). The funnel plot results show some symmetry, suggesting a low risk of publication bias, as shown in (**Figure 8C**).

Other influencing factors

Residential environmental pollution: Four studies [15, 31-33] evaluated the association

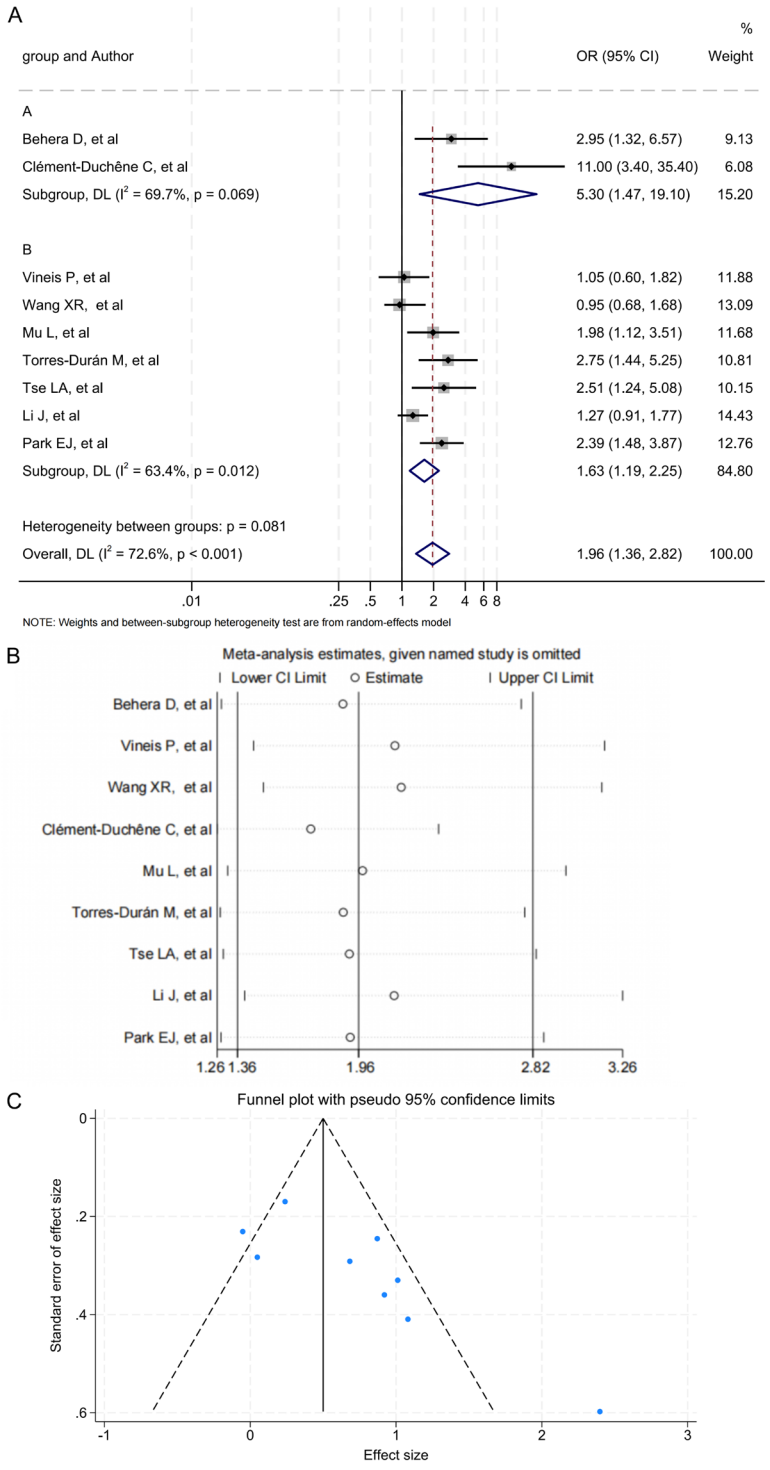

Figure 5. Meta-analysis results for ETS exposure. A. Forest map of meta-analysis of environmental tobacco exposure factors; B. Analysis of environmental tobacco exposure sensitivity; C. Funnel diagram of environmental tobacco exposure. Note: Group A: A subgroup of female non-smoking lung cancer patients; Group B: unrestricted gender subgroup. OR: Odds Ratio; CI: Confidence Interval; DL: DerSimonian and Laird method; I^2: I-squared statistic.

between residential environmental pollution and lung cancer risk in non-smokers. The pollutants included nitrogen dioxide (NO_2), particulate matter, polycyclic aromatic hydrocarbons (PAHs), and heavy metals. No significant heterogeneity was observed across the studies (I^2 = 24.7%, P = 0.263, Q = 9.83), therefore a fixed effect model was applied (**Figure 9A**). The pooled OR was 1.70 (95% CI: 1.35-2.14, z = 4.56, P < 0.001). Sensitivity analysis confirmed the robustness of the findings (**Figure 9B**), and no publication bias was observed (Begg's test: P = 0.308; Egger's test: P = 0.344), supporting the credibility of the pooled results.

Indoor occupational exposure: Indoor occupational environments is another source of carcinogenic risk. Exposure to hazardous substances such as formaldehyde and benzene, often released from asbestos or decoration materials, is a risk factor for lung cancer. Among the 22 included studies, only two studies [25, 33] explicitly reported an association between indoor chemical-related occupational exposure and lung cancer incidence in non-smokers. No significant heterogeneity was observed among the studies (I^2 = 0.0%, P = 0.892, Q = 0.02), ratifying the use of a fixed-effect model. The pooled OR was 2.92 (95% CI: 1.71-4.97, z = 3.93, P < 0.001) (**Figure 10A**). Sensitivity analysis further supported the robustness of the results, demonstrating that the association remained stable upon exclusion of individual studies (**Figure 10B**).

Low body mass index: In addition, two studies [31, 33] identified low body mass index (BMI <

