

Association Between Pulmonary Tuberculosis and Lung Cancer Risk: A Meta-Analysis

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Short Report

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Abstract

Purpose

The most common cause of cancer-related death in the world is lung cancer. It has been suggested that pulmonary tuberculosis (TB), which is caused by immunological dysregulation, scarring, and persistent pulmonary inflammation, is a separate risk factor for lung cancer. An updated analysis is necessary due to methodological limitations, such as improper pooling of heterogeneous effect measures and insufficient control for detection bias. Previous meta-analyses have reported a significant association. Using a methodologically rigorous approach, this meta-analysis is sought to estimate the pooled association between TB and lung cancer risk across cohort and case-control studies.

Methods

A thorough search of Google Scholar and PubMed turned up 4,275 records. Nine studies (8 cohort, 1 case-control; total N = 1,012,061) met predetermined eligibility criteria after duplicate removal and screening. A random-effects model with generic inverse-variance weighting on the log scale was used to aggregate effect estimates. Using the Newcastle-Ottawa Scale, study quality was evaluated.

Results

Pulmonary TB was significantly associated with increased lung cancer risk (pooled effect estimate: 2.39, 95% CI: 1.91–2.99, $p < 0.0001$). Substantial heterogeneity was observed ($I^2 = 88.7\%$). The association remained consistent across subgroup & sensitivity analyses.

Conclusion

Lung cancer is roughly 2.4 times higher in those with a history of pulmonary tuberculosis. These results emphasize the need for prospective studies to elucidate underlying mechanisms and support incorporating lung cancer surveillance into post-TB care pathways.

Introduction

Lung cancer is the leading cause of cancer-related mortality worldwide, accounting for approximately 18% of all cancer deaths (Sung et al., 2026). Pulmonary tuberculosis (TB), affecting more than 10.7 million annually (2025 Tuberculosis Global Report, n.d.), has been postulated as an independent risk factor for lung cancer through chronic inflammation, pulmonary scarring, and immune dysregulation. Prior meta-analyses reported a significant association (Hwang et al., 2022) but did not fully address methodological heterogeneity in effect measures or detection bias from early post-TB lung cancer diagnoses.

Aim:

To estimate the pooled association between pulmonary TB and lung cancer risk using a generic inverse-variance approach on the log scale to appropriately handle heterogeneous effect measures, incorporating a minimum follow-up threshold to minimize detection bias.

Methods

This meta-analysis was conducted in accordance with PRISMA 2020 guidelines Page et al. (2021). PubMed and Google Scholar were searched for studies (20 years, English) examining pulmonary tuberculosis (TB) and subsequent lung cancer risk. The complete search strategy, screening procedure, and inclusion/exclusion criteria are provided in Supplementary Tables S1-S3. Of 4,275 records identified (6 duplicates removed), 14 full-text articles were assessed against pre-specified PECO criteria (adults; history of pulmonary TB vs. no TB history; incident/fatal lung cancer; cohort or case-control design; ≥ 1 -year follow-up for cohorts, to limit detection bias). Five were excluded (outside date range, $n = 1$; mortality/prognostic outcome, $n = 2$; secondary/metastatic cancer, $n = 1$; latent TB, $n = 1$), leaving 9 studies for quantitative synthesis (Fig. 1).

For each study, the reported effect estimate (HR/OR/SIR/RR) and 95% CI were extracted. Where only stratified estimates were reported Park et al. (2010), a pooled value was derived via fixed-effect inverse-variance combination of the stratum-specific log-effect sizes. Where multiple follow-up intervals were reported Valenzuela et al. (2026), the ≥ 1 -year estimate was used. Study quality was assessed with the Newcastle-Ottawa Scale Wells et al., 2014.

Analyses used R version 4.3 Viechtbauer (2010). Log-transformed estimates were pooled via random-effects model (REML estimator), given expected heterogeneity. I^2 , τ^2 , and Cochran's Q quantified heterogeneity. Subgroup analyses (design, smoking adjustment), leave-one-out sensitivity analysis, and publication bias assessment (funnel plot, Egger's test) were performed.

Ethics Approval:

This study is a meta-analysis and systematic review of observational studies that have already been published. No human participants, animals, or biological material were directly involved. Ethical approval was therefore not required.

Clinical trial number: not applicable.

Table 1
Characteristics of included studies in the meta-analysis of pulmonary tuberculosis and lung cancer risk.

