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# The prevalence of interstitial lung disease and bronchiectasis in rheumatoid arthritis: A systematic review and meta-analysis

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**Abstract.** *Background and Aim:* Rheumatoid arthritis (RA) is associated with an increased risk of interstitial lung disease (ILD) and bronchiectasis. Understanding the prevalence of these diseases is essential for timely diagnosis and management. Our aim was to estimate the prevalence of ILD and bronchiectasis in RA patients. *Study Design and Methods:* A systematic literature search was performed on PubMed, Embase, and Google Scholar to identify all studies performing HRCT in consecutive RA patients. Articles were screened by three independent authors in accordance with PRISMA guidelines. Random-effects meta-regression was performed to estimate the prevalence according to RA duration and C-reactive protein. *Results:* Twenty-four studies comprising 2,532 RA patients were included. The estimated prevalence of ILD at the time of RA diagnosis was 8.5% (95% CI: 4.4–12.5%), increasing by 3.0 percentage points (95% CI: 2.1–3.9%) per year after RA diagnosis (P<0.0001, $R^2$=95%). The estimated prevalence of bronchiectasis at RA diagnosis was 8.2% (95% CI: 1.6–14.7%), increasing 1.1 percentage points (95% CI: 0.3–1.9) per year after RA diagnosis (P<0.01, $R^2$=34%). Bronchiectasis prevalence was strongly associated with C-reactive protein and increased by 3.1 percentage points (95% CI: 0.9–5.4) per unit increase in CRP (mg/dL) (p<0.01, $R^2$=77%) *Conclusion:* Bronchiectasis and ILD are common pulmonary manifestations of RA, particularly in patients with long-term disease. Possibly due to the cumulative effect of chronic inflammation. Therefore, HRCT for all patients with respiratory symptoms or RA duration exceeding 5 years should be considered. This approach may facilitate earlier detection of preclinical ILD and timely intervention.

**Key words:** HRCT, honeycombing, interstitial lung disease, rheumatoid arthritis, bronchiectasis

## Introduction

Rheumatoid arthritis (RA) is a chronic autoimmune disease primarily affecting synovial joints. However, multiple extra-articular manifestations are known to affect RA patients as well (1). Interstitial lung disease (ILD) and bronchiectasis (BE), detectable on chest high-resolution computed tomography (HRCT), are important pulmonary manifestations of RA. Chronic obstructive pulmonary disease also occur more frequently in RA patients possibly due to the common risk factor of tobacco smoking (2). Consequently, respiratory disease is a common cause of death in these RA patients (3,4). Patients with RA-associated ILD (RA-ILD) have a higher mortality rate than RA patients without ILD (4). HRCT findings associated with ILD include reticulation, traction bronchiectasis (TBE), honeycombing (HC), and ground-glass opacities (GGO) (5). HC

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is seen on HRCT as well-defined, clustered cystic structures, typically located in the subpleural region. HC represents the destruction and remodeling of the lung parenchyma due to inflammatory, mechanical, infectious, or iatrogenic damage (5). HC is a hallmark feature of the usual interstitial pneumonia (UIP) pattern, which is indicative of advanced pulmonary fibrosis (5). RA-ILD patients with UIP pattern on HRCT are at high risk of acute exacerbation (6,7), HRCT progression, and forced vital capacity (FVC) and diffusion capacity for carbon monoxide (DLCO) (7,8) decline compared to RA-ILD patients without UIP (9). Additionally, while reported hazard ratios vary, the presence of a UIP pattern on HRCT is typically associated with about a twofold increased risk of mortality compared to RA-ILD without UIP (10–13). Reticulation, appearing as a network of fine linear opacities on HRCT, has also been associated with radiologic progression and FVC and DLCO decline (14,15), and may be an early sign of pulmonary fibrosis in the absence of HC. Traction bronchiectasis (TBE) refers to a dilation of the bronchial lumen resulting from fibrotic retraction of the surrounding lung tissue (5). In the context of ILD, GGO are usually a sign of inflammation, but GGO may also result from other conditions such as infection and congestive heart failure (5). Interstitial lung features in asymptomatic high-risk individuals, such as RA patients, are referred to as preclinical ILD (16). The reported prevalence of RA-ILD, including preclinical cases, varies widely, ranging from around 6% to 44% of RA patients (17,18). In comparison, interstitial features on CT are observed in around 2% of the general population, with the prevalence increasing linearly with age to almost 10% in individuals older than 70 years (15). Long-standing RA has been associated with higher risk of ILD (19), possibly due to the cumulative exposure to RA-related systemic inflammation (20). Dyspnea, cough, and recurrent pulmonary infections are indicative of ILD and BE in patients with RA, and the prevalence of UIP among symptomatic RA patients may be as high as 23% (21). Knowing the prevalence of ILD and BE in patients with RA is essential for risk stratification and determining the need for HRCT. Monitoring FVC and DLCO in patients with preclinical ILD allows for timely initiation of antifibrotic therapy and, when appropriate, referral to lung transplantation (22). The prevalence of ILD in RA patients is likely underestimated due to asymptomatic cases and unrecognized lung function decline, which can be masked by physical inactivity. By pooling data from all studies that performed HRCT in consecutive RA patients, we aim to provide an accurate estimate of ILD and BE prevalence in these patients.

