

## R E V I E W

# Interstitial lung disease in psoriasis: A systematic review and meta-analysis

JONAS A. BAEKDAL<sup>1</sup>, LAURA BJERKEN<sup>1</sup>, ERIK SÖREN HALVARD HANSEN<sup>1</sup>, LAURITS K. JANNIS<sup>1</sup>, HOWRAMAN METERAN<sup>1</sup>, CHARLOTTE SUPPLI ULRIK<sup>1,2</sup>, ELISABETH BENDSTRUP<sup>3,4</sup>

<sup>1</sup>Respiratory Research Unit, Department of Respiratory Medicine, Copenhagen University Hospital – Hvidovre, Denmark; <sup>2</sup>Institute of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark; <sup>3</sup>Center for Rare Lung Diseases, Department of Respiratory Diseases and Allergy, Aarhus University Hospital, Aarhus, Denmark; <sup>4</sup>Department of Clinical Medicine, Aarhus University, Aarhus, Denmark

## ABSTRACT

**Background and aim:** Psoriatic disease is associated with several extra-cutaneous complications, including cardiovascular disease and type 2 diabetes. Whether psoriatic disease is associated with interstitial lung disease (ILD) remains uncertain. The aim of this study was to quantify the prevalence of ILD overall and across specific subtypes of psoriatic disease.

**Methods:** We systematically searched PubMed, Embase, and Scopus for original studies reporting the prevalence of ILD in adults with psoriatic disease. Pooled prevalence estimates were calculated using proportional random-effects meta-analysis, with subgroup analyses stratified by factors including psoriatic disease type, sex, and smoking history. Random-effects meta-regression was conducted to examine the influence of age and disease duration.

**Results:** Of 863 records screened, 11 studies were included. The pooled ILD prevalence in any psoriatic disease was 3.6% (95% CI: 2.1–5.0%). Meta-regression indicated that ILD prevalence increased by 0.22 percentage points per year (95% CI: 0.02–0.41) from approximately 36 years of age. Subgroup analysis showed ILD prevalences of 2.4% (95% CI: 1.1–3.6%) in psoriasis vulgaris, 5.7% (95% CI: 2.5–8.9%) in psoriatic arthritis, and 8.4% (95% CI: 6.4–10.4%) in generalized pustular psoriasis (GPP). ILD prevalence was 3.2% (95% CI: 0.1–6.3%) in never-smokers versus 7.2% (95% CI: 3.4–11.0%) in ever-smokers.

**Conclusions:** ILD may represent a clinically relevant comorbidity in patients with psoriatic disease, particularly psoriatic arthritis and GPP. This increased prevalence may reflect chronic systemic inflammation and exposures such as medications and cigarette smoke. Further research is needed to elucidate the underlying mechanisms and to assess whether early detection and targeted interventions can improve outcomes.

**Key words:** interstitial lung disease, psoriasis, psoriatic arthritis, psoriasis vulgaris, usual interstitial pneumonia



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**Correspondence:** Jonas Aggerholm Baekdal, Ph.D. fellow, MD / Respiratory Research Unit Hvidovre, Department of Respiratory Medicine, Copenhagen University Hospital – Hvidovre, Kettegård Allé 30, DK-2650, Hvidovre, Denmark / E-mail: jonas.aggerholm.baekdal.02@regionh.dk  
ORCID: 0000-0001-5414-6732

## Introduction

Psoriatic disease, most commonly presenting as psoriasis vulgaris (PsV), characterized by erythematous, scaly skin plaques, is a chronic immune-mediated condition, which affects 1-6% of the global adult population (1). Beyond its well-known effects on the skin and nails, psoriatic disease is increasingly recognized as a systemic inflammatory disorder associated with comorbidities such as psoriatic arthritis (PsA) (2), cardiovascular disease (CVD), and type 2 diabetes (3,4). Generalized pustular psoriasis (GPP) is a rare variant characterized by episodic outbreaks of widespread sterile pustules and severe skin inflammation, often accompanied by marked systemic inflammation (5). Tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) and interleukin-17 (IL-17) are key cytokines in the pathogenesis of psoriatic disease and represent important therapeutic targets (6). TNF- $\alpha$  and IL-17 inhibitors alleviate both skin and joint symptoms in psoriatic disease and have also been shown to reduce coronary inflammation and cardiovascular risk (7,8). Thus, effective treatment of psoriatic disease may reduce systemic inflammation and offer important preventive benefits beyond the skin and joints. At rest, the entire blood volume circulates through the lungs approximately once per minute (9), continuously exposing pulmonary tissue to circulating inflammatory cytokines and cells. This may explain the well-documented association between interstitial lung disease (ILD) and immune-mediated inflammatory diseases such as systemic sclerosis, Sjögren's syndrome and rheumatoid arthritis (RA) (10,11). ILD encompasses a group of lung disorders characterized by inflammation and fibrosis of the lung tissue (12), leading to restrictive impairment of lung function, impaired gas exchange and progressive respiratory symptoms (13,14). In patients with RA, the risk of ILD appears to increase with disease severity and the level of systemic inflammation (15), supporting a mechanistic link between systemic inflammation and pulmonary involvement. The association between psoriatic disease and ILD remains uncertain. Given that psoriatic disease is associated with systemic inflammation and several extracutaneous complications, it may also be associated with ILD. Several observational studies have investigated the prevalence of ILD

in this population (16–24), but so far, the data have not been synthesized in a meta-analysis. The aim of this meta-analysis is to quantify the prevalence of ILD in patients with psoriatic disease overall and in specific subtypes (PsV, PsA, GPP), thereby providing a foundation for future research.

