

Smoking cessation after diagnosis and survival in lung cancer and head and neck squamous cell carcinoma: a systematic review and meta-analysis

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ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY2026100088

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 20 October 2026 and was last updated on 20 October 2026.

INTRODUCTION

Review question / Objective In adults with lung cancer (non-small cell or small cell) or head and neck squamous cell carcinoma of the oral cavity, oropharynx, larynx or hypopharynx, is smoking cessation or abstinence assessed at or after diagnosis, compared with continued smoking, associated with better overall survival (primary question), and with better cancer-specific survival, progression- or recurrence-free survival, fewer treatment-related complications, and lower risk of second primary cancer (secondary questions)?.

Rationale Patients with lung cancer and head and neck squamous cell carcinoma frequently continue to smoke after diagnosis, and cessation is the only prognostic intervention in this setting that requires no new technology. Existing syntheses address the two cancer sites separately, define the timing of exposure differently, and have not examined how immortal time bias affects the estimates.

Treatment-related outcomes have been synthesised by treatment modality rather than alongside survival. A synthesis that harmonises the exposure definition across both sites, quantifies the influence of immortal time bias, and reports the certainty of evidence is therefore needed.

Condition being studied Lung cancer (non-small cell lung cancer, small cell lung cancer); head and neck squamous cell carcinoma (oral cavity, oropharynx, larynx, hypopharynx).

METHODS

Search strategy MEDLINE via PubMed (NCBI E-utilities), searched on 3 October 2026; English-language and human studies, no lower date limit. Four query sets were run: (A) cessation and continued-smoking behaviour terms with lung or head and neck cancer terms and prognosis or outcome terms (1,249 records); (B) smoking status or history terms with pre- and post-diagnosis

timing terms, cancer site terms and outcome terms (918); (C) cessation and continued-smoking terms with cancer site terms but without outcome terms (2,798); (D) cessation and smoking status terms with cancer site terms and systematic review or meta-analysis publication types (464). The four sets returned 5,429 records. Complete strings for all four sets are provided in Supplementary Appendix S1 of the review. Embase, the Cochrane Library and Chinese-language databases were not searched; no backward or forward citation tracking, reference-list hand-searching or grey-literature searching was performed; no formal search peer review was undertaken.

Participant or population Adults (≥ 18 years) with histologically or cytologically confirmed lung cancer (non-small cell or small cell) or head and neck squamous cell carcinoma of the oral cavity, oropharynx, larynx or hypopharynx, at any stage and receiving any treatment modality.

Intervention Smoking cessation after diagnosis, defined as quitting after diagnosis, sustained abstinence from before diagnosis, or peri-diagnostic cessation. Former smokers at diagnosis were classified according to their smoking status at the post-diagnosis time point, so that the contrast represented the absence of continued smoking at or after diagnosis. Exposure timing was categorised as at diagnosis, during treatment, after treatment, or post-diagnosis unspecified.

Comparator Continued or current smoking after diagnosis.

Study designs to be included Prospective, retrospective and registry-based cohort studies; secondary analyses of randomised controlled trials; and nested case-control studies. Cross-sectional studies, uncontrolled case series, case reports, editorials, narrative reviews, previous systematic reviews, animal and in vitro studies, and conference abstracts without extractable data were excluded.

Eligibility criteria Studies were eligible if they enrolled adults with lung cancer or head and neck squamous cell carcinoma, compared cessation or abstinence assessed at or after diagnosis with continued smoking, and reported at least one eligible outcome with a group-level effect estimate and confidence interval. Only English-language human studies with an available abstract were eligible; there was no lower date limit; conference abstracts without extractable data were excluded. When a study reported more than one estimate for the same outcome, a single estimate was selected

by a prespecified hierarchy: estimates contrasting post-diagnosis cessation with continued smoking, then estimates based on a longer duration of cessation, then multivariable-adjusted estimates; sex-stratified estimates for the same outcome were combined into one study-level estimate with a fixed-effect inverse-variance model. Where more than one report described the same cohort, the report with the most complete adjustment and the longest follow-up was retained and the other reports were used only for supplementary information.