## Methods

We systematically searched PubMed, Embase, and Google Scholar for studies that performed chest HRCT in consecutive RA patients. The protocol was registered on PROSPERO in August 2024 (ID: CRD42024581068). All search strings are included in the supplementary material. However, the initial PubMed search was considered too narrow and revised. The search, screening, and extraction processes followed the 2020 PRISMA statement (23). Title/abstract screening was performed independently by three reviewers in Covidence.org. Full-text articles were obtained successfully for all studies deemed eligible. Full-text screening was performed by two reviewers. Conflicts were solved by consulting a third reviewer for consensus. Reference lists of included studies were screened for additional eligible studies. An updated literature search conducted in April 2025 identified no additional studies. Studies were eligible if they met the following inclusion criteria: 1) Performing HRCT in consecutive RA patients. 2) Reporting the prevalence of ILD, BE or interstitial features including TBE, HC, GGO, and reticulation on HRCT. 3) Including only adult patients (≥18 years) diagnosed with RA according to the American College of Rheumatology (ACR), American Rheumatism Association (ARA), or European League Against Rheumatism (EULAR) diagnostic criteria. 4) Observational studies (cross-sectional or cohort) published between 1974 and 2025. 5) Reporting original data. Exclusion criteria were: 1) Systematic inclusion or exclusion of RA patients based on factors which could alter the risk of pulmonary involvement, such as previous chest X-ray, respiratory symptoms, or pulmonary function test results. 2) Abstracts, unpublished studies, and unoriginal data. 3) Articles not available in English.

### *Data extraction and risk of bias assessment*

Data extraction was performed independently by two reviewers using a standardized data extraction form. Disagreements were solved through

discussion until consensus was reached. Extracted information included: 1) Study characteristics, including publication year, study design, authors, and number of participants (Table 1). 2) Study population details, including median age, median RA duration, mean CRP concentration (mg/dL), and proportion of patients with respiratory symptoms and cigarette smoke exposure. 3) The total number of participants. 4) The prevalence of ILD and BE on HRCT. 5) The prevalence of specific interstitial features including TBE, HC, GGO, and reticulation on HRCT. Baseline HRCT results were extracted if sequential HRCT scans were performed. The Newcastle-Ottawa scale adapted for cross-sectional studies (24), was used for quality and risk of bias assessment. Studies were evaluated in three domains: patient selection, comparability, and outcome with a maximum score of 10 points. Studies scoring ≥7 was considered to have low risk of bias, 4-6 moderate risk of bias, and ≤3 high risk of bias. A detailed description of the risk of bias assessment is available as supplementary material.

*Statistical analysis*

Statistical analysis was performed in R (v4.3.2) using the 'Metafor' package. Random-effects proportional meta-analysis was performed to estimate overall prevalence. Between-study heterogeneity was assessed with $I^2$ statistics. Random-effects meta-regression was conducted to estimate the prevalence of ILD, BE, and specific interstitial features according to the study-specific median RA duration and mean CRP. The proportion of between-study heterogeneity explained by RA duration and CRP was quantified using $R^2$. Estimated prevalences at 0, 2, 5, 10, and 15 years of RA duration were calculated based on the meta-regression models. All estimates are reported with 95% confidence interval (CI). The meta-analysis was conducted according to MOOSE guidelines (25). Sensitivity analyses were conducted by limiting proportional meta-analyses and meta-regressions to studies with a NOS score ≥6, which was the highest threshold compatible with an adequate number of studies for meta-analysis.

## Results

The predefined search yielded 995 results. Title and abstract screening resulted in 54 articles for full-text screening. Thirty-four studies met all inclusion criteria, but 10 studies were excluded due to selection of specific RA patients (Exclusion criteria 1) (21,26–35). Thus, 24 studies comprising 2,532 patients were included in the review (Figure 1). Nineteen studies were cross-sectional (17,18,21,36–53), two were retrospective cohort studies (54,55), and three were prospective (36,56,57). NOS assessment indicated low risk of bias in 13 studies (37,41,42,45,47,49,51,53,54,56–59), and moderate risk of bias in 11 studies (17,36,39,40,43,44,46,48,50,52,55). Blinded HRCT assessment was reported in 11 studies (37,45,50–52,54–59). The remaining studies did not specify whether blinding was applied. No studies had a NOS score ≤3, due to the strict exclusion of studies at risk of selection bias (detailed risk of bias assessment is available in the supplement).

*Interstitial lung disease*

The prevalence of ILD was estimated based on 10 studies comprising 1,168 RA patients. The overall pooled prevalence was 22% (95% CI: 13–31%), with high heterogeneity ($I^2$ = 94%) (Figure 4A). In meta-regression, ILD prevalence was strongly associated with study-specific RA duration, which explained most of the observed heterogeneity ($R^2$=95%). The model predicted an ILD prevalence of 8.5% (95% CI: 4.4–12%) at the time of RA diagnosis, with an estimated increase to the ILD prevalence of 3.0 percentage points (95% CI: 2.1–3.9) per year after diagnosis (Table 2). The association between ILD prevalence and RA duration was highly significant (P<0.0001). The results were similar when the meta-analysis was restricted to studies with a NOS score ≥6. The overall prevalence of ILD was 21% (95% CI: 11–30%). Meta-regression predicted a baseline prevalence of 8.2% (95% CI: 4.3–12.1%) at the time of RA diagnosis, with an annual increase of 2.8 percentage points (95% CI: 1.9–3.8). The model explained 95% of the variance ($R^2$=95%, P< 0.0001). The association between ILD and CRP was not assessed due to few studies.

