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

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Abstract

Background Idiopathic pulmonary fibrosis (IPF) is a progressive and serious lung disease with a poor prognosis and severe clinical and humanistic burden. This systematic literature review and meta-analysis aimed to summarize and quantify the data on IPF incidence and prevalence among adults within the general population and to compare regional differences.

Methods Comprehensive searches of MEDLINE®, Embase, and the Cochrane Database of Systematic Reviews were conducted to capture available studies published in English from January 1, 2000, to November 7, 2023, that reported on the incidence or prevalence of IPF. Pooled weighted-mean incidence and prevalence estimates were calculated from studies reporting adequate epidemiological data using a DerSimonian-and-Laird random-effects model.

Results Of 4,077 records identified, 26 studies were included in the meta-analysis (17 reported both prevalence and incidence, 6 reported incidence only, 3 reported prevalence only). Most studies were retrospective, with study periods ranging from 1984 to 2021. Pooled global incidence per 100,000 (95% confidence interval) was 5.8 (4.8, 6.8; 23 studies). Pooled incidence in Asia was 4.4 (1.6, 7.2; 5 studies), 5.1 (3.9, 6.3; 13 studies) in Europe, and 9.0 (6.9, 11.1; 5 studies) in North America. Pooled prevalence (per 100,000) was 17.7 (14.0, 21.5; 20 studies) globally, 14.8 (7.1, 22.6; 6 studies) in Asia, 14.6 (9.4, 19.7; 9 studies) in Europe, and 27.2 (21.0, 33.4; 6 studies) in North America.

Conclusion This analysis confirms that IPF is a rare condition globally, but substantial heterogeneity exists across studies. Incidence and prevalence were notably high in North America compared with Europe and Asia. This finding may be explained by the use of selective source populations in North American studies, in contrast to the more general populations used in European or Asian studies. Additional contributing factors include variations in case identification algorithms, differences in diagnostic definitions and regional differences in occupational and environmental exposures. While recent multi-societal guidelines have advanced the standardization of the IPF diagnostic process, variability in clinical practice remains a challenge that affects comparisons of incidence and prevalence across regions and over time.

Keywords Idiopathic pulmonary fibrosis, Lung diseases, interstitial, Epidemiology, Incidence, Prevalence

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Introduction

Idiopathic pulmonary fibrosis (IPF) is the most common form of progressive fibrotic interstitial lung disease (ILD), with hallmark features of usual interstitial pneumonia, localized exclusively to the lungs, and not associated with other diseases (e.g., autoimmune) or identifiable causes [1]. IPF is typically progressive, with irreversible decrease in lung function, primarily affecting older patients (i.e., over 50 years old) and a high male to female ratio (3:1), and with no known cure at present [2–5]. IPF generally has a poor prognosis, with a median survival time of 3–5 years following diagnosis, with chronic hypoxemic respiratory failure being a leading cause of death [6, 7]. Five-year survival has been estimated to range from 20–40%.[7] Quality of life is severely affected due to the progressive decline in lung function, with patients experiencing difficulty performing simple daily activities; it is not uncommon for patients to require supplemental oxygen to ease the burden of normal breathing [8–10].

IPF is incurable at present [11], and treatment goals are aimed at relieving symptoms and slowing lung function decline, with palliative care provided in later stages [10, 12–15], and lung transplant a possibility in select patients [16]. Despite advances in understanding IPF pathophysiology, molecular mechanisms of disease, risk factors, and refinements in diagnostic criteria, there have been no recent approved treatments since the two antifibrotic agents, pirfenidone and nintedanib in the mid-2010s, stressing the urgent need of new therapies to alleviate the substantial burden on patients with IPF [11, 17].

The estimated incidence of IPF has previously been reported to range between 0.9 and 9 cases per 100,000 people per year in Europe and North America, and between 3.5 and 13 cases per 100,000 people per year in Asia-Pacific countries [18, 19]. Recently published evidence reported prevalence estimates (per 100,000 people) of 5.7 to 4.5 in Asia-Pacific countries, 3.3 to 25.1 in Europe, and 24.0 to 29.8 in North America [19]. IPF is considered a rare disease in all regions globally [19, 20]. Recent evidence suggests that IPF incidence and prevalence are rising globally, which may be due to the aging population, more general awareness of pulmonary fibrosis, and advances in diagnostic tools [6, 7, 18–20]. There is also growing awareness that research on IPF faces many challenges related to its low frequency, as well as the variability in data sources used to estimate incidence and prevalence [21]. A better understanding of the prevalence and incidence of this disease is needed to provide context for emerging treatments [11, 17].

Previous studies have sought to quantify the global impact of IPF but so far, no systematic review has comprehensively addressed this topic. Notably, two recent reviews on the topic have attempted to fill this gap with some limitations. One targeted review, which used a fixed-effects modeling approach, effectively highlighted the global burden of IPF but lacked the systematic methodology required to minimize biases, account for unmeasured heterogeneity and ensure comprehensive evidence synthesis [19]. The narrative review, published in 2023, provided valuable contextual insights by summarizing the epidemiology and pathogenesis of IPF, particularly in relation to environmental exposures, genetic predispositions, and potential associations with COVID-19 [20]. However, this review lacked a systematic approach, formal quality assessments, and a quantitative synthesis of the results.

By contrast, the current systematic review and meta-analysis addressed these limitations by employing rigorous and systematic approaches to quantitatively synthesize the published literature on the incidence and prevalence of IPF across different regions and globally while accounting for between-study variability through a random-effects approach.