## Methods

This systematic review was performed in accordance with the 2020 PRISMA statement (25). The protocol was registered in PROSPERO May 2025. A systematic literature search was conducted in PubMed, Embase, and Scopus to identify all studies reporting chest computed tomography (CT) or high-resolution CT (HRCT) in patients with any psoriatic disease. The search was performed in April 2025 and updated in July 2025. Searches were limited to original research articles involving human participants and published in English. Review articles, conference abstracts, and unpublished data were excluded. The complete search strings for all databases are provided in the supplementary material. Studies were considered eligible if they met the following inclusion criteria: 1) Chest CT or HRCT performed in patients with psoriatic disease; 2) Reporting the prevalence of ILD, interstitial pneumonia (IP), interstitial features including ground-glass opacities, reticulation, honeycombing, traction bronchiectasis, or named ILD patterns i.e., usual interstitial pneumonia (UIP), nonspecific interstitial pneumonia (NSIP), and organizing pneumonia (OP); 3) Inclusion of adult patients ( $\geq 18$  years); 4) Reporting original research data. Exclusion criteria were: 1) Systematically including or excluding patients based on factors influencing the risk of lung disease (e.g., pre-existing pulmonary conditions, abnormal imaging findings, or impaired lung function); 2) Non-original publications such as reviews; 3) editorials and case reports; 4) Studies not published in English.

## Study selection and data extraction

Title and abstract screening was performed independently by three authors using Covidence.org. Full-text screening was performed by three reviewers and

disagreements were resolved by consensus. Reference lists of included articles were screened for additional eligible studies. Data were extracted using a predefined data extraction form. Extracted data included: 1) Study characteristics (year, country, study design, sample size); 2) Population details (age, psoriasis subtype, smoking history, clinical symptoms, and inflammatory markers); 3) CT/ HRCT findings and reported prevalence of ILD and specific radiographic patterns; 4) Definitions used for ILD/IP and imaging features.

In this study, ILD was defined broadly to include any of the following terms or radiological patterns reported by the eligible studies: ILD, IP, UIP, NSIP, or OP.

### **Risk of bias assessment**

Risk of bias was assessed using a modified version of the Newcastle-Ottawa Scale (NOS) adapted for cross-sectional and cohort studies (26). Studies were evaluated across domains of selection, comparability, and outcome assessment. A score of  $\geq 7$  was considered indicative of low risk of bias, 4–6 as moderate, and  $\leq 3$  as high risk. The quality assessment template is provided in the supplementary material.

### **Statistical analysis**

All statistical analyses were conducted using R (version 4.3.2) with the ‘metafor’ package. A random-effects meta-analysis of proportions was used to estimate the overall prevalence of ILD and specific HRCT patterns. Heterogeneity between studies was assessed using the  $I^2$  statistic. Meta-analyses stratified by psoriatic disease type, smoking history, sex, and ILD type were conducted to explore potential sources of heterogeneity. All estimates are presented with 95% confidence intervals (95% CI). When age or disease duration were reported for separate subgroups, a weighted average for the total study population was calculated. Random-effects meta-regression was then conducted to estimate the prevalence of ILD according to the study-specific mean/median age and psoriatic disease duration. Sensitivity analyses were conducted by restricting the analysis according to the following parameters: 1) imaging performed prior to biologic therapy; 2) studies with a total NOS score  $\geq 6$ ; 3) exclusion of outliers.

## **Results**

The PubMed, Embase, and Scopus searches yielded 863 records after removal of duplicates (Figure 1). Following title and abstract screening, 23 reports were selected for full-text review. Of these, 12 fulfilled all inclusion criteria, but one study was excluded due to the exclusion of all patients with respiratory symptoms (27). Thus, 11 studies were included in the systematic review and meta-analyses (5,16,18–24,28,29). Characteristics of the included studies are summarized in Table 1. ILD definitions and diagnostic methods are summarized in Table 2. Across the included studies, the proportion of current or former smokers ranged from 20% (22) to 58% (16).

### **ILD prevalence in any psoriatic disease**

The pooled prevalence of ILD among patients with any psoriatic disease was 3.6% (95% CI: 2.1–5.0%). Between-study heterogeneity was very high ( $I^2 = 98\%$ ) (Figure 2), corresponding to a wide prediction interval of 0.0–8.7%.

When restricting the analysis to studies with a NOS score  $\geq 6$ , the prevalence increased slightly to 4.4% (95% CI: 1.6–7.3%), while heterogeneity improved slightly ( $I^2 = 80\%$ ), and when restricting the analysis to studies that performed imaging prior to the initiation of biologics (16,19,20,23,24), the prevalence of ILD further increased to 4.8% (95% CI: 2.0–7.6%), while heterogeneity remained high ( $I^2 = 80\%$ ). Meta-regression by disease duration indicated that ILD prevalence increased by 0.43 percentage points per year after approximately 10 years of disease (intercept: -4.3, 95% CI: -0.15–1.10;  $R^2 = 100\%$ ). However, the model was not statistically significant ( $P = 0.14$ ), and the number of studies reporting disease duration was limited (16,18,19,21). Meta-regression by the mean/median age of the study populations showed that ILD prevalence increased by 0.22 percentage points per year from approximately 36 years of age (intercept: -7.9, 95% CI: 0.02–0.41,  $P = 0.03$ ) (Figure 3). The model explained some between study heterogeneity ( $R^2 = 56\%$ ). The high prevalence outliers (20,22,24) included mainly patients with PsA (Table 1). When both age and the proportion of PsV patients within