### Interstitial features

The pooled prevalence of HC was based on 18 studies comprising 1,364 RA patients. The overall pooled prevalence was 5.7% (95% CI: 4.1–7.3%). Heterogeneity was low ($I^2$=36%), and there was no statically significant association with RA duration

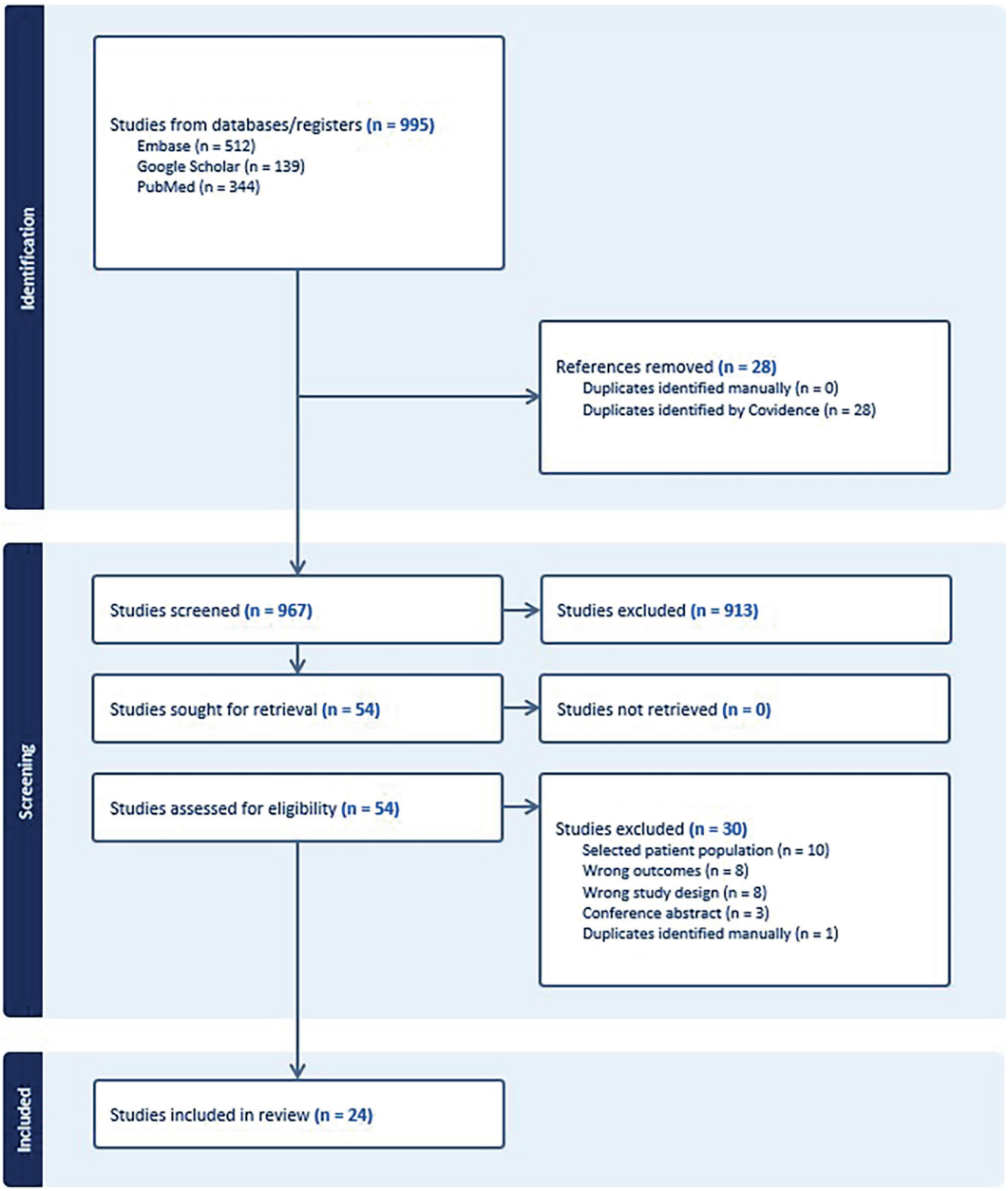


**Figure 1.** PRISMA flow diagram.

(Table 2, Figure 2A) or CRP (Figure 3A). Although, the prevalence of HC trended higher with both CRP and RA duration. The overall prevalence estimate was 4.9% (95% CI: 3.3–6.5%), with no significant association with RA duration or CRP, when the analysis was restricted to studies with a NOS score ≥6.

The pooled prevalence of GGO was based on 21 studies comprising 1,607 patients. The overall pooled prevalence was 17% (95% CI: 11–22%), and heterogeneity was high ($I^2$=91%). The high degree of heterogeneity was not explained by RA duration (Table 2, Figure 2B) or CRP (Figure 3B), although GGO prevalence trended higher with CRP. The overall prevalence of GGO remained unchanged at 17% (95% CI: 10–25%), with no significant association with RA duration or CRP, when the analysis was restricted to studies with a NOS score ≥6.

