Incidence and prevalence of idiopathic pulmonary fibrosis: a systematic literature review and meta-analysis

EPH207

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Introduction

- Idiopathic pulmonary fibrosis (IPF) is the most common form of progressive fibrotic interstitial lung disease (PF-ILD)
  - IPF affects mostly older (>50 years) males[1]
  - Prognosis is poor, with median survival time of 3-8 years[2]
- Prevalence and incidence rates of IPF are rising globally, possibly due to aging populations and improved diagnostics[3]
- Due to its rarity and variability in data sources for estimating IPF frequency, an updated analysis of incidence/prevalence is needed to provide key information for emerging treatments

Objectives

- To estimate the incidence and prevalence of IPF in adults globally and to assess regional variations

Methods

Systematic literature review

- Standard and accepted methods for conducting and reporting of systematic literature reviews[4,5,6]
  - Study eligibility criteria were defined using the CoCoPop framework (Condition, Context, Population)[6]
  - Included were English-language studies reporting incidence or prevalence of IPF in adults (≥18 years) within the general population of any country
- Database searches of MEDLINE®, Embase, and Cochrane Database of Systematic Reviews from Jan 1, 2000, to Nov 7, 2023 via OvidSP using pre-defined search strategies
  - Additional searches included bibliographies of similar literature reviews and abstracts from the American Thoracic Society, British Thoracic Society, European Respiratory Society, Canadian Society of Respiratory Therapists, American College of Rheumatology, and European Congress of Rheumatology (2021 – 2023)
- Study quality was assessed using the Joanna Briggs Institute checklist for prevalence studies[7]

Statistical analysis

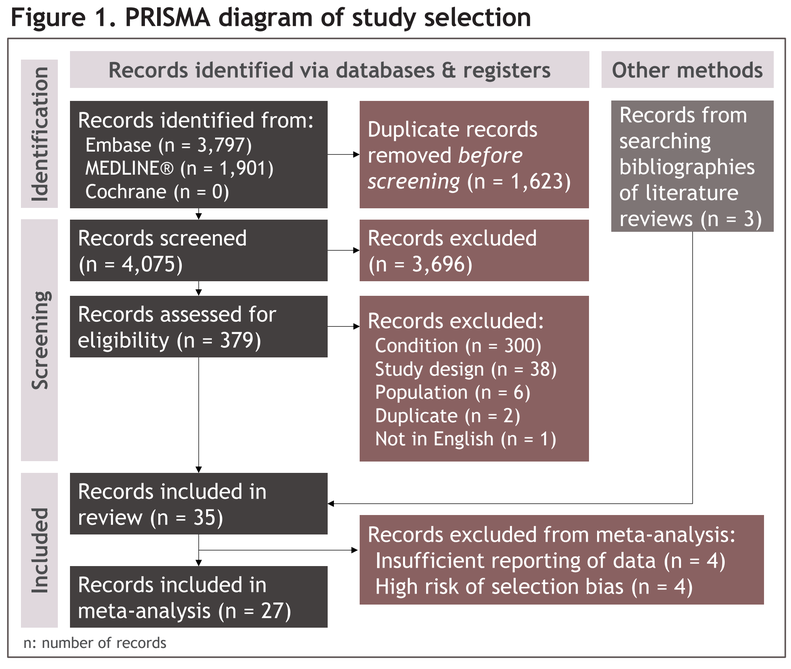
- When required, data from included studies were used to calculate denominators, numerators, and 95% confidence intervals (CIs)
  - When incidence or prevalence were reported annually, annual weighted averages were calculated over the study period; point estimates were analyzed as reported
  - Adjusted rates were prioritized over crude rates
  - Studies at high risk for selection bias[5] were excluded from meta-analyses
  - In studies reporting incidence or prevalence by year or sex, values were averaged based on population size or sex-specific sample size for each year to get a single rate per study
- Meta-analysis via DerSimonian-Laird random-effects model, an adaptation of the inverse variance method[4,8]
- Pooled weighted random-effects incidence and prevalence estimates were generated using the metafor R package[9]