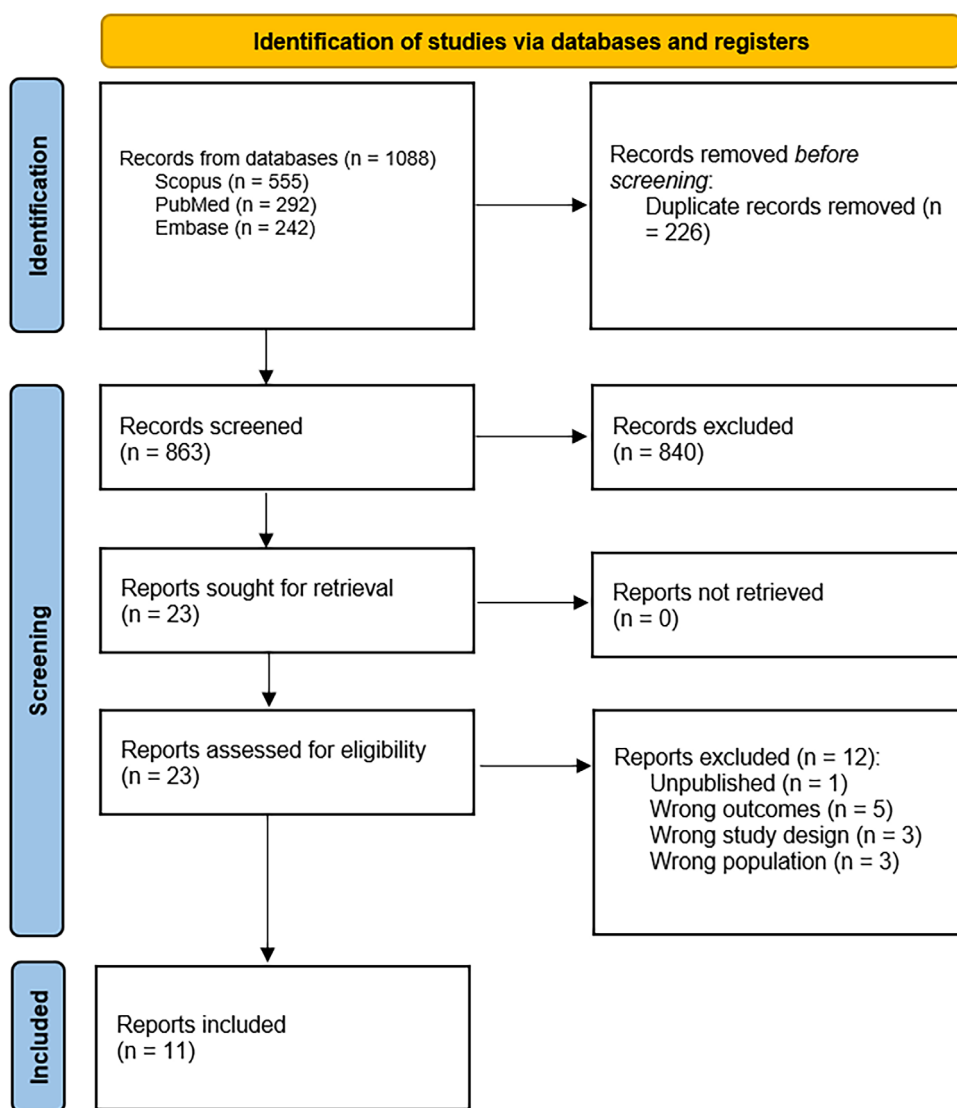


Figure 1. PRISMA flow diagram illustrating the study selection process.

each study population were included as moderators in a combined meta-regression, the model explained most of the between-study heterogeneity ( $R^2 = 87\%$ ). After adjustment for the proportion of PsV patients, the estimated increase in ILD prevalence was 0.19 percentage points per year (95% CI: 0.08–0.30,  $p < 0.001$ ). Conversely, when adjusted for age, a higher proportion of PsV patients (i.e., a lower proportion of PsA and GPP patients) was independently associated with a lower ILD prevalence. Thus, a 10% increase to the proportion of PsV patients corresponded to a 0.33 percentage point decline in ILD prevalence (95% CI: 0.09–0.57,  $p < 0.01$ ).

### Sex and smoking history

Subgroup analysis stratified according to sex showed an ILD prevalence of 4.8% (95% CI: 2.6–7.0%;  $I^2 = 61\%$ ) in male patients and 2.9% (95% CI: 0.6–5.2%;  $I^2 = 67\%$ ) in female patients. Analysis stratified according to smoking history, showed an ILD prevalence of 3.2% (95% CI: 0.1–6.3%;  $I^2 = 74\%$ ) in never-smokers, compared to 7.2% (95% CI: 3.4–11.0%;  $I^2 = 74\%$ ) among current or former smokers. Based on data from three studies (16,19,23), the pooled prevalence of concurrent emphysema among patients with psoriatic disease and ILD was 45% (95% CI: 27–63%;  $I^2 = 23\%$ ).