**Table 1.** Study characteristics

| First author, (year of publication) | RA patients, n | Median RA duration, years | Median age, years | Female, n (%) | Cigarette Smoke exposure, n (%) | Respiratory symptoms, n (%) | Study design |
|---|---|---|---|---|---|---|---|
| **Cortet et al, 1997** (36) | 68 | 12.0 | 58.8 | 54 (79%) | 16 (24%) | 47 (69%) | Prospective |
| **Gabbay et al, 1997** (37) | 36 | 1.1 | 51.8 | 25 (69%) | 20 (56%) | | Cross-sectional |
| **Dawson et al, 2001** (38) | 150 | 12.7 | 58.9 | 100 (67%) | 105 (70%) | | Cross-sectional |
| **Izumiyama et al, 2002** (39) | 123 | 10.6 | 62.0 | 101 (82%) | 6 (5%) | | Cross-sectional |
| **Bilgici et al, 2004** (40) | 52 | 8.4 | 53.6 | 44 (85%) | 13 (25%) | 21 (40%) | Cross-sectional |
| **Saracoglu et al, 2004** (53) | 40 | 9.5 | 49.2 | 31 (78%) | 20 (50%) | 12 (29%) | Cross-sectional |
| **Köker et al, 2007** (41) | 67 | 8.7 | 55.8 | 57 (85%) | 14 (21%) | | Cross-sectional |
| **Kanat et al, 2007** (42) | 54 | 9.8 | 46.9 | 46 (85%) | 12 (22%) | 22 (41%) | Cross-sectional |
| **Mori et al* (ERA group), 2008** (57) | 65 | 0.9 | 57.6 | 48 (74%) | 13 (20%) | 11 (17%) | Prospective |
| **Mori et al (LRA group), 2008** (57) | 61 | 11.8 | 62.5 | 52 (85%) | 8 (13%) | 19 (31%) | Prospective |
| **Noor et al, 2009** (17) | 63 | 14.0 | 56.7 | 56 (89%) | | 17 (27%) | Cross-sectional |
| **Youssef et al, 2011** (43) | 36 | 8.0 | 48.5 | 34 (94%) | 0 (0%) | 22 (61%) | Cross-sectional |
| **Skare et al, 2011** (44) | 71 | 11.7 | 46.5 | 63 (89%) | 24 (34%) | | Cross-sectional |
| **Habib et al, 2011** (52) | 40 | 1.5 | 37.6 | 28 (70%) | 5 (13%) | 4 (10%) | Cross-sectional |
| **Mori et al, 2012** (45) | 356 | 0.7 | 60.4 | 271 (76%) | 76 (21%) | 30 (8%) | Cross-sectional |
| **Reynisdottir et al, 2013** (50) | 105 | 0.1 | 56 | 70 (67%) | 74 (71%) | | Cross-sectional |
| **Chen et al, 2013** (51) | 103 | 4.3 | 49.1 | 76 (74%) | 2 (2%) | | Cross-sectional |
| **Baky et al, 2017** (46) | 70 | 7.3 | 44.0 | 61 (87%) | 7 (10%) | 35 (50%) | Cross-sectional |
| **Dong et al, 2019** (56) | 18 | 0.9 | 52.0 | 11 (61%) | 7 (38%) | | Prospective |
| **Shawky et al* (ERA group), 2019** (47) | 92 | 0.5 | 54.2 | 60 (65%) | 14 (15%) | 19 (21%) | Cross-sectional |
| **Shawky et al (LRA group), 2019** (47) | 82 | 6.0 | 59.4 | 57 (70%) | 16 (20%) | 35 (43%) | Cross-sectional |
| **Paulin et al, 2021** (18) | 79 | 0.3 | 46.5 | 66 (83%) | 42 (53%) | 25 (32%) | Cross-sectional |
| **Andronache et al, 2021** (48) | 92 | 15.0 | 63.8 | 73 (79%) | 39 (42%) | 65 (71%) | Cross-sectional |
| **Tanaka et al, 2022** (54) | 208 | 7.9 | 59.3 | 144 (69%) | 73 (35%) | | Retrospective |
| **Selldén et al, 2023** (49) | 30 | 0.0 | 58.0 | 25 (83%) | 12 (40%) | | Cross-sectional |
| **Chai et al, 2023** (55) | 371 | | 60.0 | 257 (69.3%) | 100 (27%) | | Retrospective |

*Abbreviations:* RA=rheumatoid arthritis. ERA=early RA. LRA=late RA. Characteristics of included studies. *Every row represents one study except Mori (2008) and Shawky (2019) which were divided into two rows each, because baseline characteristics were reported for late vs. early RA.