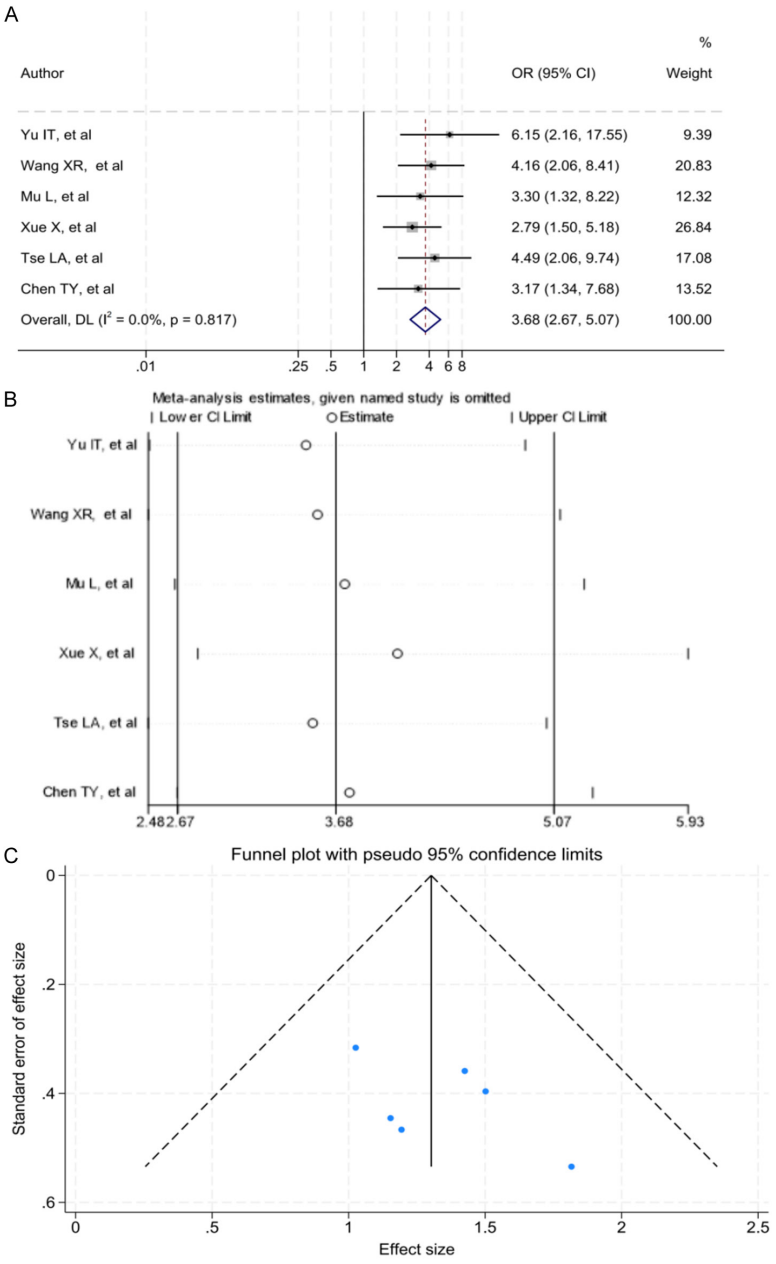

Figure 6. Meta-analysis results for cooking fumes exposure. A. Forest map of cooking fumes exposure meta-analysis; B. Analysis of cooking fumes sensitivity; C. cooking fumes funnel diagram. Note: OR: Odds Ratio; CI: Confidence Interval; DL: DerSimonian and Laird method; I^2: I-squared statistic.

18.5) as a potential risk factor for lung cancer in never-smokers. The pooled OR was 2.86 (95% CI: 1.64-4.97), with no significant heterogeneity (I^2 = 0.0%, P = 0.415, Q = 2.00), see (**Figure 11A**). Sensitivity analysis showed that the combined results were stable, as shown in (**Figure 11B**).

Discussion

According to data from the Chinese Cancer Center, lung cancer accounts for approximately 733,000 new cases, with 591,000 deaths annually, ranking first in both cancer incidence and mortality in China [34]. Environmental pollution is a major contributor to lung cancer risk. While occupational exposure is well recognized, indoor air pollution in residential environments is also a critical but often overlooked factor [35]. Research indicates that up to 68% of human diseases may be related to indoor air pollution [36]. This meta-analysis systematically assessed the relationship between indoor environmental pollution and lung cancer risk in non-smokers. The results indicate that indoor exposures, such as residential radon exposure, ETS, cooking fumes, solid fuel use, and high-temperature cooking methods, are all associated with an increased risk of lung cancer in non-smokers.

Residential radon exposure

Radon (Rn) is a colorless, odorless, and tasteless radioactive inert gas classified as a Group 1 carcinogen by the International Agency for Research on Cancer under the World Health Organization (WHO). It is currently recognized as the second leading cause of lung cancer after smoking, accounting for about 48% of indoor radiation exposure [37, 38].

Radon originates naturally from the radioactive decay of uranium in soil and rocks. It can infiltrate indoor environments through cracks and

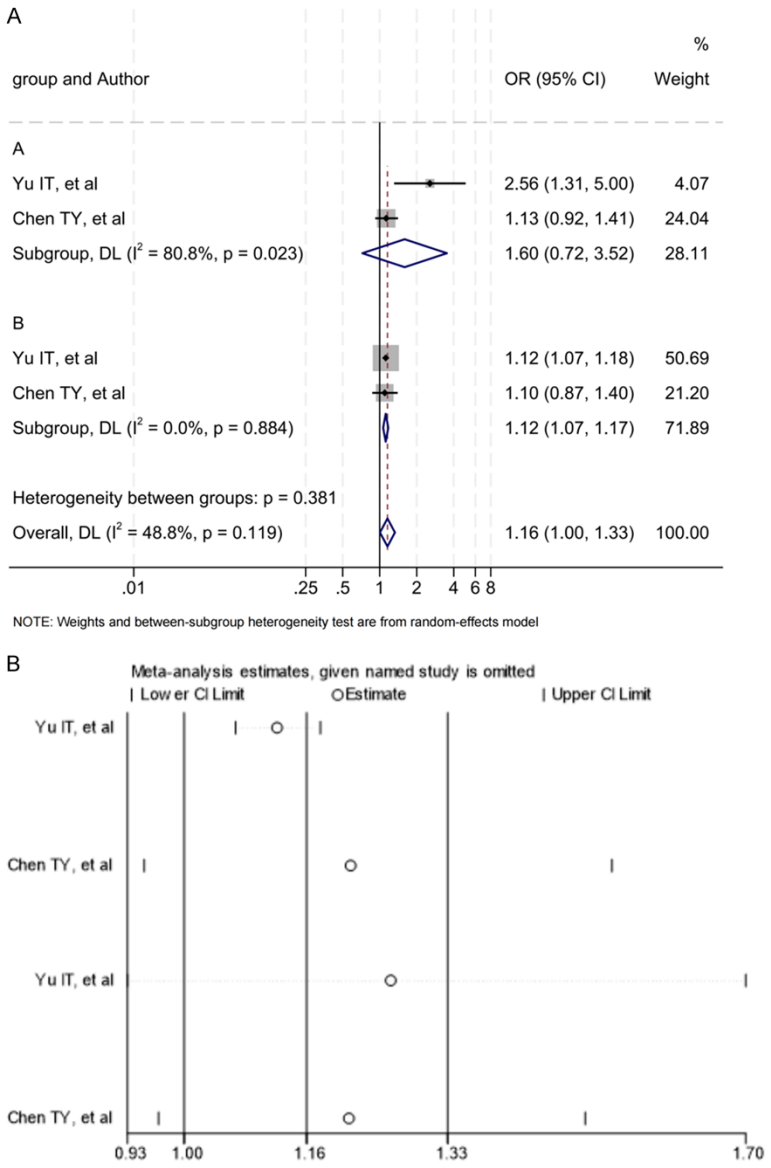

Figure 7. Meta-analysis results for cooking method. A. Forest map of cooking method meta-analysis; B. Analysis of cooking method sensitivity. Note: Group A: deep - frying; Group B: stir - frying. OR: Odds Ratio; CI: Confidence Interval; DL: DerSimonian and Laird method; I^2: I-squared statistic.

porous building materials, leading to high concentrations in enclosed areas, such as homes, schools, and workplaces [39]. An indoor radon survey covering 31 provincial capital cities in China reported an arithmetic mean (AM) and geometric mean (GM) indoor radon concentration of 65 Bq/m^3 and 55 Bq/m^3, respectively. Among them, 13.6% of the surveyed residences exceeded 100 Bq/m^3, and 0.6% exceeded 300 Bq/m^3. It is estimated that indoor radon exposure accounts for approximately 150,795 lung cancer deaths in China annually, constituting 20.30% of all lung cancer deaths (95% CI: 20.21%-20.49%) [40].