**Table 1.** Characteristics of included studies.

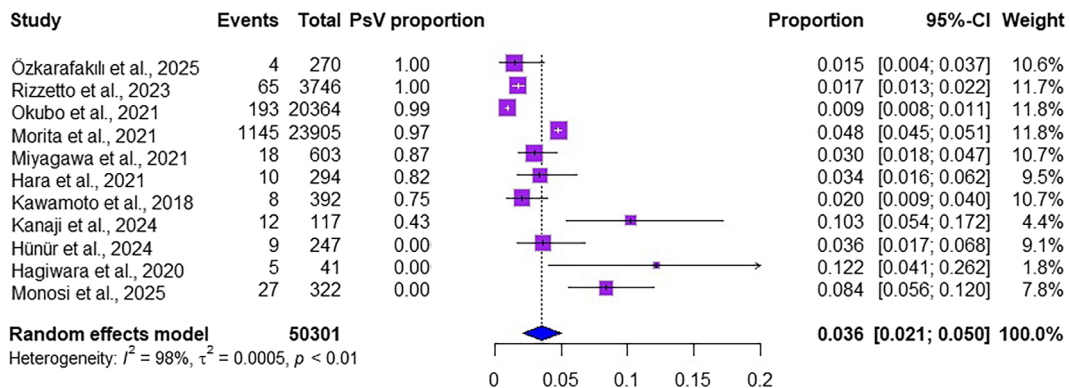
First author, country, publication year	Psoriatic disease type	Patients, n	Mean age, years	Recruitment setting	Any ILD, n (%)	UIP*, n (%) NSIP, n (%)	NOS score
<b>Kawamoto, Japan, 2018 (16)</b>	PsV (75%) PsA (21%) GPP (3%) Other (1%)	392	53.9	Retrospective review of CT scans performed prior to initiation of biologics in of psoriatic patients	8 (2%)	UIP: Na NSIP: Na	S: 2 C: 2 O: 1 <b>T: 5</b>
<b>Hagiwara, Japan, 2020 (22)</b>	PsA (100%)	41	45.6	Cross-sectional study examining consecutive patients with PsA	5 (12.2%)	UIP: Na NSIP: Na	S: 4 C: 2 O: 0 <b>T: 6</b>
<b>Hara, Japan, 2021 (19)</b>	PsV (82%) PsA (15%) GPP (2%) Other (<1%)	294	54.0	Retrospective review of CT scans performed prior to initiation of biologics in of psoriatic patients	10 (3.4%)	UIP: Na NSIP: Na	S: 2 C: 2 O: 1 <b>T: 5</b>
<b>Miyagawa, Japan, 2021 (23)</b>	PsV (87%) PsA (10%) GPP (1%) Other (2%)	603	54.0	Retrospective review of medical records of psoriatic patients prior to initiation of biologics	18 (2.5%)	UIP: Na NSIP: Na	S: 3 C: 2 O: 1 <b>T: 6</b>
<b>Morita, Japan, 2021 (5)</b>	PsV (97%) GPP (3%)	23905	62.8	Registry-based study utilizing the Japanese Medical Data Vision database which contains hospital-based claims from acute care settings	1145 (4.8%)	UIP: Na NSIP: Na	S: 0 C: 1 O: 0 <b>T: 1</b>
<b>Okubo, Japan, 2021 (28)</b>	PsV (99%) GPP (1%)	20364	42.6	Registry-based study utilizing the Japanese Medical Data Center database which contains claims data from employed and insured individuals	193 (0.9%)	UIP: Na NSIP: Na	S: 1 C: 1 O: 0 <b>T: 2</b>
<b>Rizzetto, Italy, 2023 (29)</b>	PsV (100%)	3746	Na	PsV patients with ILD identified via retrospective review of dermatology records.	65 (1.7%)	UIP: 36 (1.0%) NSIP: 19 (0.5%)	S: 2 C: 1 O: 0 <b>T: 3</b>
<b>Hünür, Turkey, 2024 (18)</b>	PsA (100%)	247	52.0	Retrospective review of hospital records.	9 (3.6%)	UIP: 2 (0.8%) NSIP: 3 (1.2%)	S: 3 C: 2 O: 1 <b>T: 6</b>
<b>Kanaji, Japan, 2024 (20)</b>	PsV (43%) PsA (56%) GPP (2%)	117	55 <sup>†</sup>	Retrospective review of hospital records. Imaging performed prior to biologics and methotrexate.	12 (10.3%)	UIP: 2 (1.7%) NSIP: 1 (0.9%)	S: 2 C: 2 O: 1 <b>T: 5</b>
<b>Özkarafakılı, Turkey, 2025 (21)</b>	PsV (100%)	270	48 <sup>†</sup>	Cross-sectional study of consecutive patients visiting the dermatology outpatient clinic	4 (1.5%)	UIP: 2 (0.7%) NSIP: 2 (0.7%)	S: 4 C: 2 O: 1 <b>T: 7</b>
<b>Monosi, Italy, 2025 (24)</b>	PsA (100%)	322	56.3	Cross-sectional study of patients with PsA from three Italian centers examined prior to initiation of biologics.	27 (8.4%)	UIP: 5 (1.6%) NSIP: 15 (4.7%)	S: 4 C: 2 O: 2 <b>T: 8</b>

*Abbreviations:* NOS = Newcastle–Ottawa Scale; S = Selection; C = Comparability; O = Outcome; T = Total; PsA = psoriatic arthritis; PsV = psoriasis vulgaris; UIP = usual interstitial pneumonia; NSIP = nonspecific interstitial pneumonia; GPP = Generalized pustular psoriasis. Maximum total NOS score is 9. \* Definite or probable UIP; † Reporting median age.

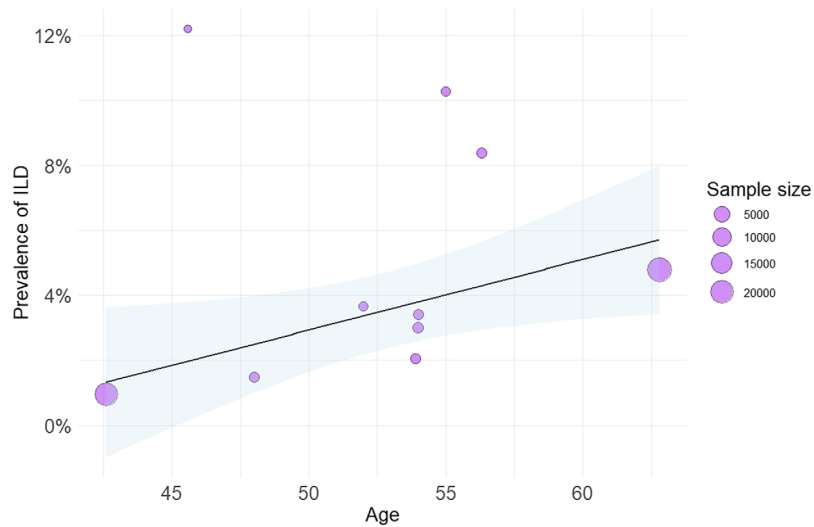
**Table 2.** ILD definitions and diagnostic method.

First Author	Study design	CT modality and coverage* (%)	ILD definition
Kawamoto et al.	Retrospective review of medical records	CT (100%)	CT scans were evaluated for features of interstitial pneumonia, including ground-glass opacities and reticulation, by two specialists from the Japanese Respiratory Society.
Hagiwara et al.	Cross-sectional	Unknown (100%)	Interstitial pneumonia definition not clarified
Hara et al.	Retrospective review of medical records	CT (Na)	Interstitial pneumonia definition not clarified
Miyagawa et al.	Retrospective review of medical records	CT (75%)	CT scans were evaluated for interstitial pneumonia by two specialists from the Japanese Respiratory Society.
Morita et al.	Retrospective registry-based cohort study	Unknown (Na)	ICD-10 codes for interstitial pneumonia
Okubo et al.	Retrospective registry-based cohort study	Unknown (Na)	ICD-10 codes for interstitial pneumonia
Rizzetto et al.	Retrospective review of medical records	Unknown (Na)	CT scans were evaluated for patterns of interstitial lung disease by two radiologists with at least 10 years of experience according to international consensus criteria.
Hünür et al.	Retrospective review of medical records	HRCT/CT (100%)	The interstitial lung disease classification was made based on the 2002 ATS/ERS consensus criteria
Kanaji et al.	Retrospective review of medical records	HRCT (63%)	Interstitial lung disease was diagnosed based on clinical features and high-resolution CT findings. scans were evaluated by a pulmonologist and a chest radiologist, with discrepancies resolved by consensus.
Özkarafaklı et al.	Cross-sectional	HRCT (100%)	HRCT scans were evaluated for patterns of UIP, probable UIP, or NSIP by two thoracic radiologists.
Monosi et al.	Cross-sectional	HRCT (100%)	Interstitial lung disease was diagnosed through a multidisciplinary approach using HRCT features, and classified into UIP, probable UIP, or NSIP patterns according to ATS/ERS guidelines.