Methods

This systematic literature review was carried out according to standard methodologies as recommended by the Cochrane Handbook for Systematic Reviews of Interventions [22]. The results of the review were reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [23]. The reporting of incidence and prevalence data adhered to the methodological guidance on systematic reviews of incidence and prevalence studies provided by the Joanna Briggs Institute (JBI) [24].

Study Eligibility

The CoCoPop framework (Condition, Context, Population) was used as a guide in defining study eligibility [24]. English-language epidemiological studies reporting on incidence and/or prevalence of adult (typically aged ≥ 18 years) IPF among the general population from any country were included.

Data sources

MEDLINE®, Embase, and the Cochrane Database of Systematic Reviews were searched using the Ovid platform from January 1, 2000, to November 7, 2023, according to pre-defined search strategies. Abstracts from relevant conferences were also searched to capture studies that were not identified from the main database searches. The conferences were from: American College of Rheumatology, American Thoracic Society, British Thoracic Society, Canadian Society of Respiratory Therapists Annual Conference, European Congress of Rheumatology, and the European Respiratory Society. Bibliographies from literature reviews identified from the main database searches were also searched. Keywords and search strategies for

MEDLINE and Embase are provided in Supplementary Table S1 and Supplementary Table S2, respectively.

Study Selection, Data Extraction, and Study Quality Appraisal

A senior reviewer was responsible for reviewing abstracts and conference proceedings in an initial screen to identify relevant studies according to the pre-defined selection criteria with oversight from a senior research scientist to ensure consistency. In the subsequent full-text screening phase, relevant studies were assessed for their eligibility for data extraction by two independent reviewers. Any discrepancies in eligibility for final inclusion by the two reviewers during full-text review were reconciled by a third independent reviewer. In the final data extraction step, relevant study and patient characteristics were extracted by a senior reviewer, and all relevant outcomes data were extracted by two independent reviewers. Data extracted included: study characteristics (including design, region, time-period), population characteristics (including age, sex, race/ethnicity) and outcomes (including incidence, prevalence, 95% confidence interval (CI) and case ascertainment method for identifying IPF cases and standard error. Study quality was appraised using the tool developed specifically by the JBI for studies reporting prevalence in systematic reviews [25]. Inclusion and exclusion of studies for the meta-analysis was determined based on this quality assessment.

Statistical analysis

Numerators, denominators and 95% CI were determined using reported data. When studies reported both crude and adjusted rates, the adjusted rate (e.g., incidence rates adjusted for age and sex) was selected for analysis. Rates reported were calculated as rates per 100,000 persons if required. If studies reported incidence and prevalence by year or by gender, these were averaged across the population size of each year or sample size of each gender to generate a single rate per study. If studies reported both a broad- and narrow-case definition of IPF, the narrow-case was typically preferred for the analysis to provide a more conservative estimate of incidence or prevalence in the general population.

Meta-analysis was carried out using the DerSimonian-and-Laird random-effects variation of the inverse variance method, as recommended by the Cochrane Handbook [22, 26], and stratified by regions or globally. Pooled rates were grouped by region, where possible. Studies with insufficient reported or derived data were not included in the meta-analysis.

Variance of reported rates was required for random-effects pooled estimates; for studies not reporting a 95% confidence interval (CI), the number of IPF cases and the population size (where available) were used to derive standard errors of reported incidence or prevalence. In studies providing annual incidence or prevalence, an average incidence or prevalence estimate over the study period weighted by population size was calculated for meta-analysis. Reported point estimates of incidence or prevalence for a study period remained as is for quantitative analysis.

The Cochrane I^2 statistic was used to estimate the degree of heterogeneity between included studies in meta-analysis and causes of heterogeneity were considered, if feasible. Pooled weighted random-effects incidence and prevalence estimates were derived using the *metafor* R-package [27].

Complementary analyses were conducted to explore the impact of varying case definitions across studies. The objective was to contrast studies that used only the ICD codes from the claims database with those that also verified the diagnosis through a clinicians' consensus process, or having access to important information from the patient charts such as high-resolution computed tomography (HRCT) scans, pathology and/or lung biopsy findings.

Results

Study Selection

A PRISMA flow diagram of the study selection procedure is presented in Fig. 1. A total of 4,077 non-duplicate records were identified, including 4,075 records from the database searches and an additional two records identified through manual searches of bibliographies of previous reviews. Following screening, 34 studies were included for qualitative evidence synthesis. Of these 34 studies, four were excluded from the meta-analysis due to insufficient reporting of incidence or prevalence epidemiological data [28–31]. For instance, when only a point estimate for incidence and/or prevalence was reported without a 95% CI and no mention of the counts of incidence or prevalence cases (i.e., numerator) or the population size (i.e., denominator) [28–31]. Another four studies were excluded for having high risk of selection bias [7, 32–34], leaving 26 studies available for meta-analysis. All studies were assessed using JBI quality assessment tool. See Supplementary Table S3 for assessment details.