According to the WHO, inhaled radon and its radioactive decay products can deposit on the bronchial epithelium, emitting heavy charged particles that damage cellular DNA, leading to uncontrolled cell proliferation and the formation of bronchopulmonary tumors [41]. Although cellular repair mechanisms exist, persistent exposure may overwhelm these defenses and increase cancer risk. A study by Ruano-Ravina, et al. [23] reported that the deletion of GSTM1 and GSTT1 genes can increase the risk of lung cancer caused by radon exposure. At the same exposure level, the deletion of these genes is associated with a higher risk of lung cancer, which further escalates with increasing radon concentration. Based on available evidence, the WHO recommends that indoor radon levels not exceed 300 Bq/m^3 and encourages national programs to adopt a target reference level of 100 Bq/m^3 to better protect public health [42].

Environmental tobacco smoke exposure

Tobacco smoke contains over 4,000 chemical compounds, including tar, carbon monoxide, and oxidative gases. Over 100 substances are harmful to human health, including approximately 50-60 known carcinogens, several mutagens, and numerous irritants or toxic substances [43]. Nicotine, a biologically active alkaloid and sympathomimetic, is the primary driver of addiction. It is absorbed primarily through inhalation and undergoes metabolic transformation in the body [44]. Combustion of tobacco generates a complex mixture of haz-

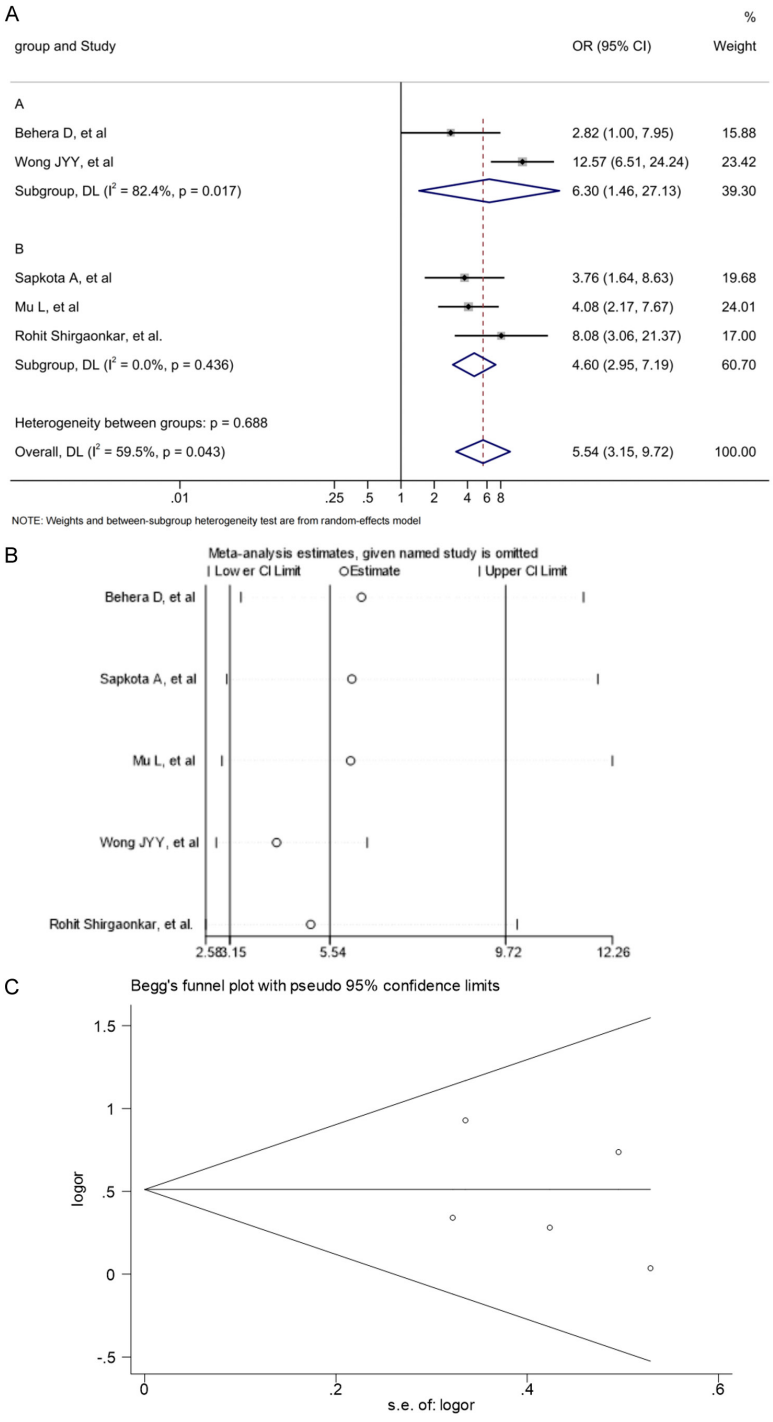

Figure 8. Meta-analysis results for solid fuel use and lung cancer risk. A. Forest map of meta-analysis of solid fuel use; B. Sensitivity analysis of solid fuel use factors; C. Funnel diagram of solid fuel usage. Note: OR: Odds Ratio; CI: Confidence Interval; DL: DerSimonian and Laird method; I^2: I-squared statistic.

ardous gases, such as carbon monoxide, nitrogen oxides, sulfur-containing gases, hydrogen cyanide, and other volatile organic compounds that irritate mucous membranes and damage the respiratory tract. Carbon monoxide reduces hemoglobin's oxygen-carrying capacity, and components like formaldehyde can be carcinogenic [45].

For non-smokers, exposure to tobacco smoke occurs primarily through passive or secondhand smoke (SHS), which is widely recognized as a major indoor air pollutant and a significant cause of preventable morbidity and mortality worldwide. It contains numerous hazardous constituents, including tar, ammonia, nicotine, particulate matter ≤ 2.5 μm (PM2.5), polonium-210, and other toxic chemicals [46]. Secondhand smoke consists of mainstream smoke (exhaled by the smoker) and sidestream smoke (produced by the burning of the cigarettes). Notably, sidestream smoke contains significantly higher concentrations of many toxicants compared to mainstream smoke: carbon monoxide (5-fold), tar and nicotine (3-fold), ammonia (46-fold), and nitrosamines (50-fold) [47].

