Supplementary Materials

Title: Air Pollution and Lung Cancer–Cardiovascular Disease Comorbidity: Epidemiological Evidence, Shared Mechanisms, and Research Gaps

Supplementary Table S1 Literature search strategy

Supplementary Table S2 Studies on air pollution and the incidence of lung cancer from 2020 to present.

Supplementary Table S3 Studies on air pollution and the incidence of CVD from 2020 to present.

Supplementary Table S1 Literature search strategy

Datebase	Pubmed, Web of Science
Timeframe	2010.1–2026.3 (Epidemiological evidence was limited to the most recent 5 years)
Search terms	Search terms were combined around four core themes using Boolean operators (AND, OR). All the search terms used in this review are as follows. **Exposure factors**: #1 Air pollution OR air Pollutants OR ambient air pollution OR particulate matter OR PM2.5 OR PM10 OR nitrogen dioxide OR ozone OR sulfur dioxide OR carbon monoxide OR polycyclic aromatic hydrocarbons **Target diseases**: #2 Lung neoplasms OR lung cancer OR lung carcinoma OR pulmonary neoplasm OR lung adenocarcinoma OR lung squamous cell carcinoma #3 Cardiovascular disease OR heart disease OR hypertension OR heart failure OR atherosclerosis OR coronary heart disease OR coronary artery disease OR myocardial infarction OR cardiac arrhythmia OR atrial fibrillation **Comorbidity association**: #4 comorbidity OR multimorbidity OR co-occurrence OR concurrent OR bidirectional association OR dual burden **Pathogenesis mechanisms:** #5 shared pathway OR common mechanisms OR signaling pathway OR signal pathway OR inflammation OR oxidative stress OR endothelial dysfunction OR reactive oxygen species OR epigenetic OR DNA methylation OR microRNA OR thrombosis OR microbiome OR microbiota Epidemiological evidence: #1 AND #2 (Supplementary Table S2), #1 AND #3 (supplementary Table S3), #1 AND #2 AND #3, #2 AND #3 AND #4. Mechanistic evidence: #1 AND #2 AND #5, #1 AND #3 AND #5, #1 AND #2 AND #3 AND #5.
Inclusion and exclusion criteria	**Inclusion Criteria:** 1. Study type: high-quality original research, meta-analyses, systematic reviews, and narrative reviews. 2. Study subjects: human epidemiological and mechanistic studies; animal mechanistic studies that can explain specific mechanistic pathways. 3. Language: articles published in English. 4. Relevance: studies covering at least one of the following core contents: research on the current status of air pollution; studies on the disease burden of lung cancer and CVD; research on the association between air pollution and the risk of lung cancer and CVD; research on the mutual association between lung cancer and CVD; studies directly exploring the association between air pollution and the co-occurrence risk of lung cancer and CVD; mechanistic studies elucidating how air pollution promotes lung cancer and CVD; research on the bidirectional promotion between lung cancer and CVD; studies proposing or evaluating public policies, screening, or therapeutic interventions that can simultaneously reduce air pollution-related risks of lung cancer and CVD. **Exclusion Criteria：** 1. Irrelevance: studies primarily focusing on cardiovascular toxicity caused by anti-tumor therapy; animal mechanistic studies that cannot be clearly linked to the human pathophysiology of comorbidity.

	2. Study type: conference abstracts, commentaries, editorials, letters, and studies for which full text cannot be obtained. 3. Non-English literature. 4. Duplicate publications: only the version with the most complete and up-to-date data is retained.
Screening process	Each section was independently searched by HY and PL. Initial screening was performed based on titles and abstracts, and any disagreements were resolved through discussion. KY made the final decision on inclusion and obtained the full texts. In addition to the predefined search strategy, a supplementary search was performed; potentially relevant articles identified through PubMed's "Similar articles" feature were screened using the same eligibility criteria and included if eligible. The final literature search was performed on March 31, 2026.

Supplementary Table S2 Studies on air pollution and the incidence of lung cancer from 2020 to present.

First Author/Year	Area	participants	Pollutants	Key Findings
Li et al, 2020 [1]	China	n = 118,551	$PM_{2.5}$	High exposure level (82.22–96.96 μg/m^3) significantly increased lung cancer risk compared with the baseline level (31.17–53.82 μg/m^3) (HR, 2.45; 95% CI: 1.83–3.29); Elderly are susceptible.
Coleman et al, 2020[2]	US	n > 8.5 million	$PM_{2.5}$	A 10μg/m^3 increase in $PM_{2.5}$ was associated with increased lung cancer risk (RR, 1.19; 95% CI, 1.09-1.30).
Bai et al, 2020 [3]	Canada	n = 4.9 million	$PM_{2.5}$ NO_2 O_3	$PM_{2.5}$ (per 5.3 μg/m^3 increase, HR,1.02, 95% CI: 1.01–1.05) and NO_2 (per 14 ppb increase: HR, 1.05, 95% CI: 1.03–1.07) are positively associated with lung cancer risk;
Huang et al, 2021 [4]	UK	n = 455,974	$PM_{2.5}$ PM_{10} NO_2	$PM_{2.5}$ (HR, 1.63; 95% CI, 1.33–2.01 per 5 μg/m^3 increase), PM_{10} (HR, 1.53; 95% CI, 1.20–1.96, per 10μg/m^3), and NO_2 (HR, 1.10; 95% CI, 1.05–1.15, per 10μg/m^3) increase lung cancer risk, genetic risk increase susceptibility.
Cheng et al, 2022 [5]	US	n = 97,288	$PM_{2.5}$ NO_2 CO	Lung cancer risk is positively associated with $PM_{2.5}$ (per 10 μg/m^3 increase, HR, 1.20, 95% CI: 1.01–1.43), but not significantly with NO_2 or CO, low-income populations are susceptible.
Liu et al, 2023 [6]	US	n = 12,429,951	$PM_{2.5}$ NO_2	$PM_{2.5}$ (per 1 μg/m^3 increase, HR = 1.008; 95% CI: 1.005, 1.011) and NO_2 (per 1 ppb increase, HR = 1.013; 95% CI: 1.012, 1.013) increase lung cancer risk. Old men