Among the four excluded high-risk bias studies, Raghu et al. (2014) [7] and Kaul et al. (2022) [32] sourced data from large administrative claims databases, specifically the US Medicare claims database and the US Veteran Administrative database, respectively; thereby included older population (aged ≥ 65 years or veterans). Similarly, Navaratnam et al. (2021) [33] used a diabetes cohort with age-matched patients from the Fremantle Diabetes Study Phase I. Lastly, Storme et al. (2017) [34] reported IPF incidence from within one small Indigenous nation from Northern Quebec, Canada. These studies considered

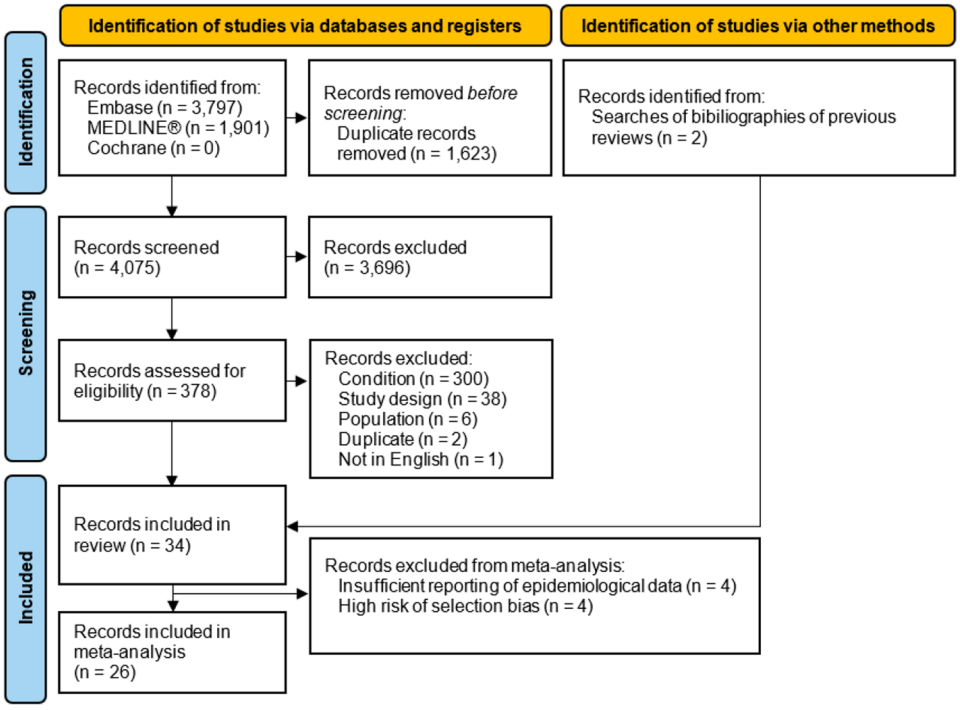

Fig. 1 PRISMA flow diagram. n: number of records

highly selective populations that were not representative of the general population and therefore excluded from the meta-analysis to avoid overestimating the incidence or prevalence of IPF to enable more reliable comparison across the regions.

Study characteristics and study quality appraisal

Of the 26 studies included in the meta-analysis, there were 23 retrospective cohort studies, two cross-sectional studies, and one prospective cohort study (Table 1). The source population size ranged from approximately 168,000 to 56 million people, with a median of approximately 6.3 million. Fourteen studies were from various European countries, six studies were conducted in North America, and six were from countries in Asia. The length of the study period ranged from 1 to 16 years, with a median of 6 years. All studies were published as full journal articles except for one study (Tang et al. 2022) [35], which was only available as a conference abstract at the time of this review; therefore, details on methodology and results from this publication were limited.

The risk of bias in the included studies was assessed using the JBI tool for prevalence studies [25], which evaluated methodological quality across several domains. Specifically, the assessment examined the representativeness of the sample population in relation to the target population and the adequacy of the sample size for generating robust estimates. The completeness of data collection, validity and reliability of methods were also examined. A summary of this appraisal is provided in Supplementary Table S3. Most studies used an appropriate sample frame for the target population, adopting appropriate sampling methods, and providing descriptions of participants and study settings in sufficient detail, using well-established definitions or diagnostic criteria. However, the use of appropriate statistical analysis was found to be unclear in nearly half of the studies, mainly due to a lack of CIs being reported. None of the epidemiological studies involved the adoption of surveys to collect self-reported data; therefore, they were not applicable in the assessment tool.

Population Characteristics

The mean age of patients in the 26 studies included in the meta-analysis ranged from 42 to 74 years (median: 70 years), and all but three studies reported on strictly adult populations [38, 44, 60]. However, data from studies including pediatric patients were still included in our analysis, as adults encompassed the large majority of the population. The proportion of male patients ranged from 34 to 73% (median: 58%). No studies included in the meta-analysis reported data on race, ethnicity and/or smoking status or habit. A summary of the population characteristics reported across studies included in the meta-analysis is provided in Supplementary Table S4.

Table 1 Study characteristics of the studies included in the meta-analysis ($n = 26$), listed in chronological orderbased on the first year of the study period