In this study, the pooled odds ratio for lung cancer associated with ETS among non-smoking females was 5.30, indicating a markedly elevated risk. Studies have shown that in female never-smokers, cumulative exposure to ETS is associated with a time-dependent accumulation of tobacco-specific carcinogens, especially 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) and its major metabolites 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL) and NNAL-

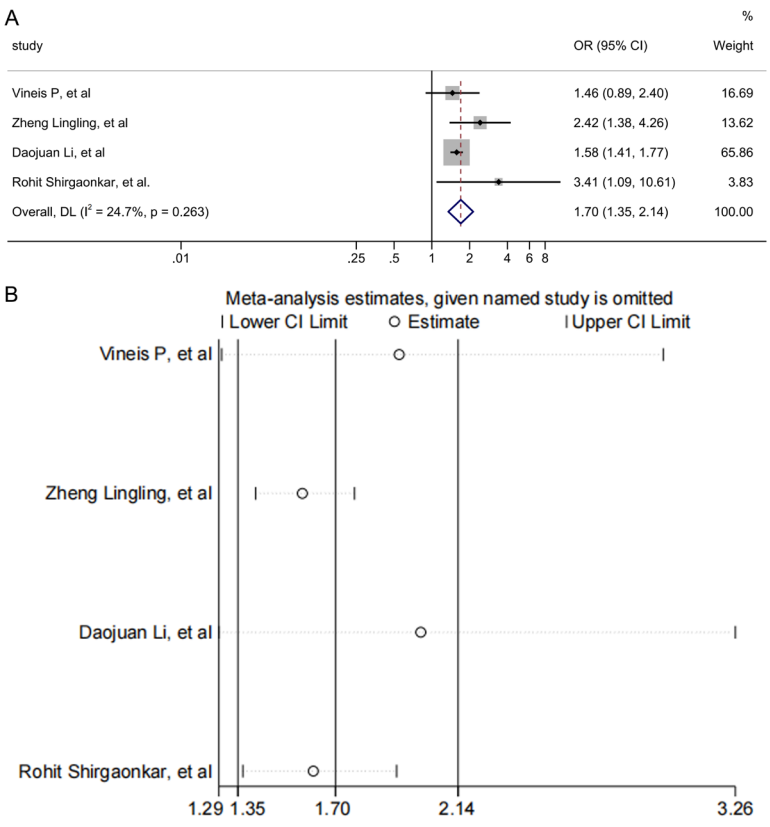

Figure 9. Meta-analysis results for environmental pollution around residential areas. A. Meta-analysis of environmental pollution around the residential area - Forest map; B. Environmental pollution around the residence. Note: OR: Odds Ratio; CI: Confidence Interval; DL: DerSimonian and Laird method; I^2: I-squared statistic.

glucuronides (NNAL-Glucs). These metabolites are potent lung carcinogens and are primarily metabolized in the liver and excreted in urine; however, under chronic ETS exposure, their accumulation in the human body can reach carcinogenic thresholds. The carcinogenicity of NNK and NNAL arises from their ability to form DNA adducts that induce mutations in critical genes such as TP53 and KRAS, leading to malignant transformation of bronchial epithelial cells. NNAL, with its long biological half-life, can persist in the body for extended periods, especially in women who may experience higher cumulative exposure due to time spent in indoor environments [48].

In female never-smokers, especially those residing in households with regular indoor smoking, the risk of lung adenocarcinoma exhibits a significant dose-dependent increase with prolonged exposure and higher internal accumulation of carcinogens. This underscores the urgent need for stricter tobacco control policies in shared indoor environments.

High-frequency cooking fumes exposure

Six studies reported that indoor cooking fume exposure was a risk factor for lung cancer in non-smoking patients, with a poled OR of 3.68 (95% CI: 2.67-5.07). Previous studies have reported that over 60% of non-smoking women diagnosed with lung cancer have a history of long-term exposure to kitchen fumes [49]. There is a dose-response relationship between exposure to kitchen fume pollution and the risk of lung cancer in female never-smokers. The study by Xue, et al. [22] further elucidated that individuals carrying the homozygous genotype of 326 Cys/Cys of the hOGG1 gene exhibited a significantly increased risk of lung adenocarcinoma (OR = 1.54). The gene-environment interaction analysis revealed that the Ser/Cys and Cys/Cys genotypes at codon 326 of the hOGG1 gene, when combined with exposure to cooking fumes, elevated the risk of lung adenocarcinoma, with the Cys/Cys genotype conferring a higher risk of lung adenocarcinoma under cooking fume exposure (OR = 2.79). These findings indicate that genetic polymorphisms may modulate individual susceptibility to the carcinogenic effects of cooking fume exposure, particularly among non-smoking women. In addition, a study has associated poor ventilation (AHR = 1.49; 95% CI: 1.15, 1.95) and exposure to cooking fumes to an increased risk of lung cancer [50]. However, accurately quantifying cumulative exposure to cooking fumes remains a challenge. In addition, fume exposure often coexists with exposure to combustion byproducts from fuel sources, making it difficult to isolate the independent effect of cooking fumes. In recognition of this, the International Agency for Research on Cancer (IARC) has classified cooking fumes as a Group 2A carcinogen [51]. Installation and proper use of range hoods can

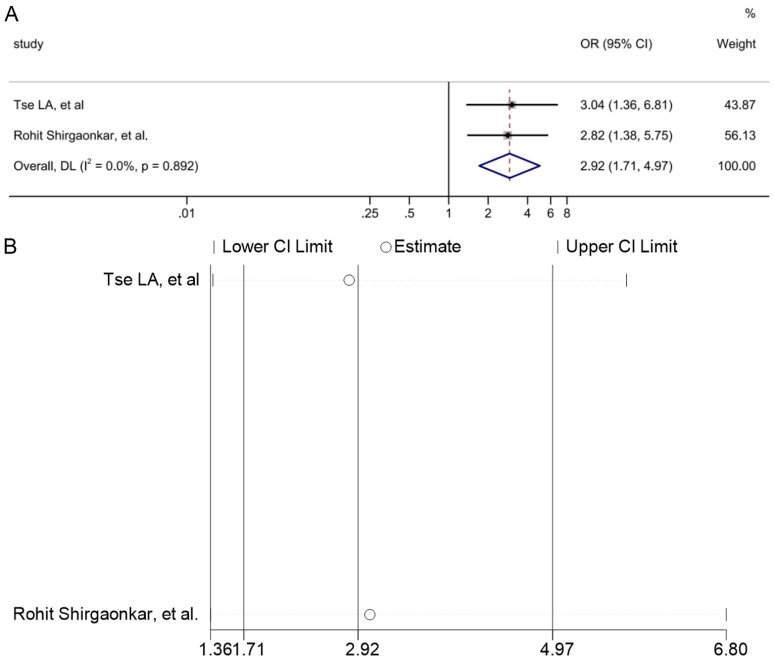

Figure 10. Meta-analysis results for indoor occupational exposure. A. Meta-analysis forest plot of indoor occupational exposure; B. Indoor occupational Exposure Sensitivity Analysis. Note: OR: Odds Ratio; CI: Confidence Interval; DL: DerSimonian and Laird method; I^2: I-squared statistic.