Study	Country	Design	TB Group N	Comparator N	Follow-up	Effect Estimate (95% CI)	Major Adjusted Variables
Yu 2011	Taiwan	Cohort	4,480	712,392	7–9 years	HR:3.32 (2.70–4.09)	Age, sex, occupation, diabetes, hypertension, dyslipidemia, COPD.
Park 2010	South Korea	Case-control	350 (cases + controls with TB history)	2,265 (cases + controls without TB history)	N/A	OR:2.77 (2.24–3.42)	Age, smoking status.
Wu 2011	Taiwan	Cohort	5,657	23,984	Mean 5.86 years (range 1–12 years)	HR:1.64 (1.20–2.15)	Age, sex, diabetes mellitus, chronic renal failure, autoimmune diseases, COPD.
Moon 2023	South Korea	Cohort	75,467	75,467 (matched controls)	Mean 4.8 years (IQR 2.9–2.15)	HR:1.68 (1.43–1.98)	Age, sex, BMI, smoking (pack-years), alcohol, exercise, income, residential area, Charlson comorbidity index.
Oh 2020	South Korea	Cohort	2,640	17,612	Mean 3.9 years	HR:3.24 (1.87–5.62)	Age, sex, education, income, smoking status, BMI, physical activity.
Hong 2024	South Korea	Cohort	35,140	General population	Mean 8.01 person-years (range 1.0–12.3)	SIR:2.04 (1.85–2.23)	Sex, age, income, smoking, alcohol, physical activity, BMI, diabetes, hypertension, stroke, heart disease, dyslipidemia, TB treatment compliance.
An 2020	South Korea	Cohort	3,776	18,880	Mean 3.9 years	HR:4.18 (3.15–5.56)	Sex, age, household income, smoking status.

Note: For Valenzuela 2026, N reflects the TB-exposed cohort only; the comparator was the general adult population of Chile (~ 17 million) during the same study period. For Hong 2024, the SIR was calculated against general population expected rates; no separate comparator was identified. For Park 2010, follow-up is not applicable as this is a case-control study. For Shiels 2011, follow-up duration reflects the study period (1985–2005); individual median follow-up was not reported. HR, hazard ratio; OR, odds ratio; SIR, standardized incidence ratio; RR, risk ratio; CI, confidence interval; BMI, body mass index; COPD, chronic obstructive pulmonary disease; HIV, human immunodeficiency virus.

Study	Country	Design	TB Group N	Comparator N	Follow-up	Effect Estimate (95% CI)	Major Adjusted Variables
Valenzuela 2026	Chile	Cohort	5,456	~ 17 million (general Chilean population)	2 years (2019–2023)	RR:1.93 (1.05–3.24)	Age, sex, alcohol use, diabetes, HIV, immunosuppression, incarceration.
Shiels 2011	Finland	Cohort	273	28,860	20 years (1985–2005)	HR:1.97 (1.46–2.65)	Age, baseline tobacco use (logcig-years).
<i>Note: For Valenzuela 2026, N reflects the TB-exposed cohort only; the comparator was the general adult population of Chile (~ 17 million) during the same study period. For Hong 2024, the SIR was calculated against general population expected rates; no separate comparator was identified. For Park 2010, follow-up is not applicable as this is a case-control study. For Shiels 2011, follow-up duration reflects the study period (1985–2005); individual median follow-up was not reported. HR, hazard ratio; OR, odds ratio; SIR, standardized incidence ratio; RR, risk ratio; CI, confidence interval; BMI, body mass index; COPD, chronic obstructive pulmonary disease; HIV, human immunodeficiency virus.</i>							

Table 2
Newcastle-Ottawa Scale quality assessment of included studies.

Cohort Studies (Newcastle-Ottawa Scale – Cohort Version)											
Study	S1 (0–1)	S2 (0–1)	S3 (0–1)	S4 (0–1)	Selection Total (0–4)	Comparability (0–2)	O1 (0–1)	O2 (0–1)	O3 (0–1)	Total (0–9)	Quality Rating
Yu 2011	1	1	1	1	4	1	1	1	1	8	Good
Wu 2011	1	1	1	1	4	1	1	1	0	7	Good
Moon 2023	1	1	1	1	4	2	1	1	0	8	Good
Oh 2020	1	1	1	1	4	2	1	1	1	9	Good
Hong 2024	1	1	1	1	4	1	1	1	1	8	Good
An 2020	1	1	1	1	4	2	1	1	1	9	Good
Valenzuela 2026	1	1	1	1	4	0	1	1	1	7	Good
Shiels 2011	0	1	1	0	2	2	1	1	1	7	Good
Case-Control Study (Newcastle-Ottawa Scale – Case-Control Version)											
Study	S1 (0–1)	S2 (0–1)	S3 (0–1)	S4 (0–1)	Selection Total (0–4)	Comparability (0–2)	E1 (0–1)	E2 (0–1)	E3 (0–1)	Total (0–9)	Quality Rating
Park 2010	1	1	0	1	3	2	1	1	0	7	Good