Author (Year); Country	Study Design	*Study Country*: Data Source	Time Period	Source Population Size	Age, Years	Males, *n* (%)
von Plessen (2003) [36]	Retrospective cohort	*Norway*: Bergen hospital district	1984–1998	250,000	Incident cases: Mean: 69.2 (SD: 17) Prevalent cases: Mean: 59.2 (SD: 19)	Incident cases: – (45) Prevalent cases: – (34)
Gribbin (2006); UK [37]	Retrospective cohort	*UK*: The Health Improvement Network (THIN)	1991–2003	6,736,382[a]	< 55: 79 (8.6%) 55-64.9: 166 (18%) 65-74.9: 290 (31.5%) 75-84.9: 302 (32.8%) > 85: 83 (9%)	568 (61.7)
Kornum (2008) [38]	Retrospective cohort	*Denmark*: The Danish National Health Service	1995–2005	5,400,000	1995–2000 Period: 0–14: 609 (5.9%) 15–39: 1449 (14%) 40–64: 3312 (32.1%) 65–79: 3584 (34.7%) 80+: 1364 (13.2%) 2001–2005 Period: 0–14: 815 (7.1%) 15–39: 1693 (14.8%) 40–64: 3737 (32.6%) 65–79: 3418 (29.9%) 80+: 1784 (15.6%)	1995–2000 Period: 6063 (58.8) 2001–2005 Period: 6576 (57.4)
Raghu (2006) [39]	Retrospective cohort	*US*: Data from a large, geographically diverse, United States' health care claims database	1996–2000	1,764,701[a]	Incident cases:– Prevalent case:–	Incident cases: 527,531 (45.3) Prevalent cases: 973,144 (45.3)
Hodgson (2002) [40]	Retrospective cohort	*Finland*: All Finnish pulmonary clinics	1997–1998	8,500,000	–	–
Fernandez-Perez (2010) [41]	Retrospective cohort	*US*: Rochester Epidemiology Project	1997–2005	168,459[a]	Mean: 73.5 (SD: 7.8)	28 (59.6)
Lai (2012) [42]	Retrospective cohort	*Taiwan*: (1) National Health Insurance (NHI), (2) national death registry	1997–2007	6,000,000	–	–
Navaratnam (2011) [43]	Retrospective cohort	*UK*: Routine death certificate data and computerized longitudinal general practice database	2000–2008	–	–	–
Strongman (2018) [44]	Retrospective cohort	*UK*: Clinical Practice Research Datalink (CPRD)	2000–2012	9,748,108	–	–
Yang (2020) [45]	Retrospective cohort	*Taiwan*: National Health Insurance Research Database (NHIRD)	2001–2011	1,916,514	–	–
Harari (2020) [46]	Retrospective cohort	*Italy*: Health Search Database (HSD)	2002–2017	1,104,307	Mean: 51.6 (SD: 19.1)	– (48.2)
Karakastani (2009) [47]	Cross-sectional	*Greece*: Departments of pneumonology with special interest in ILDs from all over Greece	2003	5,600,000	Male, Mean: 58 (SD: 0.82) Female, Mean: 59.3 (SD 0.64)	– (46.4)
Natsuizaka (2014) [48]	Retrospective cohort	*Japan*: Hokkaido prefecture	2003–2007	5,572,770	Mean: 70 (SD: 9)	402 (72.7)
Pedraza-Serrano (2017) [49]	Retrospective cohort	*Spain*: Spanish National Hospital Database (CMBD)	2004–2013	47,500,000	Mean: 73.11 (SD: 12.28)	12,739 (57.3)

Table 1 (continued)

Author (Year); Country	Study Design	*Study Country*: Data Source	Time Period	Source Population Size	Age, Years	Males, *n* (%)
Agabiti (2014) [50]	Retrospective cohort	*Italy*: Three databases from the Lazio region: (1) regional Hospital Information System (HIS), (2) regional Mortality Registry (MR), and (3) Italian National Institute of Statistics (ISTAT)	2005–2009	4,727,710	Mean: 70.3 (SD: 11.9) 18+:– (100%)	– (53)
Harari (2016) [51]	Retrospective cohort	*Italy*: DENALI; data on healthcare services since 2000 in Lombardy	2005–2010	56,180,258[a]	Incident cases: < 55: 155 (11.8%) 55–59: 83 (6.3%) 60–64: 142 (10.8%) 65–69: 185 (14.1%) 70–74: 216 (16.5%) 75–79: 238 (18.2%) 80–84: 186 (14.2%) 85+: 104 (7.9%) Prevalent cases: < 55: 306 (14.6%) 55–59: 161 (7.7%) 60–64: 217 (10.3%) 65–69: 302 (14.4%) 70–74: 348 (16.6%) 75–79: 354 (16.9%) 80–84: 278 (13.3%) 85+: 131 (6.2%)	Incident cases: 772 (59) Prevalent cases: 1193 (56.9)
Raghu (2016) [52]	Retrospective cohort	*US*: Optum's Clinformatics™ Data Mart for Multiplan Database	2005–2010	40,000,000	Mean: 41.7	– (48.4)
Esposito (2015) [53]	Retrospective cohort	*US*: Health Core Integrated Research Database	2006–2012	3,672,370	Mean: 73.1 (SD: 10.93)	2303 (50.1)
Kondoh (2022) [54]	Retrospective cohort	*Japan*: Medical Data Vision (MDV) database	2008–2019	28,000,000	–	–
Lee (2016) [55]	Retrospective cohort	*South Korea*: Korean Health Insurance Review and Assessment (HIRA)	2010–2013	51,038,893	–	–
Hopkins (2016) [56]	Retrospective cohort	*Canada*: Two national mandatory administrative databases from Canadian Institute for Health Information (CIHI)	2011	34,110,000[a]	–	1784 (58.4)
Lee (2023) [57]	Retrospective cohort	*South Korea*: Korean Health Insurance Review and Assessment (HIRA)	2011–2019	51,499,951	–	45,837 (70.3)
Duchemann (2017) [58]	Retrospective cohort	*France*: (1) Hospital and community physicians for clinical data, (2) Seine-Saint-Denis Social Security	2012	1,194,601	Mean: 55.6 (SD: 0.6)	417 (49.2)
Tang (2022) [35]	Retrospective cohort	*Canada*: Ontario Health Insurance Program (OHIP)	2013, 2017	10,278,388[a]	–	–
Iommi (2022) [59]	Prospective cohort	*Italy*: (1) regional hospital discharge database, (2) regional drug prescriptions database	2014–2019	7,789,720	–	521 (68)
Kreuter (2022) [60]	Retrospective cohort	*Germany*: German regional healthcare provider AOK PLUS	2016–2019	3,400,000	Mean: 72.1 (SD: 10.4)	1173 (67.5)

