International Platform of Registered Systematic Review and Meta-analysis Protocols

INPLASY

Malignancy-associated interstitial lung disease: a systematic review protocol

INPLASY202580088
doi: 10.37766/inplasy2025.8.0088
Received: 28 August 2025
Published: 28 August 2025

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ADMINISTRATIVE INFORMATION

Support - This review received no specific grant from any funding agency.

Review Stage at time of this submission - Preliminary searches.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202580088

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 28 August 2025 and was last updated on 28 August 2025.

INTRODUCTION

Review question / Objective In patients with malignancy, what are the characteristics, incidence, risk factors, and outcomes of associated interstitial lung disease(ILD)?
• To estimate the incidence and prevalence of ILD in cancer populations.
• To identify risk factors for malignancy-associated ILD.
• To describe radiologic and histopathologic patterns of ILD in malignancy.
• To summarize outcomes including mortality, survival, and treatment strategies.

Rationale ILD may occur in cancer patients either as a paraneoplastic manifestation or as a result of anticancer therapy (chemotherapy, radiotherapy, targeted therapy, immunotherapy). The association between malignancy and ILD is clinically significant but remains poorly defined across cancer types and treatment modalities. This review will systematically synthesize existing evidence to clarify epidemiology, risk factors, ILD patterns, and outcomes.

Condition being studied Malignancy-associated interstitial lung disease (ILD) is a form of ILD that occurs in patients with cancer. It may result directly from the malignancy itself, from anti-cancer treatments such as chemotherapy, radiotherapy, immunotherapy, or targeted therapy, or from shared biological mechanisms between cancer and fibrotic lung disease. This condition is clinically important because it increases morbidity, complicates oncologic treatment decisions, and is associated with worse survival. Despite its relevance, current evidence is fragmented, and no comprehensive synthesis is available.

METHODS

Search strategy

Draft PubMed strategy:
("Interstitial Lung Diseases"[MeSH] OR ILD OR "interstitial pneumonia" OR "diffuse parenchymal lung disease")

AND
("Neoplasms"[MeSH] OR malignancy OR cancer OR carcinoma OR lymphoma OR leukemia OR myeloma OR sarcoma)
AND
(associated OR comorbid* OR concurrent OR secondary OR paraneoplastic OR therapy-induced)
No language restriction at search stage. Date range: database inception → August 2025.
Draft PubMed strategy:
("Interstitial Lung Diseases"[MeSH] OR ILD OR "interstitial pneumonia" OR "diffuse parenchymal lung disease")
AND
("Neoplasms"[MeSH] OR malignancy OR cancer OR carcinoma OR lymphoma OR leukemia OR myeloma OR sarcoma)
AND
(associated OR comorbid* OR concurrent OR secondary OR paraneoplastic OR therapy-induced)
No restriction on publication year; English-language publications only for analysis.

Participant or population • Inclusion: Adults (≥18 years) with malignancy (solid or hematologic) and reported ILD (clinical, radiologic, histopathologic diagnosis).
• Exclusion: Pediatric populations; non-malignant causes of ILD without documented cancer.

Intervention Presence of malignancy or anticancer therapy (e.g., chemotherapy, immune checkpoint inhibitors, targeted agents, radiotherapy).

Comparator
• Cancer patients without ILD (where available). • No comparator required for descriptive epidemiology.

Study designs to be included • Observational studies (cohort, case-control, cross-sectional)• Interventional studies if reporting ILD outcomes in cancer populations• Systematic reviews will be excluded but their references will be screened• Case reports/series with <10 patients excluded.

Eligibility criteria
Inclusion:
• Adults (≥18 years) with malignancy and reported ILD
• Observational studies (cohort, case-control, cross-sectional)
• Interventional studies reporting ILD as outcome
• Any diagnostic definition of ILD (clinical, HRCT, pathology)
Exclusion:
• Case reports/series with <10 patients
• Pediatric populations
• Reviews, commentaries, editorials.

Information sources
Databases: PubMed/MEDLINE, EMBASE, Cochrane Library, Web of Science, Scopus
Grey literature: ClinicalTrials.gov, WHO ICTRP, conference abstracts (ATS, ERS, ASCO).

Main outcome(s) .
Primary outcome(s)
• Incidence and prevalence of ILD in malignancy
• Risk factors (demographic, treatment-related, genetic/serological)
Time frame: any follow-up duration.

Additional outcome(s)
Secondary outcome(s)
• Mortality (all-cause, ILD-related)
• Progression-free survival, overall survival
• Radiological patterns (UIP, NSIP, OP, HP-like, etc.)
• Treatment strategies and responses
• Quality of life (where reported).

Data management All search results will be imported into EndNote and duplicates will be removed. Titles, abstracts, and full texts will be screened independently by two reviewers using Rayyan. Data will be extracted with a standardized form and stored in secure, password-protected files. Disagreements will be resolved through discussion or a third reviewer.

Quality assessment / Risk of bias analysis • Observational studies: Newcastle–Ottawa Scale (NOS). • RCTs: Cochrane RoB 2 tool. • Two independent reviewers; conflicts resolved by consensus.

Strategy of data synthesis
• Narrative synthesis summarizing epidemiology, risk factors, ILD subtypes, and malignancy types.
• Meta-analysis: if ≥3 studies are sufficiently homogenous (e.g., incidence of ILD with a specific cancer therapy), pooled prevalence or risk ratios will be calculated using a random-effects model.
• Heterogeneity: assessed with I^2 statistic (I^2 >50% = substantial heterogeneity).
• Subgroup analyses: by cancer type, therapy class, geographic region.
• Sensitivity analyses: excluding high-risk of bias studies.
• Publication bias: funnel plots & Egger's test if ≥10 studies.
Software: RevMan, Stata, or R.

Subgroup analysis • By cancer type (solid vs hematologic) • By therapy type (chemotherapy,

radiotherapy, immunotherapy, targeted therapy) • By ILD pattern (UIP, NSIP, OP, etc.).

Sensitivity analysis Sensitivity analyses will be conducted by sequentially excluding studies with high risk of bias, small sample sizes, or low methodological quality to assess the robustness of the pooled results. Additional analyses will be performed by excluding individual studies one at a time to evaluate their influence on overall outcomes.

Language restriction English.

Country(ies) involved Viet Nam.

Other relevant information No additional relevant information.

Keywords Interstitial lung disease; cancer; malignancy; comorbidity; systematic review; meta-analysis.

Dissemination plans Results will be submitted to a peer-reviewed journal and presented at ATS, ERS, and oncology/pulmonology meetings.

Contributions of each author

Author 1 - DONG PHU CAU - Author 1 drafted the manuscript.
Email: dongphucauhvqy@gmail.com
Author 2 - DONG KHAC HUNG - The author provided statistical expertise.
Author 3 - DINH VAN LUONG - The author contributed to the development of the selection criteria, and the risk of bias assessment strategy.
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