Results

Nine studies (8 cohort, 1 case-control; total N = 1,012,061) were included (Yu et al., 2010) (Park et al., 2010) (Wu et al., 2011) (Moon et al., 2023) (Oh et al., 2020) (Hong et al., 2024) (An et al., 2020) (Valenzuela et al., 2026) (Shiels et al., 2011), all rated good quality on the Newcastle-Ottawa Scale (scores 7–9/9; Table 2) “[Insert Table 1 here]”. The pooled estimate demonstrated a statistically significant association between prior pulmonary TB and increased lung cancer risk (pooled effect estimate: 2.39, 95% CI: 1.91–2.99, $p < 0.0001$; Fig. 2), consistent with the direction of effect reported in prior meta-analyses Hwang et al. (2022), though our pooled estimate differs in magnitude owing to methodological differences in effect-measure handling and inclusion criteria. Substantial heterogeneity was observed ($I^2 = 88.7\%$, $\tau^2 = 0.074$, $p < 0.001$). Subgroup analyses by study design and smoking-adjustment status yielded closely comparable pooled estimates (range 2.24–2.77 across strata), and leave-one-out sensitivity analysis confirmed the result was not driven by any single study (range: 2.22–2.51). Sensitivity analyses excluding the SIR study (Hong 2024; pooled = 2.49, 95% CI: 1.91–3.24) and the OR study (Park 2010; pooled = 2.34, 95% CI: 1.84–2.98) yielded estimates consistent with the primary analysis, supporting the validity of combining heterogeneous effect measures. Restriction to HR studies only ($n = 6$) produced a comparable estimate (HR: 2.47, 95% CI: 1.77–3.43). No significant publication bias was detected (Egger’s $p = 0.71$), though power was limited with $k = 9$ studies.

Discussion

This meta-analysis shows a statistically significant pooled effect estimate of 2.39 (95% CI: 1.91–2.99) for lung cancer risk among patients with pulmonary TB across nine geographically and methodologically diverse studies, consistent with a prior meta-analysis (Hwang et al., 2022) and a slight increase that may be attributed to differences in inclusion criteria and the methodologically rigorous pooling of heterogeneous effect measures on the log scale.

The heterogeneity ($I^2 = 88.7\%$) is large but is consistent with previous publications in the field (Hwang et al., 2022) and probably reflects real differences in study populations, geographic TB burden, follow-up duration, smoking prevalence, and degree of confounder adjustment. Heterogeneity in estimates was not explained by subgroup analyses by study design and smoking adjustment status (range: 2.24–2.77).

Biological plausibility for this association is provided by evidence that chronic TB-related inflammation causes pulmonary fibrosis, generates reactive oxygen species, and triggers pro-carcinogenic pathways such as NF- κ B signalling and cytokine dysregulation. The ≥ 1 -year follow-up criterion was used to minimize detection bias, as lung cancer diagnosed within a short period after TB diagnosis likely to reflect pre-existing disease detected during TB-related imaging rather than TB-induced carcinogenesis (Valenzuela et al., 2026).

Limitations include substantial between-study heterogeneity, variable confounder adjustment across studies, and inability to exclude residual confounding by unmeasured variables including occupational exposures and comorbidities, and the inability to perform sensitivity analyses at longer post-TB latency thresholds (≥ 2 or ≥ 3 years) owing to limited availability of time-stratified effect estimates across included studies.

Conclusion

Prior pulmonary tuberculosis is associated with an approximately 2.4-fold increased risk of lung cancer (pooled effect estimate: 2.39, 95% CI: 1.91–2.99, $p < 0.0001$), with consistent findings across study design and sensitivity

analyses. These findings support further prospective evaluation of lung cancer risk among tuberculosis survivors and suggest that heightened clinical awareness of lung cancer symptoms in this population may be warranted, pending evidence from prospective studies on the benefits and cost-effectiveness of formal surveillance programmes.

Declarations

Clinical trial number: not applicable.

Conflict of interest:

Authors declare no conflict of interests.

Ethics Approval:

This study is a systematic review and meta-analysis of observational studies previously published. No human participants, animals, or biological material were directly involved. Ethical approval was therefore not required.

Consent to participate:

Not applicable. This study is a meta-analysis of previously published data and did not involve direct human participants.

Consent for Publication:

Not applicable. This study is a meta-analysis of previously published data and did not involve direct human participants.