[a]Estimated denominator determined based on reported data.–: Not reported. *ILD* Interstitial lung disease, *UK* United Kingdom, *US* United States

Incidence and Prevalence of IPF

Among the 26 studies included in the meta-analysis, 17 reported both incidence and prevalence, six studies reported only on incidence, and three studies reported only on prevalence.

Incidence of IPF

A meta-analysis of the 23 studies reporting incidence data showed a pooled global incidence of 5.8 per 100,000 (95% CI: 4.8, 6.8; I^2: 99.7%, range [min– max]: 0.6–14.6; Fig. 2). Pooled incidence was 9.0 per 100,000 (95% CI: 6.9, 11.1; I^2: 98.8%, range: 6.1–14.6) across the five studies in North America, while the pooled rate across thirteen

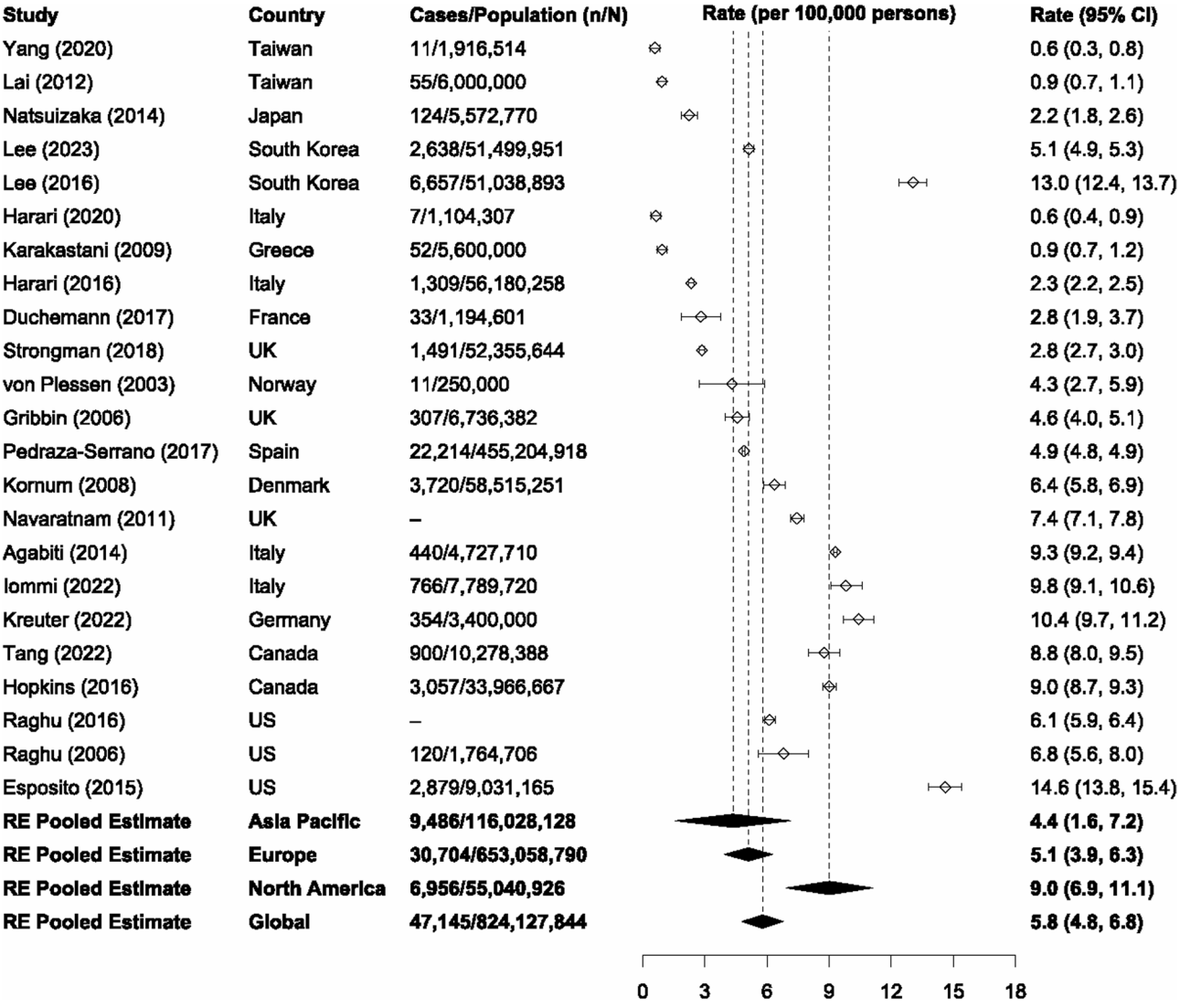

Fig. 2 Forest plot of incidence rate of IPF by region ($n = 23$). Not reported; CI: Confidence interval; RE: Random effects; UK: United Kingdom; US: United States

studies in Europe was 5.1 (95% CI: 3.9, 6.3; I^2: 99.7%, range: 0.6–10.4), and 4.4 (95% CI: 1.6, 7.2; I^2: 99.8%, range: 0.6–13.0) across five studies in Asia (Fig. 2).