*Abbreviations:* CT = computed tomography; HRCT = high-resolution computed tomography; ICD-10 = International Classification of Diseases, 10th revision; ATS = American Thoracic Society; ERS = European Respiratory Society; UIP = usual interstitial pneumonia; NSIP = nonspecific interstitial pneumonia. \*Coverage refers to the proportion of patients who underwent CT or HRCT.



**Figure 2.** The prevalence of ILD in any psoriatic disease. *Abbreviations:* ILD = interstitial lung disease; PsV = psoriasis vulgaris. Forest plot showing the pooled prevalence of ILD in patients with any psoriatic disease. The studies are arranged according to the proportion of the study population with PsV. The diamond represents the overall pooled prevalence estimate with its 95% confidence interval, calculated using a random-effects model.



**Figure 3.** Prevalence of any ILD by mean/median age. *Abbreviations:* ILD = Interstitial lung disease. Meta-regression of ILD prevalence according to mean/median age. Each point represents a study, with point size proportional to the number of included subjects. The black line represents the meta-regression, and the shaded area indicates the 95% confidence interval.

### HRCT patterns

The pooled prevalence of the UIP pattern among patients with any psoriatic disease was 1.0% (95% CI: 0.7–1.3%;  $I^2 = 0\%$ ), and the prevalence of the NSIP pattern was 1.3% (95% CI: 0.2–2.4%;  $I^2 = 70\%$ ) (Figure 4).

### Psoriatic disease subtypes

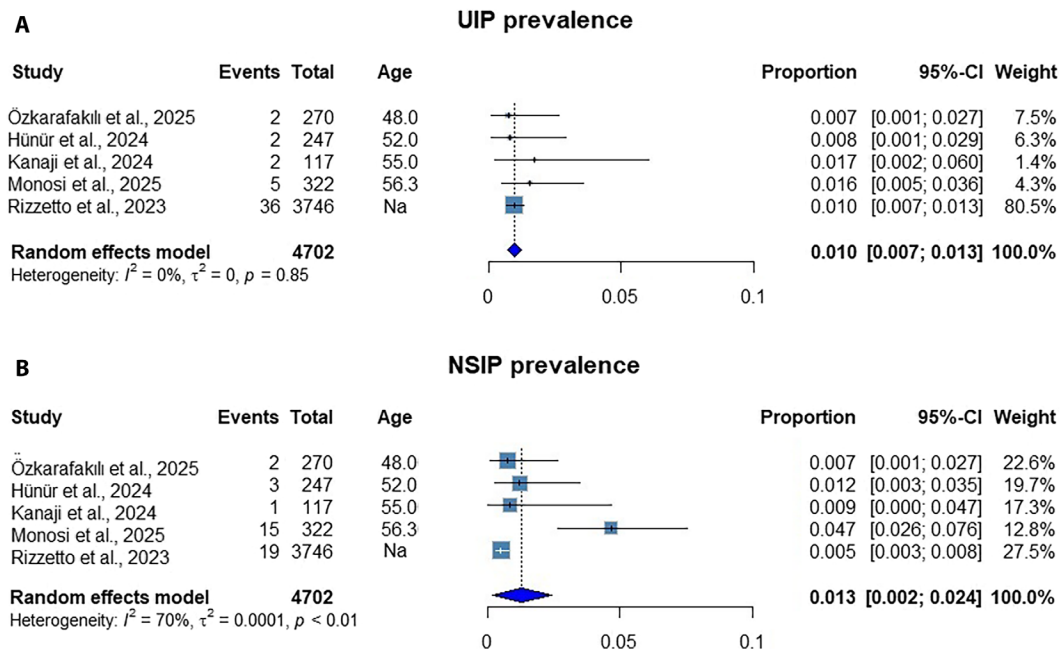
Among patients with PsV, the pooled prevalence of ILD was 2.4% (95% CI: 1.1–3.6%;  $I^2 = 99\%$ ) (Figure 5A). Exclusion of the outlier study by Kanaji et al. (20) slightly reduced the prevalence estimate to 2.2% (95% CI: 0.9–3.4%). However, heterogeneity remained high ( $I^2 = 99\%$ ). When restricting to studies that performed imaging prior to the initiation of biologics (16,19,20), the prevalence of ILD in patients with PsV was 2.8% (95% CI: 0.1–5.5%;  $I^2 = 68\%$ ) (Figure 6A).

Among patients with PsA, the pooled prevalence of ILD was 5.7% (95% CI: 2.5–8.9%;  $I^2 = 73\%$ ) (Figure 5B). When restricting to studies that performed imaging prior to the initiation of biologics (16,19,20,24), the prevalence of ILD was 5.9% (95% CI: 1.6–10.1%;  $I^2$

= 81%) (Figure 6B). Among patients with GPP, the pooled prevalence of ILD was 8.4% (95% CI: 6.4–10.4%;  $I^2 = 0\%$ ) (Figure 5C). No sensitivity analysis was performed due to absence of outliers and few studies.

### Discussion

This meta-analysis is, to the best of our knowledge, the first to systematically synthesize data on the prevalence of ILD in patients with psoriatic disease. The pooled ILD prevalence in patients with any psoriatic disease was 3.6%. In comparison, the estimated prevalence of ILD in the general population is less than 0.1% (30). However, caution is warranted when comparing this prevalence estimate to the background population, given potential differences in demographic characteristics and exposures such as medication, work environment, and smoking history. Thus, ILD prevalence may reach up to 5% in individuals from the general population with a smoking history of  $\geq 10$  pack-years, as reported in the COPDGene study (31).