The pooled prevalence of reticulation was based on 16 studies comprising 1,236 RA patients. The overall prevalence was 24% (95% CI: 19–30%), and heterogeneity was high ($I^2$=80%). The prevalence of reticulation increased with RA duration (Table 2, Figure 2C), which explained some of the heterogeneity ($R^2$=35%). Notably, the prevalence of reticulation was strongly associated with median study CRP in meta-regression (Figure 3C). Thus, reticulation prevalence increased with 6.2 percentage points (95% CI:

**Table 2.** Predicted prevalence of interstitial lung disease, bronchiectasis, and interstitial features according to duration of rheumatoid arthritis

| | 0 years | 2 years | 5 years | 10 years | 15 years | $R^2$ | P-value |
|---|---|---|---|---|---|---|---|
| **ILD** | 8.5% (95% CI: 4.4 – 12.5%) | 14.4% (95% CI: 10.9 – 18%) | 23.4% (95% CI: 19.0 – 27.7%) | 38.3% (95% CI: 30.4 – 46.1%) | Na* | 95% | P<0.0001 |
| **BE** | 8.2% (95% CI: 1.6 – 14.7%) | 10.3% (95% CI: 4.9 – 15.7%) | 13.6% (95% CI: 9.4 – 17.8%) | 19.0% (95% CI: 14.4 – 23.6%) | 24.4% (95% CI: 17.0 – 31.8%) | 34% | P<0.01 |
| **Interstitial features** | | | | | | | |
| **HC** | 4.4% (95% CI: 1.6 – 7.3%) | 4.8% (95% CI: 2.4 – 7.1%) | 5.3% (95% CI: 3.5 – 7.1%) | 6.2% (95% CI: 4.1 – 8.3%) | 7.1% (95% CI: 3.8 – 10.4%) | 11% | P=0.3 |
| **GGO** | 17% (95% CI: 6.2 – 27.9%) | 16.8% (95% CI: 8 – 25.7%) | 16.5% (95% CI: 9.8 – 23.2%) | 15.9% (95% CI: 8.6 – 23.3 %) | 15.4% (95% CI: 3.3 – 27.5 %) | 0% | P=0.9 |
| **TBE** | 5.1% (95% CI: 0.0 – 11.7 %) | 6.9% (95% CI: 1.9 – 12 %) | 9.7% (95% CI: 6.5 – 12.9 %) | 14.2% (95% CI: 9.7 – 18.8 %) | Na* | 100% | P=0.06 |
| **Reticulation** | 11.1% (95% CI: 0.3 – 22 %) | 14.2% (95% CI: 5.3 – 23.1 %) | 18.7% (95% CI: 12.3 – 25.1 %) | 26.3% (95% CI: 21.1 – 31.5 %) | 33.9% (95% CI: 25.2 – 42.6 %) | 35% | P<0.01 |

*Abbreviations:* ILD=Interstitial lung disease. BE=Bronchiectasis. HC=Honeycombing. GGO=ground glass opacities. TBE: Traction bronchiectasis. Predicted prevalence of ILD, BE, HC, GGO, and TBE at 0, 2, 5, 10 and 15 years of RA duration according to random-effects meta-regression. *Not reported due to lacking studies with this duration of RA.

1.8-10.6) per unit increase in median CRP (mg/dL) according to the regression model. The association was highly significant (P<0.001) and explained a significant proportion of the observed between-study heterogeneity ($R^2$=61%). When restricting the analysis to studies with a NOS score ≥6, the overall prevalence of reticulation was 20% (95% CI: 14–27%). The association with RA duration remained statistically significant, with an estimated annual increase in reticulation prevalence of 1.2 percentage points (95% CI: 0.4–2.5) per year, ($R^2$=28%, P=0.04). Similarly, CRP remained significantly associated with reticulation, showing an increase of 4.7 percentage points (95% CI: 0.5–8.9) per unit increase in CRP (P=0.03). The pooled prevalence of TBE was based on 4 studies with 418 RA patients. The overall prevalence was 11% (95% CI: 8–14%), $I^2$=34%. The prevalence of TBE seemed to increase with RA duration (Figure 2D), although not reaching statistical significance in meta-regression (Table 2).

*Bronchiectasis*

The pooled prevalence of BE was based on 16 studies comprising 1,348 RA patients. The overall prevalence was 16% (95% CI: 11%–20%), with substantial heterogeneity ($I^2$=86%) (Figure 4B). RA duration explained some of the heterogeneity in BE prevalence ($R^2$=34%), with an estimated increase to the BE prevalence of 1.1 percentage points (95% CI: 0.3–1.9) per year after diagnosis (Table 2). The prevalence of BE was strongly associated to CRP and the model accounted for a substantial proportion of the between-study heterogeneity ($R^2$=77%) (Figure 3D). According to the model prevalence of BE increased by approximately 3.1 percentage points (95% CI: 0.9–5.4) per unit increase in CRP (p<0.01). When restricting the analysis to studies with a NOS score ≥6, the overall BE prevalence was 15% (95% CI: 9–21%). The association with RA duration remained statistically significant, with an estimated annual increase in BE prevalence of 1.1 percentage points (95% CI: 0.1–2.1) ($R^2$=28%, P=0.02). Similarly, CRP remained significantly associated with BE, showing an increase of 3.4 percentage points (95% CI: 0.9–6.0) per unit increase in CRP, ($R^2$ =74%; P<0.01).