The subgroup analysis of studies that used verified cases of IPF compared to those that used only ICD codes showed only marginal difference in the pooled incidence estimates, with a similarly high I^2 estimate indicating persistent heterogeneity.

Prevalence of IPF

In the meta-analysis of 20 studies, the pooled global prevalence of IPF was 17.7 per 100,000 persons (95% CI: 14.0, 21.5; I^2: 99.9%, range: 2.7–58.7). The pooled prevalence of IPF across five studies from North America was 27.2 (95% CI: 21.0, 33.4; I^2: 99.7%, range: 14.0–58.7), while the pooled estimate across six studies in Asia was 14.8 (95% CI: 7.1, 22.6; I^2: 100.0%, range: 2.7–32.0), and 14.6 (95% CI: 9.4, 19.7; I^2: 99.8%, range: 2.7–31.6) for nine studies in Europe (Fig. 3). The subgroup analysis for prevalence likewise showed only marginal differences between studies that used a verified diagnosed IPF criteria and those that used simple ICD code, with similarly high heterogeneity.

Discussion

This review provides a comprehensive overview and quantitative assessment of the incidence and prevalence of IPF across different countries in Europe, North America, and Asia, using data from studies published between January 2000 and November 2023. Pooled global incidence (5.8 per 100,000 persons) and prevalence (17.7 per 100,000 persons) suggest that IPF is quite rare. The meta-analyses indicated approximately 2-fold higher incidence

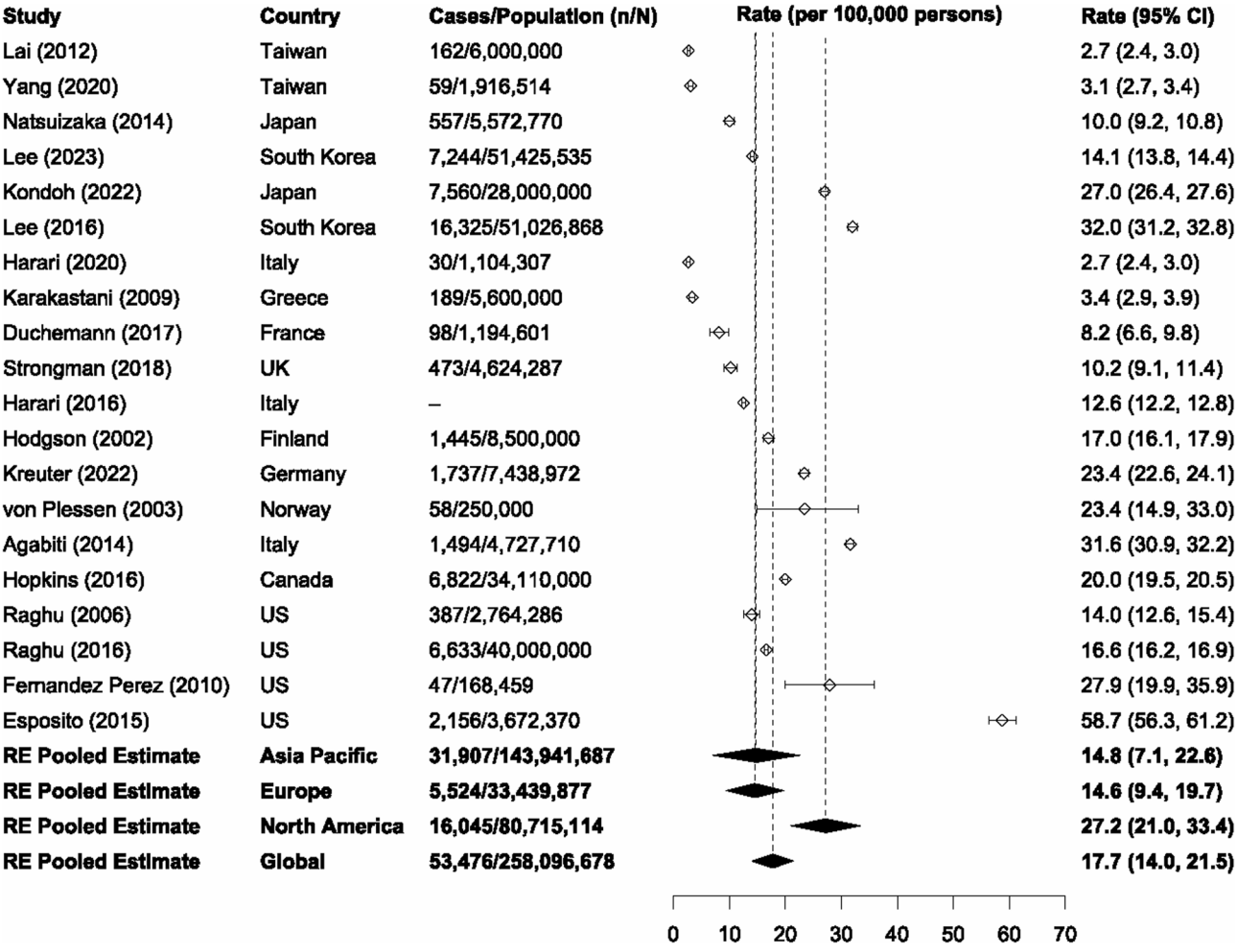

Fig. 3 Forest plot of prevalence of IPF by region ($n = 20$). Not reported; CI: Confidence interval; RE: Random effects; UK: United Kingdom; US: United States

and prevalence of IPF in North America compared with Europe and Asia.