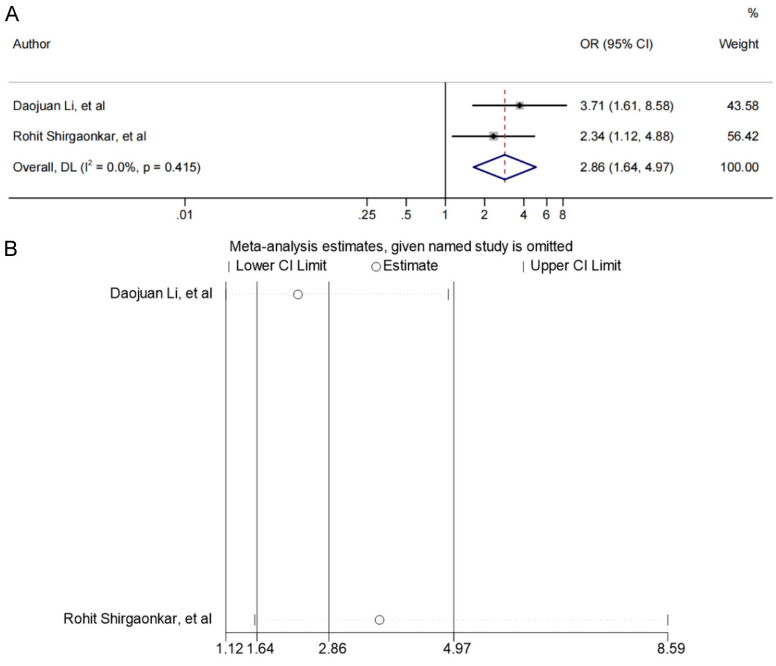

Figure 11. Meta-analysis results for low body mass index. A. Meta-analysis forest plot of low body mass index; B. Low body mass index Sensitivity Analysis. Note: OR: Odds Ratio; CI: Confidence Interval; DL: DerSimonian and Laird method; I^2: I-squared statistic.

reduce indoor fume concentrations and may play a protective role.

Cooking methods

The results of this study suggest that both deep-frying and stir-frying are associated with varying degrees of increased lung cancer risk in non-smokers. High-temperature deep frying produces substances such as heterocyclic amines (HCAs) and polycyclic aromatic hydrocarbons (PAHs). HCAs have been shown to possess carcinogenic properties in animal models, while PAHs - organic compounds containing two or more fused benzene rings - include several well-established human carcinogens [52].

During stir-frying, when cooking oil reaches a temperature of approximately 150°C, acrolein becomes the predominant volatile component released, which is a potent mucosal irritant affecting the nasal passages, eyes, and respiratory tract. At higher temperature at 350°C, in addition to acrolein, oil mist aggregates are produced, which are capable of inducing chronic toxicity and have been implicated in the development of malignancies in the respiratory and digestive systems. Common household cooking oils such as canola oil and soybean oil begin to emit significant amounts of oil mist when heated to 270°C to 280°C. The smoke is difficult to dissipate and can be inhaled over long periods, contributing to health risks [53].

Solid fuel use

This study identified solid fuel use as a key risk factor for lung cancer in non-smokers, with a pooled OR of 5.08 (95% CI: 2.58-10.00). Solid fuels include

biomass fuels such as plant material, animal dung, wood, charcoal, and crop residues, as well as coal. Combustion of these fuels releases a range of toxic pollutants, including carbon oxides, nitrogen oxides, sulfur oxides, incompletely combusted hydrocarbons, PM, and polycyclic organic compounds.

Biomass smoke is particularly rich in inhalable particles, primarily PM10 (≤ 10 μm) and PM2.5 (≤ 2.5 μm) [54]. The four studies included in this analysis were conducted in China and India, two developing countries where many rural kitchens lack proper ventilation, exacerbating the concentration of pollutants. Quantitatively, the PM concentrations from cooking with solid fuels can reach levels as high as 1000 μg/m^3, greatly exceeding recommended air quality standards.

Although biomass smoke does not contain nicotine, its composition and health effects are comparable to those of tobacco smoke. Oxidative stress in the airways and alveoli stimulates alveolar macrophages and damages the epithelial membranes, leading to the activation of inflammatory cells and inflammation. Furthermore, alveolar macrophages ingesting carbon particles from smoke may increase the risk of respiratory infections. The pathogenic pathway leading to lung cancer induced by solid fuel smoke may share similar mechanisms with tobacco smoke-induced carcinogenesis [55]. In recent years, with the improvement of economic conditions and living standards in China, the use of solid fuels has significantly reduced. The increased adoption of clean energy sources, such as natural gas and electricity, and the widespread installation of range hoods in rural households have helped mitigate indoor air pollution. These improvements are likely contributing to a decline in lung cancer risk attributable to solid fuel combustion.

Other factors

Residential environmental pollution around the place of residence is also a potential source. Pollutants generated from industrial activities and traffic emissions, including polycyclic aromatic hydrocarbons, nitrogen oxides, and PM, can infiltrate indoor air through atmospheric dispersion, sedimentation, and ventilation pathways. Chronic exposure to such pollutants can cause continuous damage to lung tissues, trigger oxidative stress reactions, and sustained inflammatory reactions in cells, thereby promoting carcinogenesis. Vineis et al. [15] conducted a prospective survey of 520,000 healthy volunteers in 10 European countries, demonstrating that NO_2 concentrations and residential proximity to high-traffic roads are reliable indicators for assessing the impact of air pollution on lung cancer risk. Zheng Lingling et al. [31] found that the presence of polluting enterprises near residential areas was significantly associated with increased lung cancer risk in non-smoking populations. Similarly, Shirgaonkar et al. [33] found that individuals living within 3 km of heavy industrial plants had a 3.5-fold higher risk of lung cancer compared to those residing farther away. These findings underscore the need to reduce the infiltration of outdoor pollutants into residential environments, especially in high-risk populations. Targeted public health measures - such as stricter regulation of industrial emissions and traffic-related pollution - are crucial for improving environmental quality and mitigating lung cancer risk in never-smokers.

Occupational exposure also contributes to environmental risk. Tse et al. [25] showed that employment in sectors such as construction, decoration, shipbuilding, auto repair, professional driving, and engine operation increased with elevated lung cancer risk. Shirgaonkar et al. [33] identified chemical and construction work as high-risk occupations. From a biological mechanism perspective, chemical substances such as formaldehyde and benzene possess well-established cytotoxic and genotoxic properties. These substances can directly damage DNA, induce gene mutations and chromosomal aberrations, and disrupt normal cellular metabolism and proliferation, thus increasing the risk of cancer. Asbestos can persist in lung tissue for extended periods and trigger chronic inflammation, leading to the massive generation of ROS, which causes oxidative DNA damage and chromosomal instability and further contributes to carcinogenesis [56]. Additionally, mutations in oncogenes such as ras have been shown to correlate with elevated serum level of p21 protein in lung cancer patients exposed to asbestos [57]. However, in this meta-analysis, only two studies assessed occupational exposure, highlighting the need for further research. Future studies should

expand sample sizes, include diverse occupational groups, and explore carcinogenic mechanisms across varying exposure conditions to provide a more robust basis for formulating precise occupational health interventions.

In addition, it is worth noting that there was an association between a low BMI and the risk of lung cancer in non-smoking patients. This may be associated with impaired immune function, reducing the body's ability to defend against environmental carcinogens. Subsequent studies need to further explore the biologic mechanisms underlying the association between low BMI and increased vulnerability to indoor environmental pollution.