**Figure 4.** The prevalence of UIP and NSIP patterns in any psoriatic disease. *Abbreviations:* UIP = usual interstitial pneumonia; NSIP = nonspecific interstitial pneumonia. Forest plot showing the pooled prevalence of UIP (A) and NSIP (B). Prevalence estimates are presented as proportions. The diamond represents the overall pooled prevalence estimate with its 95% confidence interval, calculated using a random-effects model.

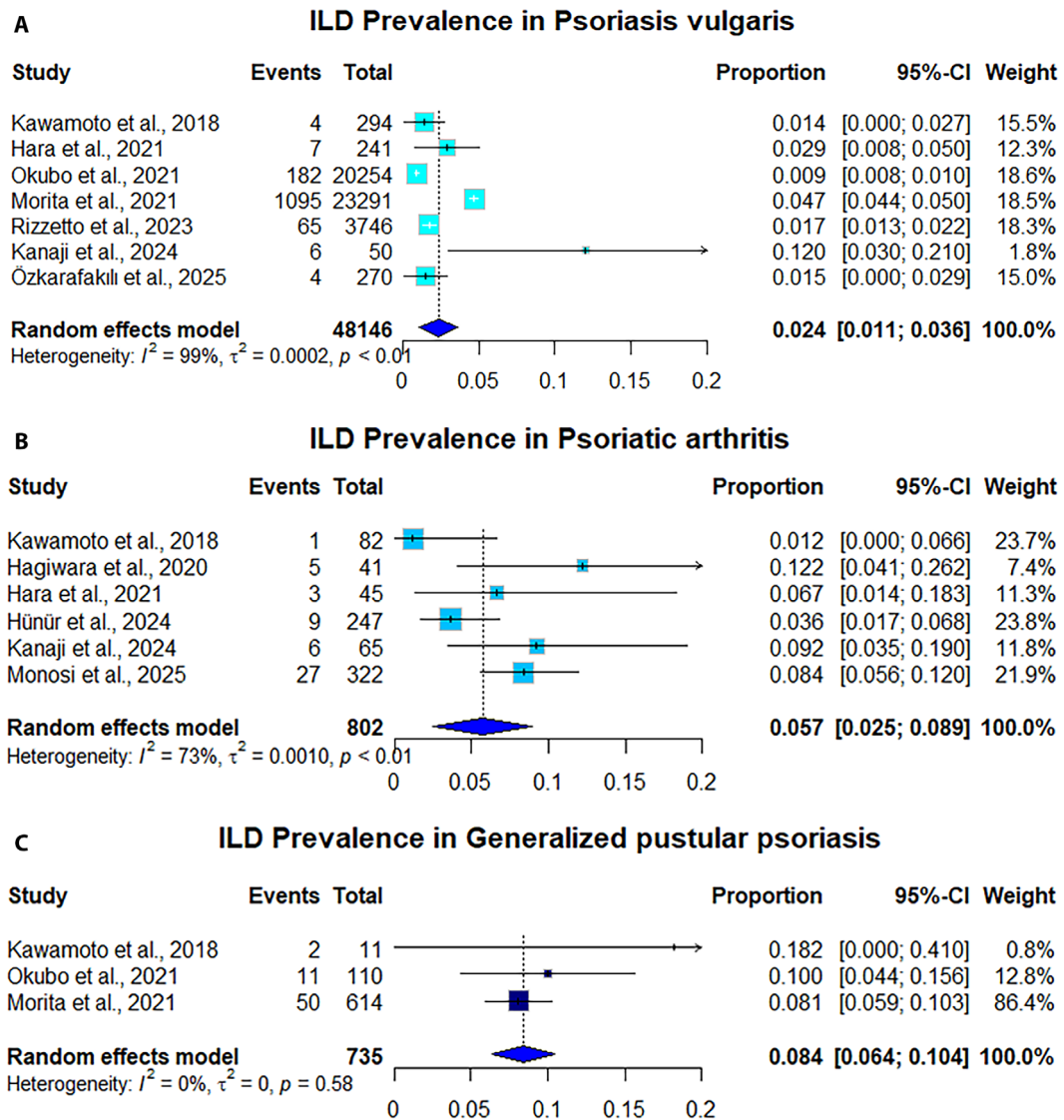
### Risk of ILD across psoriasis subtypes

ILD prevalence varied notably between psoriatic disease subtypes, with estimated rates of 2.4% in PsV, 5.7% in PsA, and 8.4% in GPP. Similar patterns have been observed in an American registry-based study, where patients with PsA had a significantly higher ILD risk compared to both matched controls (relative risk 1.9) and PsV (relative risk 1.5) (32). When comparing PsA to PsV, immunosuppressive therapies were included in the matching, along with smoking, age, sex, race, and body mass index, implying that the observed difference in ILD risk is unlikely to be explained by these factors alone. Similarly, a Nordic registry-based study reported a fourfold increased risk of ILD in patients with PsA who were treated with biologics, compared to matched controls. Among these patients, concomitant methotrexate use was associated with a hazard ratio of 0.9 for ILD. Thus, methotrexate co-medication did not appear to increase ILD risk in this study (33). While the evidence consistently indicates an increased risk of ILD in PsA patients, findings for PsV are conflicting (5,28,32), and further research

is needed to establish whether the risk of ILD is increased in these patients.