Of the remaining studies included in the meta-analysis, most were retrospective cohort studies using data obtained from large populations at a national or wide regional level, as indicated by the observed median population in this study of approximately 5.8 million. While studies using hospital databases [40, 46, 49, 58, 60–62] can provide access to precise information regarding the clinical symptoms and severity of cases with a valid diagnosis of IPF, they are prone to a selection bias toward including the most severe cases, and are often limited by the difficulty in estimating precisely the source population (i.e., the hospital catchment area). Studies using IPF registry databases [41, 47, 50] have been developed to provide precise information on a selected group of patients; however, these registries are often based on voluntary participation which may bias the summary information. Further, patients' follow-up may vary, limiting their use for establishing prognosis at a population level [51].

Studies included in the meta-analysis that used claim databases [37, 39, 42–44, 52–57, 59] tended to vary in size. Claims database studies relied heavily on ICD codes for diagnosis of IPF without including other diseases in the ILD subgroup, which makes it difficult to accurately identify IPF versus non-IPF cases [63]. In addition, they often lacked detailed information such as lab, imaging findings, patient history, and risk factors or confounding factors, such as smoking status or work exposure [51]. These factors limits the ability to fully understand the disease context. Furthermore, large claim databases may also suffer from selection bias, focusing on specific groups of patients such as the elderly in Medicare, care seekers in insurance databases, or profession in the US Veterans database. This selective sampling can skew the estimates. Challenges in identifying IPF cases from administrative claims databases using ICD codes are well-recognized, and the accuracy of these codes in identifying IPF cases has been questioned. Esposito et al. (2015) validated their IPF identification algorithms based on medical records and provided positive predictive

values [53]. These researchers demonstrated that even the most rigorous algorithm to identify patients with IPF ultimately led to the selection of a group of patients that included 40% false positives; with even the strictest definition, the positive predictive value was only 60%, leading to overestimation of IPF incidence and prevalence [53]. These findings underscore the importance of validating ICD-based case definitions and highlight the need for careful considerations of the accuracy of administrative data when interpreting results from database-driven studies. Further validation is essential to ensure the reliability of IPF estimates.

Another important point to consider when evaluating IPF incidence and prevalence estimates across studies is the disparity in the definitions of IPF. The definition used will heavily depend on the data source. For example, in one Italian hospital-based study [61], charts were reviewed by a multidisciplinary group of specialists using defined clinical criteria. In contrast, a German study using insurance claims data covering approximately 4% of the German population, identified IPF cases using the German Modification of the ICD-10-GM code J84.1 for interstitial pulmonary diseases [56]. Furthermore, even the choice of ICD code to define IPF may vary. For instance, a large US Medicare claims database study (patients aged ≥ 65 years) identified patients who had one claim with the ICD-9-CM diagnosis code of 516.3[7], a general category of pulmonary diseases within which IPF's code is 516.31.

Previous reviews on the incidence and prevalence of IPF have been published; however, our review stands as the most recent, most complete, and systematic. A targeted literature review and survey by Maher et al. (2021) [19] included studies published between 2009 and 2020. Authors reported ranges of adjusted IPF incidence (per 10,000 persons) between 0.35 and 1.30 in Asia-Pacific countries, 0.09 and 0.49 in Europe, and 0.75 and 0.93 in North America. Ranges of adjusted IPF prevalence (per 10,000 persons) ranged from 0.57 to 4.51 in Asia-Pacific countries, 0.33 to 2.51 in Europe, and 2.40 to 2.98 in North America. Although the estimates by Maher et al. were adjusted for between-study differences where possible, their estimates are broadly comparable with those of the current study, confirming higher IPF incidence and prevalence in North America compared with Europe. It should be noted that the present study can be considered more comprehensive as it was based on a systematic literature review, including results from 24 and 21 studies for incidence and prevalence, respectively (following removal of biased studies), compared with 15 incidence and 18 prevalence studies included by Maher et al.

In another systematic review of IPF incidence and mortality published in 2015 by Hutchinson et al. (2015), authors reported a conservative (age-adjusted with narrow case definition criteria) range of incidence rates for studies published between 2000 and 2012, ranging between 3 and 9 cases per 100,000 persons per year in Europe and North America. Lower rates were observed in East Asia and South America [18]. Although their survey of the literature identified 34 records, they did not conduct a meta-analysis; hence, it is difficult to directly compare our results to theirs.

The present review has several strengths. First, all stages of this review adhered to standard recommendations for performing literature reviews, thus ensuring the rigorousness and robustness of the methodologies utilized. Second, the literature search and screening were comprehensive; a substantial evidence base spanning two major electronic databases, as well as gray literature sources, were searched during the study selection process. Moreover, publications were not restricted to specific countries to obtain a more comprehensive understanding of the epidemiology of IPF. Further, the included studies were generally conducted with high methodological quality. A limitation of our analysis concerns the restriction of study selection to records published in the English language. This potentially missed valuable insights into epidemiology-related evidence on IPF that are published in non-English journals. However, we included any study with at least the title and/or abstract available in English, and therefore we expect the language bias to be minimal. It should also be noted that inherent limitations of meta-analysis based on mixed-source epidemiological studies apply [64]; however, although the different data sources have their own strengths and limitations, this review and analysis identified informative and consistent patterns.