Preventive measures

This study revealed that specific indoor environmental exposures significantly increase the risk of lung cancer in never-smokers, emphasizing the importance of incorporating environmental risk factors into clinical evaluation and lung cancer risk assessment. These findings provide a scientific basis for refining clinical screening strategies and facilitating early identification of high-risk individuals. Future research should focus on integrating environmental exposure data with clinical and molecular indicators to develop personalized risk prediction models and support precision oncology in lung cancer care.

Therefore, it is crucial to minimize exposure to these environmental risk factors through primary prevention (etiological prevention) as a key strategy in lung cancer prevention. Smoking bans in public places and households should be enforced to reduce secondhand smoke exposure among never-smokers. Public health campaigns can raise awareness of the health hazards associated with environmental tobacco smoke. Improving indoor environment by reducing pollution caused by home renovations is also essential. For example, increasing indoor ventilation is an effective strategy to reduce radon levels; studies have shown that natural ventilation can lower indoor radon concentrations by over 90% [58].

At the policy level, stricter indoor air quality standards can be implemented, along with providing economic subsidies and technical support to promote comprehensive management of indoor pollution. Actively promoting clean energy alternatives, such as natural gas, liquefied petroleum gas (LPG), and electricity as primary energy sources, and improving kitchen ventilation can reduce harmful byproducts produced by the combustion of solid fuels, including PM2.5, CO, and PAHs.

Improving kitchen ventilation through the use of high-efficiency range hoods can help reduce airborne pollutants. In addition, low-emission cooking methods (e.g., steaming, boiling, braising) should be encouraged over high-temperature techniques like deep-frying and stir-frying.

Choosing healthy oils with high smoke points and avoiding the reuse of frying oil can help reduce smoke production. Additionally, environmental protection should be strengthened. From a residential design perspective, installing double-glazed windows in areas with high external pollution can reduce the indoor penetration of NO_2 and traffic-derived particulate matter. During periods of good air quality, regular window ventilation can help maintain indoor air freshness. At the urban planning and regulatory level, efforts should be made to optimize residential layouts, separate residential zones from industrial and traffic-heavy areas, and enforce stricter oversight of industrial emissions to ensure compliance with environmental regulations. When choosing a place to live, residents should avoid living in close proximity to pollution-intensive enterprises when possible. Protection measures and occupational safeguards for occupational workers who are in long-term contact with harmful substances and gases should be strengthened, and direct contact should be avoided as much as possible. Future research should further examine the cumulative effects of multi-pollutant exposure and optimize the prevention and control strategies for lung cancer among non-smokers.

Research limitations and future directions

Limitations of this study were as follows. First, the geographic distribution of the included studies was restricted, with a relative scarcity of data from specific regions, and the overall sample size was moderate. Second, the control of confounding factors - such as individual genetic susceptibility and detailed lifestyle factors - was often insufficient. Additionally, some studies failed to provide detailed pollutant con-

centration data, instead categorizing exposures based solely on fuel types, cooking behaviors, or living environments. This hindered the accurate assessment of exposure-response relationships, thereby reducing the comparability and generalizability of the findings.

Future research should prioritize multi-center, large-scale prospective cohort studies with long-term follow-up to precisely evaluate the cumulative and time-dependent effects of various indoor pollutants. Further exploration is also needed into the interactions between genetic susceptibility and environmental pollution, as well as the synergistic effects of multiple pollutants.

Conclusion

This meta-analysis demonstrated that residential radon exposure, environmental tobacco smoke exposure, cooking fumes, high-temperature cooking methods, and solid fuel combustion are significantly associated with an increased lung cancer risk in non-smoking populations. In lung cancer prevention efforts, focus should be placed on reducing exposure to these risk factors in daily life, strengthening smoking control in public places, improving indoor ventilation conditions, optimizing cooking methods, and promoting the use of clean energy to safeguard public health.

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Disclosure of conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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References

[1] Leiter A, Veluswamy RR and Wisnivesky JP. The global burden of lung cancer: current status and future trends. Nat Rev Clin Oncol 2023; 20: 624-639.

[2] He Y, Tang X, Yang F, Jiang Q, Deng L and Lang W. Exploring resistance to initial chemotherapy in small cell lung cancer: the role of bone metastasis and other clinicopathologic characteristics. Medicine (Baltimore) 2025; 104: e41953.

[3] LoPiccolo J, Gusev A, Christiani DC and Jänne PA. Lung cancer in patients who have never smoked - an emerging disease. Nat Rev Clin Oncol 2024; 21: 121-146.

[4] Liu Y, Xu Y, Xu W, He Z, Fu C and Du F. Radon and lung cancer: current status and future prospects. Crit Rev Oncol Hematol 2024; 198: 104363.

[5] Barta JA, Farjah F, Thomson CC, Dyer DS, Wiener RS, Slatore CG, Smith-Bindman R, Rosenthal LS, Silvestri GA, Smith RA and Gould MK. The American Cancer Society National Lung Cancer Roundtable strategic plan: optimizing strategies for lung nodule evaluation and management. Cancer 2024; 130: 4177-4187.

[6] Xue Y, Wang L, Zhang Y, Zhao Y and Liu Y. Air pollution: a culprit of lung cancer. J Hazard Mater 2022; 434: 128937.

[7] Chen KC, Tsai SW, Shie RH, Zeng C and Yang HY. Indoor air pollution increases the risk of lung cancer. Int J Environ Res Public Health 2022; 19: 1164.

[8] Zhou RX, Liao HJ, Hu JJ, Xiong H, Cai XY and Ye DW. Global burden of lung cancer attributable to household fine particulate matter pollution in 204 countries and territories, 1990 to 2019. J Thorac Oncol 2024; 19: 883-897.

[9] Jovičić-Bata J, Sazdanić-Velikić D, Ševo M, Milanović M, Tubić T, Bijelović M, Milošević N and Milić N. Lifestyle, environmental, occupational, and dietary risk factors in small-cell vs. non-small-cell advanced lung cancer patients: is there a connection? Cancers (Basel) 2025; 17: 864.

[10] Li L, Coull BA, Zilli Vieira CL and Koutrakis P. High-resolution national radon maps based on