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Author Contribution

Riya Rajendra Shirote was in charge of conceptualization, methodology, formal analysis, data curation, drafting, review and editing. Dr. Parth Sarthi Sen Gupta provided formal analysis as well as review and editing. Dr. Ramendra Pati Pandey contributed to conceptualization, data curation, and formal analysis. All authors have read and agreed to the published version of the manuscript.

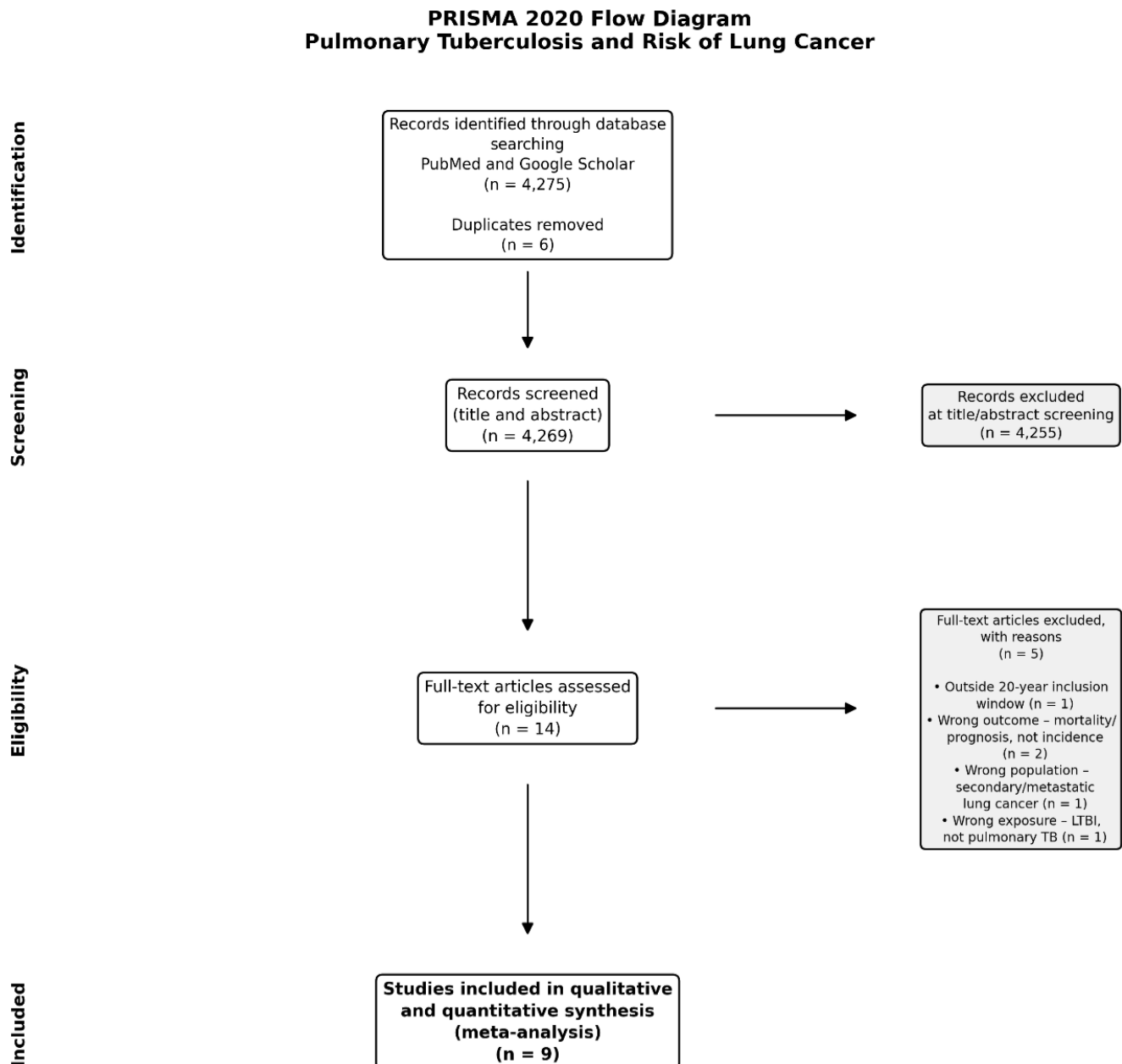
Data availability:

All data analyzed in this study are derived from previously published studies listed in the list of references. The extracted data set and the R analysis script are available from the corresponding author on request.

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PRISMA 2020 flow diagram illustrating the systematic search and study selection process for the meta-analysis of pulmonary tuberculosis and subsequent lung cancer risk. Records were identified through PubMed and

Google Scholar (n = 4,275). Following removal of duplicates (n = 6), title/abstract screening, and full-text assessment, nine studies were included in the quantitative synthesis.