### Potential pathophysiological mechanisms and risk factors

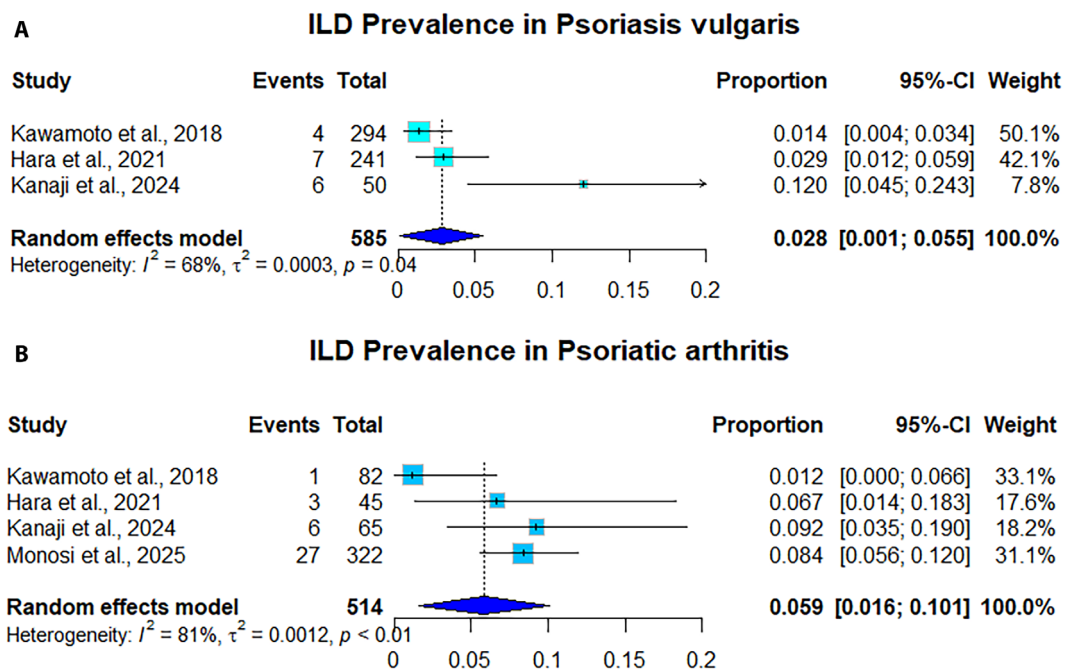
PsA has been associated with an increased risk of cardiovascular disease, type 2 diabetes, and hyperlipidemia compared to PsV (34). This may reflect a greater systemic inflammatory burden of PsA (35,36), and longer psoriatic disease duration, as PsV often precedes PsA (37) leading to increased cumulative exposure to systemic inflammation. Moreover, a swollen joint count >3 has been linked to an increased risk of ILD in patients with PsA (24), supporting that severe psoriatic disease may increase ILD risk. Our meta-regression analyses demonstrated that age was associated with a higher prevalence of ILD. Although the association did not reach statistical significance, ILD prevalence appeared to increase with disease duration as well. Disease duration, disease severity and systemic inflammation have been associated with an increased risk of ILD in patients with RA (15). Similarly,



**Figure 5.** The prevalence of ILD in Psoriasis vulgaris, Psoriatic arthritis and generalized pustular psoriasis. *Abbreviation:* ILD = interstitial lung disease. Forest plots showing the pooled prevalence of ILD in patients with psoriasis vulgaris (A), psoriatic arthritis (B), and generalized pustular psoriasis (C). The blue diamonds illustrate the overall pooled prevalence estimates with 95% confidence interval, calculated using a random-effects model.

systemic inflammation has been linked to a higher risk of ILD in primary Sjögren's syndrome (11), as well as increased mortality in RA-associated ILD (RA-ILD), IPF, and systemic sclerosis-associated ILD (SSc-ILD) (38). Further research is needed to clarify whether disease duration, disease severity and systemic inflammation are also associated with an increased risk if ILD in patients with psoriatic disease. The estimated prevalence of ILD was approximately twice as high among

patients with any psoriatic disease who had a history of tobacco smoking. Thus, tobacco smoking may increase ILD risk, consistent with observations in primary Sjögren's syndrome, RA and IPF (11,15,39,40). However, confidence intervals did overlap, limiting firm conclusion. In this meta-analysis, 45% of patients with psoriatic disease and ILD also exhibited emphysema, a prevalence comparable to that observed in RA-ILD and IPF patients (41), likely reflecting the



**Figure 6.** ILD prevalence in Psoriasis vulgaris and Psoriatic arthritis prior to treatment with biologics. *Abbreviations:* ILD = interstitial lung disease; PsA = psoriatic arthritis PsV = Psoriasis vulgaris. Forest plots showing the pooled prevalence ILD prior to initiation of biologics in patients with A) psoriasis vulgaris and B) psoriatic arthritis. The diamond represents the overall pooled prevalence estimate with its 95% confidence interval, calculated using a random-effects model.

shared risk factor of cigarette smoking. Thus, cigarette smoking and psoriatic disease may have an additive effect in causing ILD as observed in other immune-mediated diseases (11,15). While cigarette smoking appears to increase the risk of ILD, Rizzetto et al. reported that more than one-third of psoriatic patients with a UIP pattern were never-smokers (29), indicating that fibrotic ILD may develop even in the absence of cigarette smoke exposure. Both IPF and RA-ILD with UIP patterns are known to carry a poor prognosis (42–46), and further studies are needed to determine whether UIP in the context of psoriatic disease is associated with similar outcomes. The prevalence of ILD appeared to be higher in male patients. This is consistent with findings in both RA-ILD and IPF, where male sex is a recognized risk factor (33,47–49). This association may, in part, reflect sex-related differences in health-related behaviors, including cigarette smoking. Drug-induced ILD has been reported as a complication of various drugs including disease-modifying anti-rheumatic drugs (DMARDs) and biologics (17,23,50–56). Traditionally, it has been defined,

according to Camus et al. (57), as ILD with a temporal association to a drug known to cause ILD, the absence of any alternative plausible cause, and improvement upon drug withdrawal. However, the diagnosis of drug-induced ILD remains challenging, especially in patients with systemic inflammatory diseases, where an undiagnosed underlying ILD could be misinterpreted as drug-induced. To establish the diagnosis with certainty in these patients, it would require relevant imaging demonstrating no signs of ILD immediately prior to drug initiation, followed by the onset of ILD with a clear temporal relationship to the drug in question and improvement upon drug withdrawal. In practice, the diagnosis is rarely established on such a solid basis, as pre-treatment imaging is not routinely available and other interventions or comorbidities may confound the temporal association. Consequently, the attribution of ILD to drug exposure often remains presumptive rather than definitive, highlighting the inherent challenges in distinguishing drug-induced ILD from ILD caused by the underlying systemic inflammatory disease. Recent studies indicate that methotrexate