Information sources PubMed (NCBI E-utilities) only; searched on 3 October 2025. No other databases, trial registers, preprint servers or grey-literature sources were searched, and no reference lists or citing articles were screened.

Main outcome(s) Overall survival (all-cause mortality), the primary outcome.

Additional outcome(s) Cancer-specific survival; progression- or recurrence-free survival; treatment-related complications (postoperative complications, chemoradiotherapy toxicity, hospitalisation during treatment); second primary cancer.

Data management Records were merged and de-duplicated by PubMed identifier (1,470 duplicates removed; 3,959 unique records). Title and abstract screening was performed by one reviewer; uncertain records were carried forward rather than excluded, and all records retained at screening were independently re-assessed by a second reviewer. Data were extracted from published abstracts into a standardised form by one reviewer, and every value was checked verbatim against the source abstract by a second independent pass (172 outcome-level data points; 99.1% verbatim agreement); disagreements were resolved by consensus. Full texts were not retrieved, so no full-text verification was performed (reported as a protocol deviation). Four estimates whose contrast direction or reference group could not be determined were recorded as unclear and were not pooled. The extracted dataset and analysis scripts can be provided on reasonable request.

Quality assessment / Risk of bias analysis Risk of bias was assessed with a modified Newcastle–Ottawa Scale comprising six domains: representativeness of the cohort; ascertainment of exposure and exposure timing; ascertainment of outcome and completeness of follow-up; adjustment for key confounders; immortal time bias; and selective reporting or small sample size.

Each domain was rated low, high or unclear; overall risk was high when two or more domains were high, moderate when one domain was high or two or more were unclear, and low otherwise. The immortal time bias domain was added because several exposure definitions require survival to a post-diagnosis or post-treatment landmark before cessation can be classified. Certainty of evidence was rated with GRADE for each outcome.

Strategy of data synthesis Estimates were combined on the natural logarithm scale with hazard ratios as the common metric; risk and odds ratios were pooled with hazard ratios after direction harmonisation and treated as approximations (in the primary overall survival analysis, 21 of 23 estimates were hazard ratios and 2 were risk ratios). Random-effects meta-analysis used the DerSimonian–Laird estimator, with Hartung–Knapp adjusted confidence intervals and fixed-effect estimates calculated for comparison. Heterogeneity was quantified with Cochran Q, I^2 and τ (the square root of τ^2), and a 95% prediction interval was calculated for each analysis with at least four contributing studies. An outcome was pooled when at least three studies provided a compatible estimate; where pooling was not appropriate, findings were synthesised narratively. Small-study effects were assessed with Egger’s test.

Subgroup analysis Prespecified subgroup analyses of overall survival were performed by cancer site (lung vs head and neck), exposure timing (at diagnosis vs during or after treatment), study design (prospective vs retrospective or registry-based), and adjustment (adjusted vs unadjusted estimates).

Sensitivity analysis Sensitivity analyses excluded studies at high overall risk of bias; excluded studies at high risk of immortal time bias; excluded both; compared random-effects with fixed-effect estimates; and used a leave-one-out approach. A planned sensitivity analysis excluding abstract-only studies was not feasible because all data were abstract-level.

Language restriction English.

Country(ies) involved China.

Other relevant information This protocol was registered retrospectively; no prospective registration was obtained and the review was not registered in PROSPERO. Protocol deviations are reported in the manuscript: data were extracted from published abstracts without full-text retrieval;

the planned exclusion of abstract-only studies was not feasible; subgroup analyses by stage, treatment modality and region were not performed because of missing data; and a modified Newcastle–Ottawa Scale with an added immortal time bias domain replaced ROBINS-E.

Keywords Smoking cessation; lung neoplasms; squamous cell carcinoma of head and neck; survival analysis; prognosis; systematic review; meta-analysis.

Dissemination plans The extracted dataset and analysis scripts will be made available on reasonable request. The final publication will cite the INPLASY registration number and DOI, and all protocol deviations will be reported in the published article.

Contributions of each author

Author 1 - Mao Sun - Conceptualization, Methodology, Writing – original draft, Writing – review & editing.

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