## Discussion

In this comprehensive review, we have synthesized data from 24 studies to estimate the prevalence

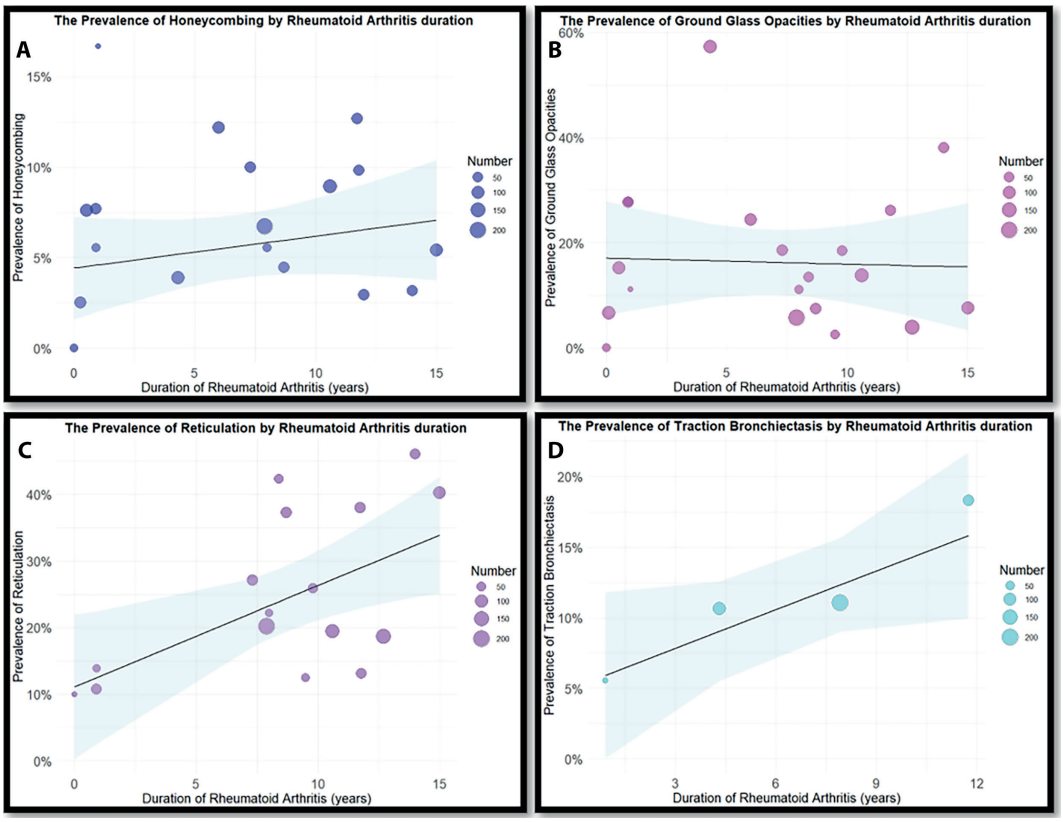


**Figure 2.** Random-effects meta-regression of the prevalence of (A) honeycombing, (B) ground-glass opacities, (C) reticulation, and (D) traction bronchiectasis according to study-specific median duration of rheumatoid arthritis. Each point represents one study. The size of the point is determined by the number of study participants. Only reticulation was significantly associated with RA duration. The shaded area around the regression line represents the 95% confidence interval of the meta regression.

of BE and ILD in RA patients. The overall pooled prevalence of BE was 16%, slightly lower than previous estimates (60). However, prevalence of BE did increase to 19-24% in patients with long-term RA. The prevalence of BE correlated strongly with CRP. One possible explanation is that RA patients with BE experience more frequent infections or chronic colonization with airway pathogens, leading to a higher CRP in RA patients with BE on average. Alternatively, RA patients with high level of systemic inflammation or recurrent infections may be more at risk of developing bronchiectasis. Both explanations may be true hereby by creating a self-reinforcing cycle where inflammation promotes airway damage, and airway damage predisposes to infections leading to systemic inflammation. Moreover, immunosuppressive therapies, a cornerstone in RA treatment, may further increase the risk of opportunistic and chronic infections (61). Clinicians must be aware of the increased risk of pulmonary infections in these patients. The overall prevalence of ILD was 22%, with marked variation depending on RA duration. Based on the meta-regression model, ILD prevalence increased from 8.5% at RA diagnosis to 38.5% at 10 years. The high prevalence observed in this meta-analysis, compared to previous estimates (62), is likely due to the systematic use of HRCT in all included studies, which enabled the detection of all RA-ILD cases, including preclinical RA-ILD. In contrast, registry-based studies may underestimate ILD prevalence due to reliance on diagnostic coding of RA-ILD patients identified in clinical settings, which likely results in underestimation of preclinical RA-ILD prevalence. Reticulation was the most prevalent interstitial feature, and its prevalence increased significantly with both RA duration and CRP. The association with CRP seemed to be stronger than RA duration suggesting that chronic systemic inflammation may be a