Another key limitation of this review is the lack of data from other regions like Africa, the Middle East or South and Central America. No studies from these regions met the inclusion criteria which likely reflects a scarcity of published epidemiological research on IPF in these regions, possibly due to the absence of formal disease surveillance systems, limited research infrastructures, or reduced awareness or recognition of IPF. The omission of such large and diverse regions limits the global representation of the findings and may introduce potential bias in the overall pooled estimates.

The Cochrane I^2 statistic of the pooled studies for both incidence and prevalence meta-analyses showed considerable heterogeneity, as per the "rough guide to interpretation" provided by the Cochrane Handbook for Systematic Reviews of Interventions [22]. The heterogeneity is likely driven by the unmeasured or unaccountable variability among studies across different parameters, such as definitions for identifying IPF cases, populations included, and various follow-up durations, data sources, and inclusion criteria for enrolling study participants.

None of the included studies reported about known risk factors for IPF [65] which includes genetic predisposition; [66, 67] co-morbid conditions, such as esophageal reflux; [68] occupational and environmental risk factors; [69] or behavioral factors, such as smoking habits [70]. These factors could contribute to the figures reported in one region, and may also explain the differences between regions. This omission likely contributes to the observed heterogeneity across studies, beyond differences in how IPF patients are defined and selected.

As a result, these inconsistencies contribute to substantial variation in reported incidence and prevalence estimates. For example, the use of databases that include sub-populations rather than the true general population (e.g., Optum's Clinformatics™ Data Mart for Multiplan Database) introduces a systematic selection bias [71], which may further contribute to overestimations and variation of reported incidence and prevalence. Perhaps a major source of this heterogeneity is the evolving nature of IPF diagnostic guidelines, which have contributed to the inconsistencies in case identification. In earlier years, a definitive diagnosis required on histopathology via surgical lung biopsy, with the emphasis on excluding other known causes of ILD, as recommended in the 2000 international consensus statement released by the American Thoracic Society (ATS) and European Respiratory Society (ERS) in 2000 [72]. In 2011, the ATS, ERS, Japanese Respiratory Society and Latin American Thoracic Association expanded and updated the entry IPF guidelines to incorporate HRCT, provided that scans indicated probable usual interstitial pneumonia. They also emphasized the value of multidisciplinary discussion in improving diagnostic accuracy [73]. In 2018, a systematic review and expert consensus led to further updates, allowing a first-line diagnosis of IPF based on HRCT findings of typical or probably usual interstitial pneumonia. Most recently, a 2022 joint societal update recommended transbronchial lung cryobiopsy as an alternative to surgical lung biopsy for histopathological diagnosis of IPF [1]. Despite the presence of heterogeneity as a limitation, the value of understanding the global impact of IPF through a systematic and rigorous approach brings cohesion to the diverse regional estimates. While individual study results may vary due to methodological and population differences, the overall pooled values provide crucial insights into the overall burden of IPF. These aggregated estimates, when considered alongside regional findings, offer valuable information on the disease's impact.

Conclusions

Current pooled estimates suggest that IPF remains a relatively rare condition globally. However, our review reveals substantial heterogeneity across regions with notably higher incidence and prevalence reported in North America compared with Europe and Asia. This variability is likely attributable to differences in case identification methods, particularly the use of unvalidated diagnosis algorithms. Our findings highlight the critical need for standardized validated definitions of IPF and the establishment of clear guidelines for identifying cases across diverse databases. They also emphasize the paramount importance of reporting the main risk factors associated with IPF in each study, as differences in environmental pollution, smoking behavior or genetic predisposition for instance, could explain differences across regions. Such standardization would enhance the comparability of IPF epidemiological data across regions and enable the assessment of temporal trends. Furthermore, a unified definition is essential for advancing research on this vulnerable patient population and for evaluating the effectiveness of therapeutic interventions more reliably and efficiently.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12890-025-03836-1.

Additional file 1. Supplementary Table S1: Search strategy for MEDLINE®. A supplementary table of the search strategy for MEDLINE database

Additional file 2. Supplementary Table S2: Search strategy for Embase (via OvidSP). A supplementary table of the search strategy for Embase database

Additional file 3. Supplementary Table S3: Summary of the Joanna Briggs Institute quality assessment tool for studies included in the literature review (n = 34). A supplementary table of a summary of the Johanna Briggs Institute quality assessment took for the included studies

Additional file 4. Supplementary Table S4: Population characteristics of studies included in the meta-analysis (n = 26). A supplementary table of the population characteristics of the included studies for the meta-analysis

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Authors' contributions

Negar Golchin, Aditya Patel, Julia Scheuring, Jean-Paul Collet, Brandon Elpers, and Tamara Lesperance were involved in the conception and design of the work. Victoria Wan, Kimberly Hofer, and Jean-Paul Collet acquired and analyzed the prevalence and incidence data and were major contributors in the writing of the original manuscript. All authors were involved in interpretation of the prevalence and incidence data and editing of the draft manuscripts. All authors read and approved the final manuscript.

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Data availability

The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication
Not applicable.

Competing interests
Negar Golchin, Aditya Patel, Julia Scheuring, and Tamara Lesperance are employees and/or shareholders of Bristol Myers Squibb; Brandon Elpers was an employee and/or shareholder of Bristol Myers Squibb at the time of this study. 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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