and biologics are not associated with an increased risk of ILD in RA and may even have a protective effect (15,58,59), whereas corticosteroids may increase the risk of ILD in RA patients (15). In the present meta-analysis, five studies (16,19,20,23,24) reported ILD prevalence prior to the initiation of biologic therapy. Restricting the analysis to these studies resulted in a slightly higher estimated prevalence of ILD in both PsV and PsA, indicating that ILD is typically present in psoriatic patients prior to initiation of biologic therapy. Future studies could explore whether biologic therapies might exert a protective effect on the lungs by reducing systemic inflammation, analogous to findings in psoriasis and CVD where biologics have been shown to reduce coronary artery inflammation and the risk of CVD (7,8). Only Kanaji et al (20) assessed ILD prevalence before initiation of any treatment associated with drug-induced lung injury, including DMARDs and biologics. Consequently, it remains uncertain to what extent DMARD-induced lung injury may have contributed to the reported ILD prevalence, and further studies are warranted to determine whether DMARDs increase the risk of ILD in psoriatic patients. Regardless of etiology, the seemingly increased prevalence of ILD in patients with psoriatic disease, particularly PsA and GPP, highlights the importance of clinical vigilance. To ensure early identification of parenchymal changes or pulmonary function impairment, healthcare providers should remain aware of the potential for pulmonary involvement in patients with psoriatic disease. We suggest that clinicians consider pulmonary evaluation, including pulmonary function testing and HRCT, in psoriatic patients presenting with unexplained respiratory symptoms such as progressive dyspnea, particularly when additional risk factors such as older age or cigarette smoking are present. Future research may help clarify whether PsV is associated with ILD, as well as elucidate the potential pathophysiological mechanisms linking psoriatic disease and ILD. In addition, further studies could explore the clinical relevance and prognosis of different HRCT patterns, such as UIP and NSIP, within this patient population. Finally, future research could investigate the utility of lung ultrasound (LUS) as a screening tool for ILD in psoriatic patients. A growing body of literature has investigated the diagnostic utility

of LUS in Connective Tissue Disease-associated ILD (CTD-ILD), with reported sensitivities often around 80% (60–63), but the current European Respiratory Society (ERS) / European Alliance of Associations for Rheumatology (EULAR) guidelines suggest not to replace HRCT with lung ultrasound (LUS) for CTD-ILD screening (64). LUS presents several advantages: it is readily available, radiation-free, and economically viable compared to HRCT. Consequently, LUS could potentially serve as a valuable alternative screening method in the future. The primary limitation of LUS is its inherent user-dependent nature. Furthermore, HRCT would still be required subsequently to verify the diagnosis and accurately quantify parenchymal involvement. Therefore, LUS could potentially serve as an initial screening tool when the suspicion of ILD is low to moderate, but high-risk patients should probably proceed directly to HRCT.

## Limitations

Differences in study methodology, ILD definitions, CT modality and population characteristics, including psoriatic disease subtype and mean age, likely contributed to the substantial heterogeneity observed in the meta-analysis of ILD prevalence in any psoriatic disease. Meta-regression including both mean/median age and the proportion of PsV patients explained most of the between-study heterogeneity ( $R^2 = 87\%$ ), highlighting that both age and psoriatic disease subtype contribute substantially to the between-study variability in reported ILD prevalence. Therefore, the overall ILD prevalence estimate in any psoriatic disease reported in this meta-analysis should be interpreted with caution, as without consideration of psoriatic disease subtype and age, its clinical relevance is likely limited. The meta-regression method has certain limitations which should also be considered. First, the use of study-level rather than individual patient data introduces the risk of ecological fallacy, where associations observed at the study level may not reflect true relationships at the individual level (65). Second, the meta-regression assumes a linear relationship between age and ILD prevalence, which may not hold true across the entire lifespan, and non-linear patterns or

thresholds could remain undetected due to the limited number of studies. Most of the included studies were based on hospital cohorts, which may have led to selection of patients with more severe psoriatic disease and an overestimation of ILD prevalence. Conversely, CT or HRCT was rarely performed in all study participants, and older studies often relied on CT rather than HRCT, potentially leading to underestimation of ILD prevalence. Accordingly, Kanaji et al. (20), who employed HRCT, reported a higher prevalence of ILD, although most cases were mild, with only four out of 12 involving  $\geq 20\%$  of the lung fields, and just three meeting criteria for definite or probable UIP or NSIP. Finally, most studies were conducted in Japanese populations, limiting the generalizability of the findings to other countries and ethnic groups. Differences in ethnic and genetic background, environmental exposures, clinical awareness, and ILD definitions may contribute to geographical variations in ILD prevalence. Additional studies from geographically and ethnically diverse populations are therefore needed to clarify whether the observed ILD prevalence reflects a universal pattern or is specific to certain regions or ethnic groups.

## Conclusion

ILD appears to be a clinically relevant comorbidity in patients with psoriatic disease, particularly among those with PsA and GPP, with estimated prevalences of 5.7% and 8.4%, respectively. The estimated prevalence among patients with PsV was lower at 2.4%, and whether this represents an increased risk compared to the general population remains uncertain. Approximately 1% of patients exhibited a UIP pattern on HRCT, which may be of prognostic relevance given the poor outcomes typically associated with UIP. Male sex, a history of cigarette smoking and old age may be important risk factors of ILD. Future research could investigate how disease duration and severity, may influence ILD risk in this population, and whether biologics may confer a protective effect. These results should be interpreted with caution due to methodological heterogeneity and the observational nature of the data. Nonetheless, ILD may represent a potential comorbidity in patients with

psoriatic disease, particularly in those with respiratory symptoms or established risk factors. In such cases, further diagnostic evaluation, including HRCT and pulmonary function testing, should be considered.

**Data Availability:** The data extraction templates and datasets analyzed during the current study are available from the corresponding author upon reasonable request.

**Conflict of Interest:** Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

**Declaration on the Use of AI:** During the preparation of this work, the authors used Gemini 1.5 Pro (Google) to improve the language and readability of the manuscript. After using this tool, the authors carefully reviewed, edited, and verified the content. The authors take full responsibility for the final content of the publication.

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