Results

Study Selection

- 4,075 records were identified from databases; 3 were captured from manual searches (**Figure 1**)
- 35 studies were reviewed for meta-analysis
  - 4 studies were excluded from the meta-analysis due to insufficient reporting of epidemiological data (i.e., lack of reported sample size)[10-13]
  - Another 4 were excluded due to high risk of selection bias[2,14-16]; 2 US studies used potentially incorrect ICD codes to identify cases[2,14]
- 27 studies were selected for meta-analysis

Figure 1. PRISMA diagram of study selection



Study characteristics

- Of 27 studies included for meta-analysis, most (24 studies) were retrospective; 2 cross-sectional,[17,18] 1 prospective[19]
- Sample size of the source population ranged from ~168,000[20] to ~56 million persons[21] (median: 5.8 million)
- Studies were conducted in Europe (14 studies),[17-19,21-31] North America (7 studies),[20,32-37] and Asia (6 studies)[38-43]
- Study period ranged from 1[18,22,34] to 16 years[24] (median: 6 yrs)

Population characteristics

- Across studies included for meta-analysis, mean or median age ranged from 42[35] to 74 years[20] (median: 64 years)
- Proportion of males ranged from 34%[31] to 73%[42] (median: 54%)

Incidence of IPF

- Higher pooled incidence was observed within North America (9.0 per 100,000 [95% CI: 7.1, 10.9]) compared with Europe (5.1 [3.9, 6.3]) and Asia (4.4 [1.6, 7.2]; **Figure 2**)

Prevalence of IPF

- Pooled prevalence of 25.4 per 100,000 (95% CI: 19.9, 30.9) from North America was higher than the pooled estimate for Asia (14.8 [7.1, 22.6]) and Europe (14.6 [9.4, 19.7]; **Figure 3**)

Discussion

- Incidence and prevalence estimates were generally consistent across studies, except for **4 outliers** which were excluded from meta-analysis due to biased data sources
  - Outliers used highly selected populations such as large administrative claims databases in the US or Veterans' database
  - Claims databases (e.g., US Medicare) often rely on ICD codes, which may overestimate IPF incidence or prevalence via misclassification
- IPF was typically defined by clinical assessment or ICD codes; disparities in definitions complicate comparisons of results
- **STRENGTHS**: rigorous methodologies, comprehensive literature review, selection of high-quality studies
- **LIMITATIONS**: heterogeneity across studies, non-validated tools for IPF case identification, restriction to English articles

Pooled global incidence of IPF was 5.9 per 100,000 persons (95% CI: 4.9, 6.9); pooled global prevalence was 17.7 per 100,000 persons (95% CI: 14.1, 21.3)

Figure 2. Forest plot of incidence of IPF by region (24 studies)