massive indoor measurements in the United States. Proc Natl Acad Sci U S A 2025; 122: e2408084121.
[11] Fiordalisi CV, Borsky A, Chang S, Gerrity M, Schmidt AM and Guise JM. Improving health systems' access to high-quality evidence: AHRQ EPC 2018 Pilot Projects Summary [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US) 2019; Report No.:19-EHC015-EF.
[12] Behera D and Balamugesh T. Indoor air pollution as a risk factor for lung cancer in women. J Assoc Physicians India 2005; 53: 190-2.
[13] Darby S, Hill D, Auvinen A, Barros-Dios JM, Baysson H, Bochicchio F, Deo H, Falk R, Forastiere F, Hakama M, Heid I, Kreienbrock L, Kreuzer M, Lagarde F, Mäkeläinen I, Muirhead C, Oberaigner W, Pershagen G, Ruano-Ravina A, Ruosteenoja E, Rosario AS, Tirmarche M, Tomásek L, Whitley E, Wichmann HE and Doll R. Radon in homes and risk of lung cancer: collaborative analysis of individual data from 13 European case-control studies. BMJ 2005; 330: 223.
[14] Yu IT, Chiu YL, Au JS, Wong TW and Tang JL. Dose-response relationship between cooking fumes exposures and lung cancer among Chinese nonsmoking women. Cancer Res 2006; 66: 4961-7.
[15] Vineis P, Hoek G, Krzyzanowski M, Vigna-Taglianti F, Veglia F, Airoldi L, Overvad K, Raaschou-Nielsen O, Clavel-Chapelon F, Linseisen J, Boeing H, Trichopoulou A, Palli D, Krogh V, Tumino R, Panico S, Bueno-De-Mesquita HB, Peeters PH, Lund EE, Agudo A, Martinez C, Dorronsoro M, Barricarte A, Cirera L, Quiros JR, Berglund G, Manjer J, Forsberg B, Day NE, Key TJ, Kaaks R, Saracci R and Riboli E. Lung cancers attributable to environmental tobacco smoke and air pollution in non-smokers in different European countries: a prospective study. Environ Health 2007; 6: 7.
[16] Sapkota A, Gajalakshmi V, Jetly DH, Roychowdhury S, Dikshit RP, Brennan P, Hashibe M and Boffetta P. Indoor air pollution from solid fuels and risk of hypopharyngeal/laryngeal and lung cancers: a multicentric case-control study from India. Int J Epidemiol 2008; 37: 321-8.
[17] Wang XR, Chiu YL, Qiu H, Au JS and Yu IT. The roles of smoking and cooking emissions in lung cancer risk among Chinese women in Hong Kong. Ann Oncol 2009; 20: 746-51.
[18] Clément-Duchêne C, Vignaud JM, Stoufflet A, Bertrand O, Gislard A, Thiberville L, Grosdidier G, Martinet Y, Benichou J, Hainaut P and Paris C. Characteristics of never smoker lung cancer including environmental and occupational risk factors. Lung Cancer 2010; 67: 144-50.
[19] Tang L, Lim WY, Eng P, Leong SS, Lim TK, Ng AW, Tee A and Seow A. Lung cancer in Chinese women: evidence for an interaction between tobacco smoking and exposure to inhalants in the indoor environment. Environ Health Perspect 2010; 118: 1257-60.
[20] Bräuner EV, Andersen CE, Sørensen M, Andersen ZJ, Gravesen P, Ulbak K, Hertel O, Pedersen C, Overvad K, Tjønneland A and Raaschou-Nielsen O. Residential radon and lung cancer incidence in a Danish cohort. Environ Res 2012; 118: 130-6.
[21] Mu L, Liu L, Niu R, Zhao B, Shi J, Li Y, Swanson M, Scheider W, Su J, Chang SC, Yu S and Zhang ZF. Indoor air pollution and risk of lung cancer among Chinese female non-smokers. Cancer Causes Control 2013; 24: 439-50.
[22] Xue X, Yin Z, Lu Y, Zhang H, Yan Y, Zhao Y, Li X, Cui Z, Yu M, Yao L and Zhou B. The joint effect of hOGG1, APE1, and ADPRT polymorphisms and cooking oil fumes on the risk of lung adenocarcinoma in Chinese non-smoking females. PLoS One 2013; 8: e71157.
[23] Ruano-Ravina A, Pereyra MF, Castro MT, Pérez-Ríos M, Abal-Arca J and Barros-Dios JM. Genetic susceptibility, residential radon, and lung cancer in a radon prone area. J Thorac Oncol 2014; 9: 1073-80.
[24] Torres-Durán M, Ruano-Ravina A, Parente-Lamelas I, Leiro-Fernández V, Abal-Arca J, Montero-Martínez C, Pena-Álvarez C, González-Barcala FJ, Castro-Añón O, Golpe-Gómez A, Martínez C, Mejuto-Martí MJ, Fernández-Villar A and Barros-Dios JM. Lung cancer in never-smokers: a case-control study in a radon-prone area (Galicia, Spain). Eur Respir J 2014; 44: 994-1001.
[25] Tse LA, Yu IT, Rothman N, Ji BT, Qiu H, Wang XR, Hu W, Au JS and Lan Q. Joint effects of environmental exposures and familial susceptibility to lung cancer in Chinese never smoking men and women. J Thorac Oncol 2014; 9: 1066-72.
[26] Lorenzo-González M, Ruano-Ravina A, Torres-Durán M, Kelsey KT, Provencio M, Parente-Lamelas I, Leiro-Fernández V, Vidal-García I, Castro-Añón O, Martínez C, Golpe-Gómez A, Zapata-Cachafeiro M, Piñeiro-Lamas M, Pérez-Ríos M, Abal-Arca J, Montero-Martínez C, Fernández-Villar A and Barros-Dios JM. Lung cancer and residential radon in never-smokers: a pooling study in the Northwest of Spain. Environ Res 2019; 172: 713-718.
[27] Wong JYY, Downward GS, Hu W, Portengen L, Seow WJ, Silverman DT, Bassig BA, Zhang J, Xu J, Ji BT, Li J, He J, Yang K, Tian L, Shen M, Huang Y, Vermeulen R, Rothman N and Lan Q. Lung cancer risk by geologic coal deposits: a case-control study of female never-smokers from Xuanwei and Fuyuan, China. Int J Cancer 2019; 144: 2918-2927.

[28] Chen TY, Fang YH, Chen HL, Chang CH, Huang H, Chen YS, Liao KM, Wu HY, Chang GC, Tsai YH, Wang CL, Chen YM, Huang MS, Su WC, Yang PC, Chen CJ, Hsiao CF and Hsiung CA. Impact of cooking oil fume exposure and fume extractor use on lung cancer risk in non-smoking Han Chinese women. Sci Rep 2020; 10: 6774.

[29] Li J, Xu HL, Yao BD, Li WX, Fang H, Xu DL and Zhang ZF. Environmental tobacco smoke and cancer risk, a prospective cohort study in a Chinese population. Environ Res 2020; 191: 110015.

[30] Park EJ, Lee H, Kim HC, Sheen SS, Koh SB, Park KS, Cho NH, Lee CM and Kang DR. Residential radon exposure and cigarette smoking in association with lung cancer: a matched case-control study in Korea. Int J Environ Res Public Health 2020; 17: 2946.

[31] Zheng LL and Cai L. Case-control study of risk factors for lung cancer among nonsmokers. Cancer Research on Prevention and Treatment 2011; 38: 1306-1310.

[32] Li D, Shi J, Dong X, Liang D, Jin J and He Y. Epidemiological characteristics and risk factors of lung adenocarcinoma: a retrospective observational study from North China. Front Oncol 2022; 12: 892571.

[33] Shirgaonkar R, Mohapatra PR, Panigrahi MK, Mishra P, Bhuniya S, Sarkar S, Girija A, Shaik A, Mohanty S and Moorthy A. Evaluation of risk factors for lung cancer among never smokers and their association with common driver mutations. Cureus 2024; 16: e56024.

[34] Wu F, Wang L and Zhou C. Lung cancer in China: current and prospect. Curr Opin Oncol 2021; 33: 40-46.