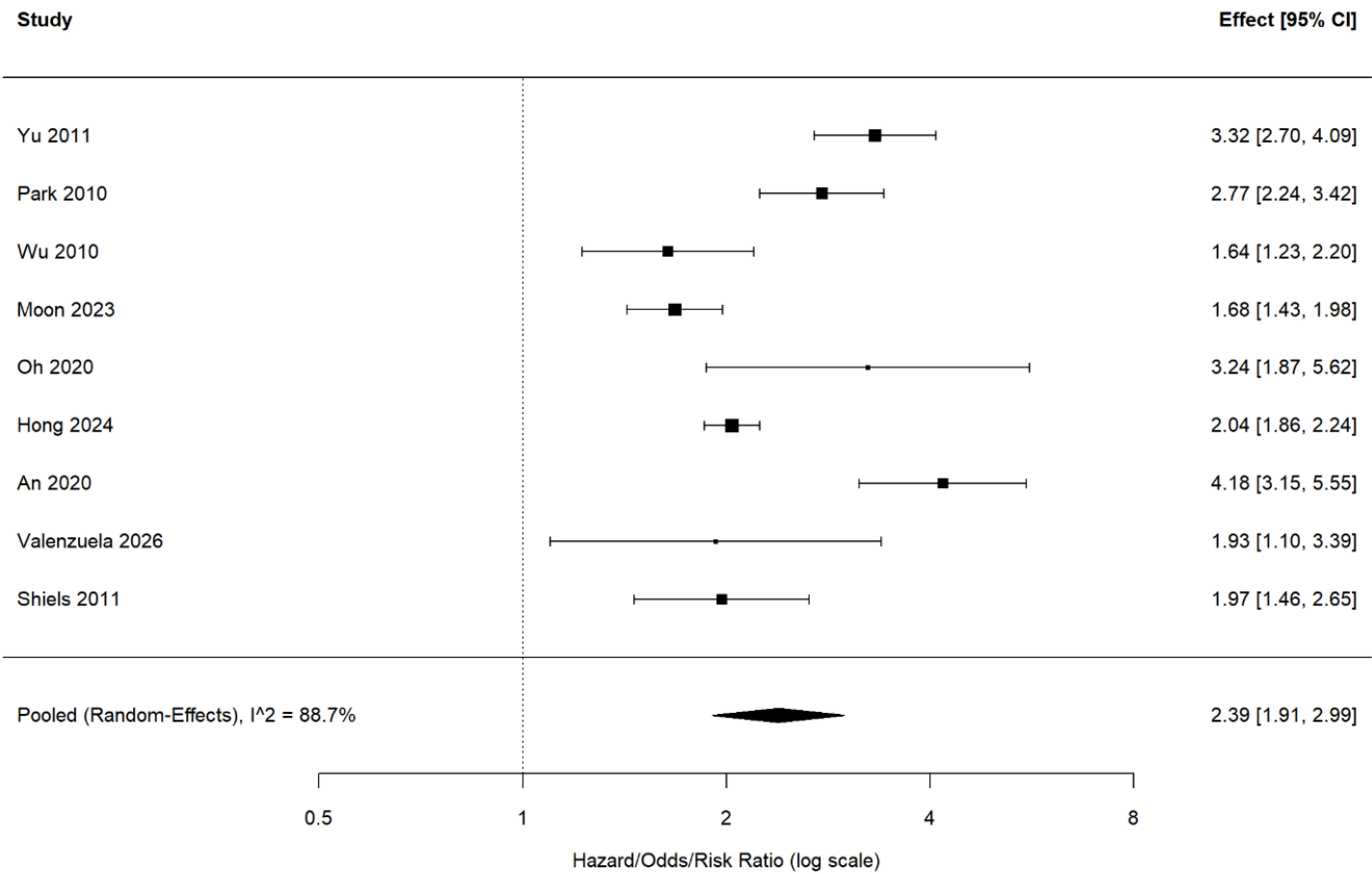


Figure 2

Forest plot illustrating the pooled association between prior pulmonary tuberculosis and lung cancer risk across nine included observational studies. Individual study effect estimates and 95% confidence intervals are displayed on a log scale. The size of each square reflects the study’s relative weight in the pooled analysis. The diamond represents the overall pooled-random-effects estimate (pooled effect = 2.39, 95% CI: 1.91-2.99, $p < 0.0001$; $I^2 = 88.7\%$). HR, hazard ratio; OR, odds ratio; RR, risk ratio; SIR, standardized incidence ratio; CI, confidence interval; REML, restricted maximum likelihood.

Supplementary Files

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