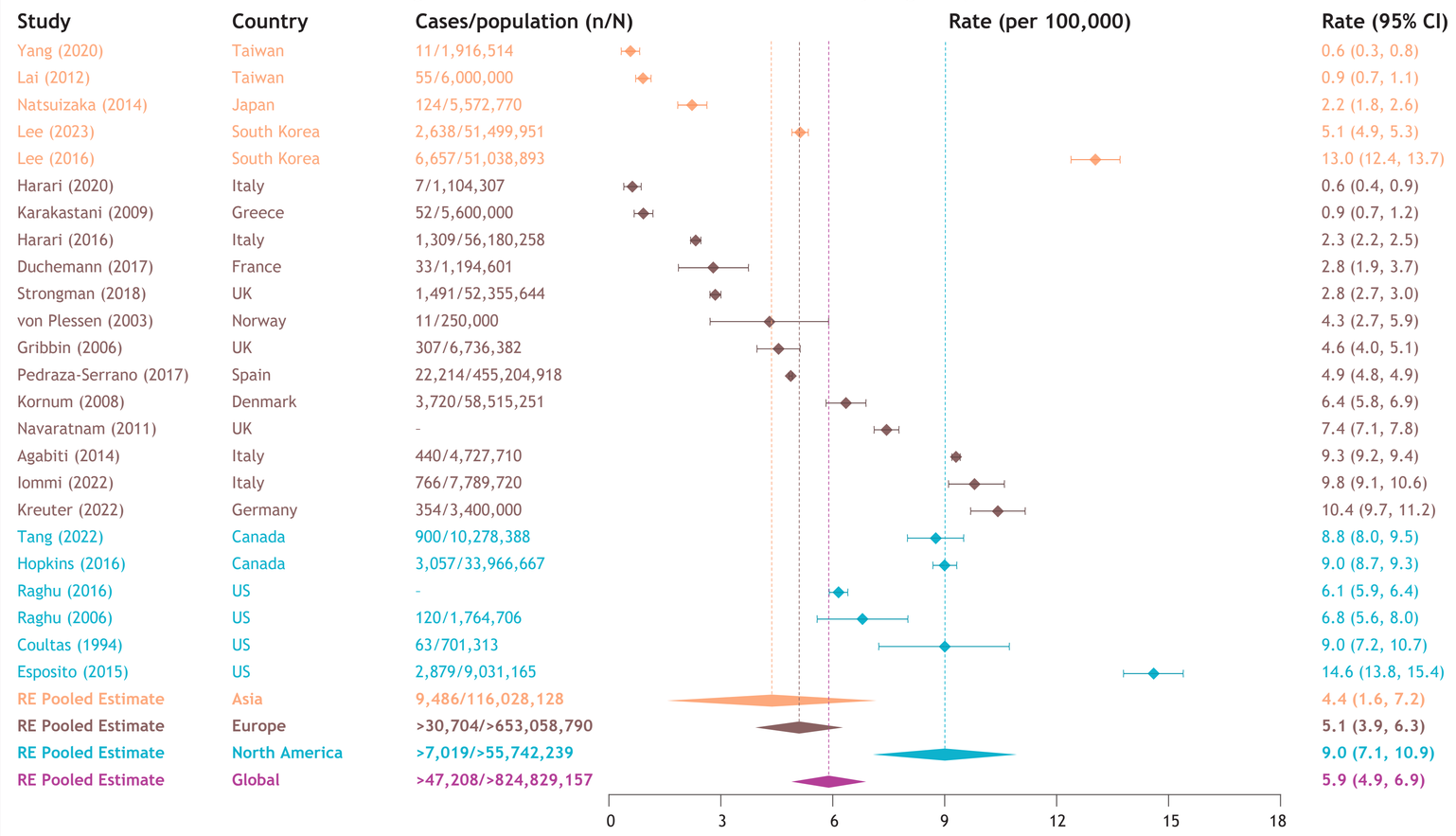
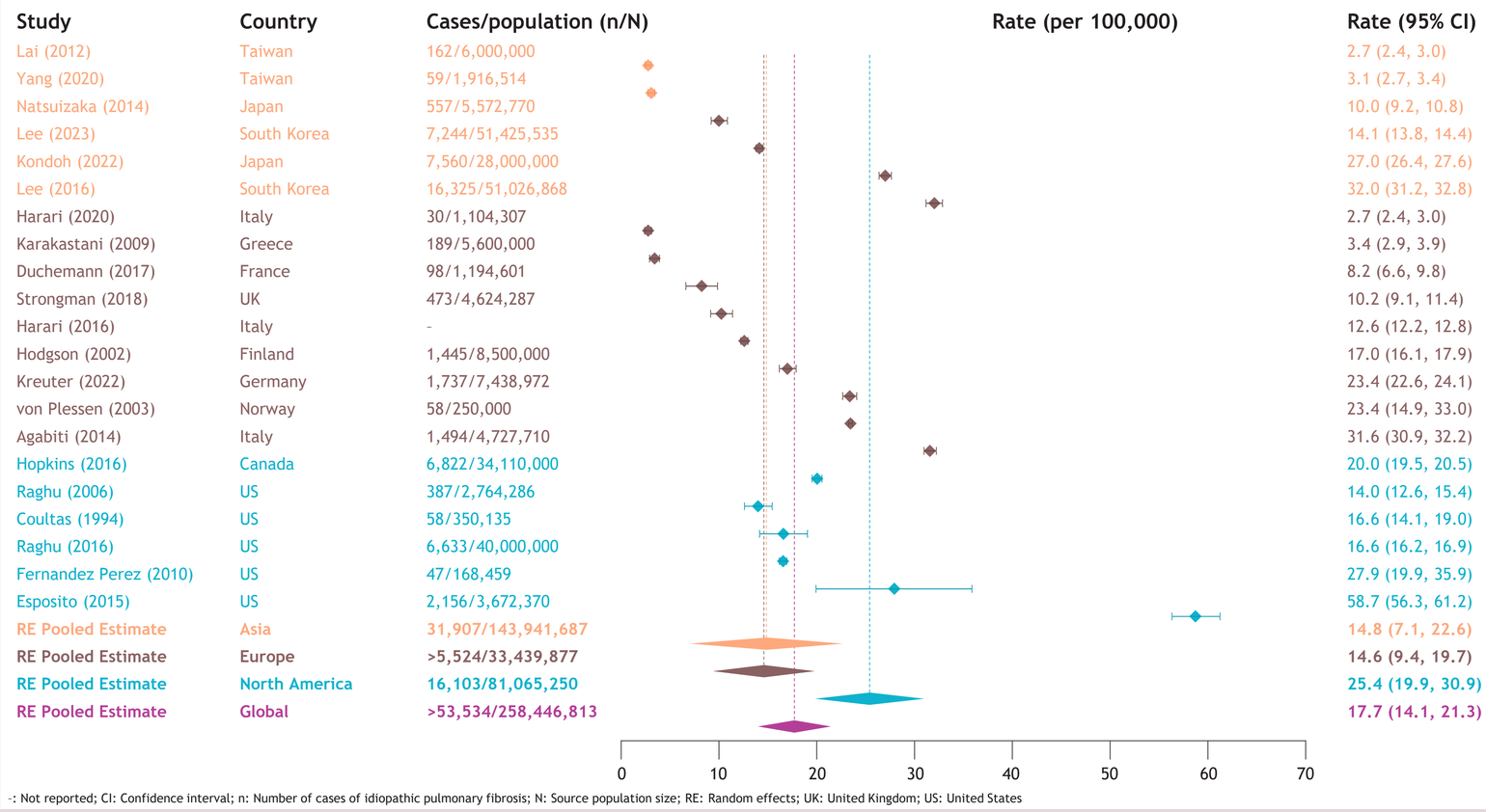


Figure 3. Forest plot of prevalence of IPF by region (21 studies)



-: Not reported; CI: Confidence interval; n: Number of cases of idiopathic pulmonary fibrosis; N: Source population size; RE: Random effects; UK: United Kingdom; US: United States

Conclusion

- This study found an approximately 2-fold higher incidence and prevalence of IPF in North America compared with Europe and Asia
  - Difference may be explained by use of selective databases which may have biased results toward higher estimates in North America
- Important to develop standardized and validated definitions to identify patients with IPF across various databases
  - Such development will facilitate future comparisons of IPF prevalence and incidence across geographic regions and allow assessment of trends over time
  - This is particularly critical to facilitate ongoing research to develop new, effective treatments for this vulnerable patient population

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Conflicts of Interest

- Negar Golchin, Tamara Lesperance, Julia Scheuring, Aditya Patel, and Brandon Elpers* are employees and/or shareholders of Bristol Myers Squibb. *At the time of the analysis
- Victoria Wan, Kimberly Hofer, and Jean-Paul Collet are employees of Evidinno Outcomes Research Inc. (Vancouver, BC, Canada), which was contracted by Bristol Myers Squibb to conduct this study

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