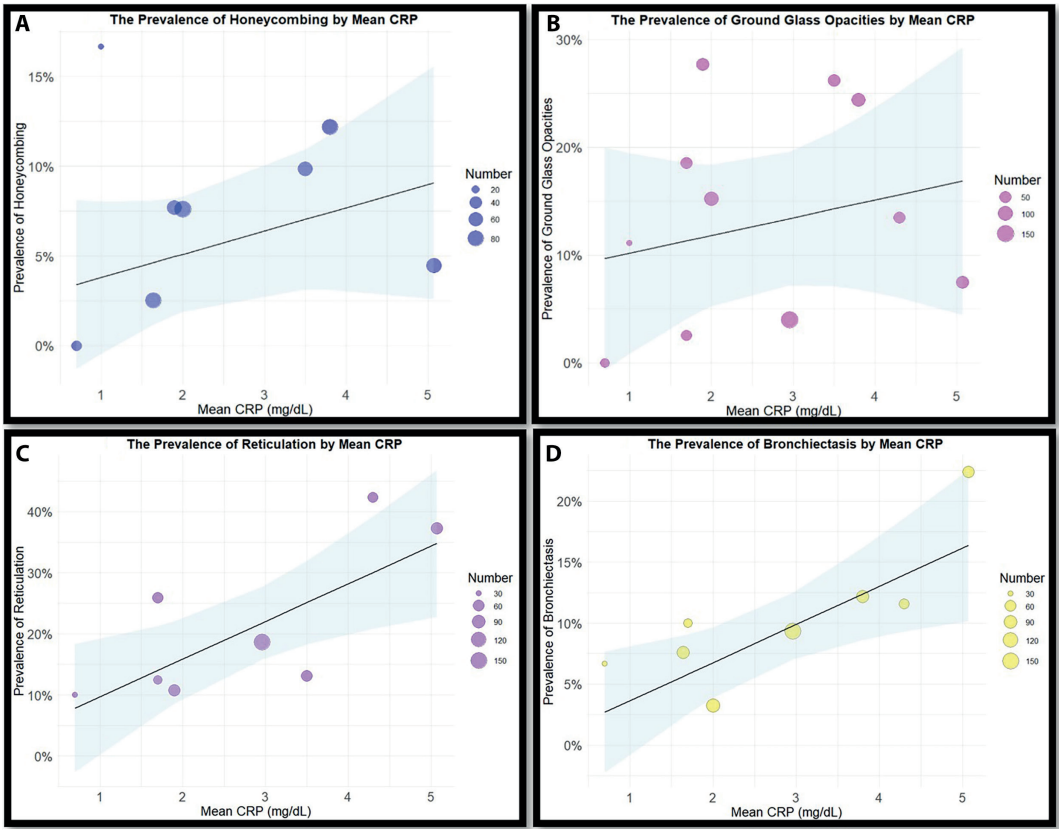


**Figure 3.** Random-effects meta-regression of the prevalence of (A) honeycombing, (B) ground-glass opacities, (C) reticulation, and (D) bronchiectasis according to study-specific mean CRP. Each point represents one study. The size of the point is determined by the number of study participants. Only reticulation and bronchiectasis were significantly associated with CRP. The shaded area around the regression line represents the 95% confidence interval of the meta regression.

key driver of reticulation. Thus, reticulation may be a result of cumulative RA related inflammation which leads to gradual fibrosing and permanent structural alterations to the parenchyma. GGO was present in 17% of patients but did not show a statistically significant association with RA duration or CRP, although prevalence trended higher with CRP. The lacking association with RA duration may reflect the reversible nature of GGO. The pooled prevalence of HC around 5%, and although it increased slightly with RA duration the association was not statistically significant. This may reflect the poor prognosis of HC and UIP (10–13), as conditions with limited long-term survival are less likely to accumulate in the population over time. The estimated prevalence of 4.4% at the time of RA diagnosis is noteworthy and suggests that some RA patients may have radiologic signs of pulmonary fibrosis prior to RA diagnosis. This has clinical relevance as ILD debut prior to RA diagnosis and UIP on HRCT both seem to be associated with an increased risk of acute exacerbation of ILD, which is a common cause of death in these patients (6).Identification of ILD at the preclinical stage may be beneficial, as both preclinical and clinical RA-ILD patients appear to be at high risk of HRCT progression and FVC and DLCO decline within few years (9,33,55,63,64). Chest HRCT could be considered for all patients with RA of more than five years' duration, as approximately one in four may have developed ILD by this time. Additionally, annual lung function testing and DLCO measurement in all patients with RA-ILD, including those with preclinical disease, may enable earlier detection of ILD progression and timely initiation of antifibrotic therapy. Furthermore, UIP seems to be highly prevalent among RA patients with respiratory symptoms (21). Therefore, respiratory symptoms should be addressed routinely. In RA patients with