[35] Iles IA, Nan X, Ma Z, Butler J, Feldman R and Wang MQ. Self-affirmation does not change smokers' explicit or implicit attitudes toward smoking following exposure to graphic cigarette warning labels. Commun Res Rep 2021; 38: 53-65.

[36] Li C, Lei S, Ding L, Xu Y, Wu X, Wang H, Zhang Z, Gao T, Zhang Y and Li L. Global burden and trends of lung cancer incidence and mortality. Chin Med J (Engl) 2023; 136: 1583-1590.

[37] Ruano-Ravina A, Varela Lema L, García Talavera M, García Gómez M, González Muñoz S, Santiago-Pérez MI, Rey-Brandariz J, Barros-Dios J and Pérez-Ríos M. Lung cancer mortality attributable to residential radon exposure in Spain and its regions. Environ Res 2021; 199: 111372.

[38] Kurkela O, Nevalainen J, Pätsi SM, Kojo K, Holmgren O and Auvinen A. Lung cancer incidence attributable to residential radon exposure in Finland. Radiat Environ Biophys 2023; 62: 35-49.

[39] Urrutia-Pereira M, Chatkin JM, Chong-Neto HJ and Solé D. Radon exposure: a major cause of lung cancer in nonsmokers. J Bras Pneumol 2023; 49: e20230210.

[40] Miao X, Su Y, Hou C, Song Y, Ding B, Cui H, Wu Y and Sun Q. Indoor radon survey in 31 provincial capital cities and estimation of lung cancer risk in urban areas of China. Biomed Environ Sci 2024; 37: 1294-1302.

[41] Kerpel-Fronius A, Tammemägi M, Cavic M, Henschke C, Jiang L, Kazerooni E, Lee CT, Ventura L, Yang D, Lam S and Huber RM; members of the Diagnostics Working Group; ED and Screening Committee. Screening for lung cancer in individuals who never smoked: an international association for the study of lung cancer early detection and screening committee report. J Thorac Oncol 2022; 17: 56-66.

[42] Folesani G, Galetti M, Ranzieri S, Petronini PG, La Monica S, Corradi M and Cavallo D. Interaction between occupational radon exposure and tobacco smoke: a systematic review. Expert Rev Respir Med 2022; 16: 787-800.

[43] Kratzer TB, Bandi P, Freedman ND, Smith RA, Travis WD, Jemal A and Siegel RL. Lung cancer statistics, 2023. Cancer 2024; 130: 1330-1348.

[44] Aredo JV, Luo SJ, Gardner RM, Sanyal N, Choi E, Hickey TP, Riley TL, Huang WY, Kurian AW, Leung AN, Wilkens LR, Robbins HA, Riboli E, Kaaks R, Tjønneland A, Vermeulen RCH, Panico S, Le Marchand L, Amos CI, Hung RJ, Freedman ND, Johansson M, Cheng I, Wakelee HA and Han SS. Tobacco smoking and risk of second primary lung cancer. J Thorac Oncol 2021; 16: 968-979.

[45] Corrales L, Rosell R, Cardona AF, Martín C, Zatarain-Barrón ZL and Arrieta O. Lung cancer in never smokers: the role of different risk factors other than tobacco smoking. Crit Rev Oncol Hematol 2020; 148: 102895.

[46] Forder A, Zhuang R, Souza VGP, Brockley LJ, Pewarchuk ME, Telkar N, Stewart GL, Benard K, Marshall EA, Reis PP and Lam WL. Mechanisms contributing to the comorbidity of COPD and lung cancer. Int J Mol Sci 2023; 24: 2859.

[47] Huang J, Yue N, Shi N, Wang Q, Cui T, Ying H, Wang Z, Leng J, Sui Z, Xu Y, Wei B and Jin H. Influencing factors of lung cancer in nonsmoking women: systematic review and meta-analysis. J Public Health (Oxf) 2022; 44: 259-268.

[48] Shih YM, Chang YJ, Cooke MS, Pan CH, Hu CH, Chao MR and Hu CW. Alkylating and oxidative stresses in smoking and non-smoking patients with COPD: Implications for lung carcinogenesis. Free Radic Biol Med 2021; 164: 99-106.

[49] Maung TZ, Bishop JE, Holt E, Turner AM and Pfrang C. Indoor air pollution and the health of

vulnerable groups: a systematic review focused on Particulate Matter (PM), Volatile Organic Compounds (VOCs) and their effects on children and people with pre-existing lung disease. Int J Environ Res Public Health 2022; 19: 8752.

[50] Bhurosy T, Marium A, Karaye IM and Chung T. Where there are fumes, there may be lung cancer: a systematic review on the association between exposure to cooking fumes and the risk of lung cancer in never-smokers. Cancer Causes Control 2023; 34: 509-520.

[51] Lee KK, Bing R, Kiang J, Bashir S, Spath N, Stelzle D, Mortimer K, Bularga A, Doudesis D, Joshi SS, Strachan F, Gumy S, Adair-Rohani H, Attia EF, Chung MH, Miller MR, Newby DE, Mills NL, McAllister DA and Shah ASV. Adverse health effects associated with household air pollution: a systematic review, meta-analysis, and burden estimation study. Lancet Glob Health 2020; 8: e1427-e1434.

[52] Prakasham K, Gurrani S, Wu CF, Wu MT, Hsieh TJ, Peng CY, Huang PC, Krishnan A, Tsai PC, Lin YC, Tsai B, Lin YC and Ponnusamy VK. Rapid identification and monitoring of cooking oil fume-based toxic volatile organic aldehydes in lung tissue for predicting exposure level and cancer risks. Chemosphere 2023; 339: 139704.

[53] Torres-Cadavid E, Pérez-Ríos M, Candal-Pedreira C, Guerra-Tort C, Rey-Brandariz J, Provencio-Pulla M, Kelsey K and Ruano-Ravina A. Lung cancer risk associated with occupations in women: a pooling study. Occup Med (Lond) 2024; 74: 348-354.

[54] Mehta SS, Elizabeth Hodgson M, Lunn RM, Ashley CE, Arroyave WD, Sandler DP and White AJ. Indoor wood-burning from stoves and fireplaces and incident lung cancer among sister study participants. Environ Int 2023; 178: 108128.

[55] Cheng ES, Chan KH, Weber M, Steinberg J, Young J, Canfell K and Yu XQ. Solid fuel, secondhand smoke, and lung cancer mortality: a prospective cohort of 323,794 Chinese never-smokers. Am J Respir Crit Care Med 2022; 206: 1153-1162.

[56] Greco SL, MacIntyre E, Young S, Warden H, Drudge C, Kim J, Candido E, Demers P and Copes R. An approach to estimating the environmental burden of cancer from known and probable carcinogens: application to Ontario, Canada. BMC Public Health 2020; 20: 1017.

[57] Avramescu ML, Potiszil C, Kunihiro T, Okabe K and Nakamura E. An investigation of the internal morphology of asbestos ferruginous bodies: constraining their role in the onset of malignant mesothelioma. Part Fibre Toxicol 2023; 20: 19.

[58] Matthaios VN, Liu M, Li L, Kang CM, Vieira CLZ, Gold DR and Koutrakis P. Sources of indoor $PM_{2.5}$ gross α and β activities measured in 340 homes. Environ Res 2021; 197: 111114.