				and low-income populations are susceptible.
Liang et al, 2023 [7]	UK	n = 367,623	$PM_{2.5}$ NO_2	Each interquartile range (IQR) increase was associated with elevated lung cancer risk for $PM_{2.5}$ (HR, 1.22; 95% CI: 1.15–1.30) and NO_2 (HR, 1.19; 95% CI: 1.10–1.27). Unhealthy lifestyle & genetic risk increase susceptibility.
Lim et al, 2023 [8]	Australia	n = 11,679	$PM_{2.5}$ NO_2	At $PM_{2.5}$ concentrations of 5 μg/m^3 vs 1 μg/m^3, lung cancer risk increased (HR 1.45; 95% CI: 1.03–2.03); no significant association was found for NO_2. Old men are susceptible
Diver et al, 2026 [9]	US	n = 122,442	$PM_{2.5}$ NO_2 SO_2 O_3 CO	$PM_{2.5}$ (HR, 1.15, 95% CI: 1.04–1.27), NO_2 (HR, 1.04; 95% CI 1.00–1.08), SO_2 (HR, 1.05; 95% CI 1.01–1.12) and O_3 (HR, 1.07; 95% CI 1.00–1.14) are associated with lung cancer.

Supplementary Table S3 Studies on air pollution and the incidence of CVD from 2020 to present.

First Author/Year	**Area**	**participants**	**Pollutants**	**Key Findings**
Short-time effect				
Ishii et al, 2021 [10]	Japan	n = 137,678	$PM_{2.5}$	A 10μg/m^3 increase in $PM_{2.5}$ was associated with admission for acute myocardial infarction (AMI) (OR, 1.060; 95% CI: 1.038–1.082).
Khajaviet al, 2021 [11]	Iran	n = 4,580	PM_{10} NO_2 SO_2 CO O_3	All pollutants had immediate but directionally inconsistent effects on blood pressure.
Chen et al, 2022 [12]	China	n = 1,292,880	$PM_{2.5}$ PM_{10} NO_2 SO_2 CO O_3	Each IQR increase in PM2.5, NO2, SO2, and CO was associated with a significantly increased risk of acute coronary syndrome (ACS), with NO_2 showing the largest increase (3.89%, 95% CI: 3.41%–4.37%). Elderly are susceptible.
Lin et al, 2025 [13]	China and UK	n = 1.5 million	$PM_{2.5}$ PM_{10} NO_2 SO_2 CO O_3	Each IQR increase in pollutants was associated with a 9–16% increased risk of ACS, with $PM_{2.5}$ showing the largest effect (OR, 1.66; 95% CI, 1.079–1.261). Mediation analysis indicated that inflammation played a major role, with the elderly and females being more susceptible.
Long-time effects				
Prabhakaran et al,	India	n = 5,342	$PM_{2.5}$	Each IQR increase in $PM_{2.5}$ exposure was associated with a mean increase of 3.33 mmHg in

2020 [14]				systolic blood pressure (95% CI: 1.12–5.52). Obese individuals are susceptible
Alexeeff et al, 2023 [15]	US	n = 3.7 million	$PM_{2.5}$	A 10 μg/m^3 increase in $PM_{2.5}$ was associated with a 12% (95% CI: 7%–18%) higher risk of incident AMI, low socioeconomic status more susceptible
Yuan et al, 2023 [16]	China	n = 109,374	$PM_{2.5}$	A 10 μg/m^3 increase in $PM_{2.5}$ was associated with Atherosclerotic cardiovascular disease (HR, 1.24; 95% CI: 1.19 - 1.30)
Wang et al, 2023 [17]	China	n = 36,948	NO_2	Each 10 μg/m^3 increase in NO_2 was associated with a HR of 1.558 (95% CI: 1.477–1.642) for total CVD and 1.521 (95% CI: 1.419–1.631) for hypertension, with urban residents and obese individuals being more susceptible.
Liang et al, 2024 [18]	China	n = 30,226	O_3	Each 10 ppb increase in O_3 was associated with hypertension (HR, 1.10; 95% CI, 1.03–1.18), with males and urban areas being more susceptible.
Cheng et al, 2025 [19]	UK	n = 491,305	$PM_{2.5}$ PM_{10} NO_2	Under high genetic risk, each one-quintile increase in $PM_{2.5}$, PM_{10}, and NO_2 was associated with arrhythmia: HR 4.51 (95% CI: 3.66–5.56), 4.28 (95% CI: 3.52–5.22), and 4.90 (95% CI: 3.97–6.03), respectively. Genetic risk increase susceptibility.
Cui et al, 2025 [20]	UK	n = 411,807	$PM_{2.5}$	Each IQR increase in $PM_{2.5}$ was associated with HF (HR, 1.50; 95% CI: 1.46–1.54). Genetic risk increase susceptibility.

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