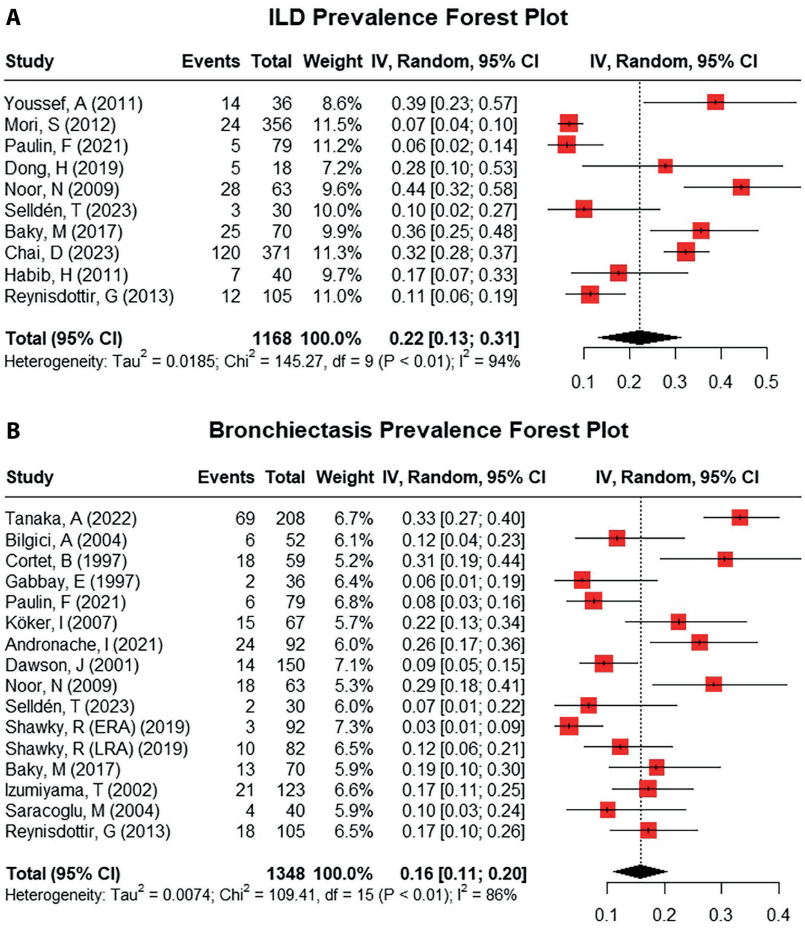


**Figure 4.** ERA = early rheumatoid arthritis; LRA = late rheumatoid arthritis. Forest plots showing the pooled prevalence of (A) interstitial lung disease and (B) bronchiectasis based on random-effects proportional meta-analysis. The squares represent the point estimates, and the horizontal lines indicate the 95% confidence intervals. Square size is proportional to the weight of the study in the meta-analysis.

respiratory symptoms, we recommend lung function testing, DLCO measurement, and chest HRCT regardless of RA duration, since 4% of patients seem to have HC at the time of RA diagnosis.

*Strengths and limitations*

By focusing exclusively on studies which performed HRCT in consecutive RA patients, all cases of RA-ILD (including preclinical) were identified. This approach resulted in a higher ILD prevalence estimate compared to previous studies, which have relied on other methods, such as diagnostic coding and registry-based data (4,62). Heterogeneity was generally high in the overall prevalence estimates. However, Meta-regression by CRP or RA duration accounted for most of the observed heterogeneity. The remaining heterogeneity may have reflected differences in study settings, inclusion criteria, or patient population characteristics such as RA disease severity and smoking history. We explored smoking history as a potential contributor to the heterogeneity but found no significant association between the proportion of patients with smoking history in each study and the prevalence of HRCT findings. This may reflect limitations in the smoking data, which lacked information on cumulative exposure and current smoking status. Thus, statistical analyses based on study-level data may obscure individual-level associations, as this method os inherently limited by the potential for ecological fallacy (65). The diagnosis of bronchiectasis implies irreversible bronchial dilatation (5). Determining irreversibility can be challenging in cross-sectional studies relying on a single

HRCT scan. Imaging features such as bronchial wall thickening, peribronchial fibrosis, lack of tapering, and cystic or varicose bronchial morphology may strongly suggest chronic structural changes. However, in the absence of these features, chronicity can be difficult to establish without sequential HRCTs. Therefore, some cases labelled as bronchiectasis in our analysis may represent reversible bronchial dilatation. Since the patients in this meta-analysis have been included mostly from hospital settings, they likely represent more severe cases than the average RA patient. This potential selection bias may have resulted in a higher observed ILD and BE prevalence compared to the RA population in general. Several studies lacked information on HRCT coverage and whether assessments were blinded, which may introduce selection and detection bias. These limitations could affect the reported prevalence estimates and should be considered when interpreting the findings. Finally, only the prevalence was considered in this study. The extent of reported HRCT findings is equally important in a clinical setting.

## Conclusion

With this systematic review and meta-analysis, we provide updated estimates of pulmonary involvement in patients with RA. The pooled prevalence of BE and ILD was 16% and 22%, respectively, with higher rates observed in patients with longstanding RA. Both CRP and RA duration were positively correlated with the prevalence of bronchiectasis and reticulation, supporting the key role of chronic systemic inflammation in the development of airway and parenchymal pulmonary disease. Given the strong association between ILD prevalence and RA duration, with an estimated prevalence of around 23% after 5 years of RA, we suggest considering HRCT in all patients with RA lasting more than 5 years—particularly in those with chronically elevated systemic inflammation. This approach may facilitate earlier detection of preclinical ILD which allows for proper monitoring and timely intervention.

**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:** The authors declare that they have 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.

**Authors' Contribution:** JAB and CSU conceived and designed the study. JAB, CSU, and LKJ collected and curated the data. JAB performed the statistical analyses and drafted the manuscript. CSU, EB, HM, and ESHH critically revised the manuscript for important intellectual content. All authors reviewed and approved the final version of the manuscript.

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