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REVIEW ARTICLE

Diagnosis Delay of Diffuse Parenchymal Lung Disease and its Associated Factors - A Scoping Review

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ABSTRAK

Penyakit 'Diffuse Parenchymal Lung Disease' (DPLD) telah menjadi cabaran yang signifikan kepada golongan doktor, dengan kelewatan mendiagnosis penyakit sebagai salah satu isu yang sering terjadi. Kajian ini bertujuan untuk mengkaji secara menyeluruh literatur mengenai tempoh masa yang diambil untuk mendiagnosis penyakit dan faktor-faktor kelewatan dalam diagnosis. Carian literatur sistematik telah dijalankan dengan menggunakan pangkalan data MEDLINE dan Web of Sciences bagi mengenal pasti kajian-kajian yang berkaitan. Sebanyak 13 kajian dimasukkan dalam kajian skop ini. Kebanyakan kajian menunjukkan bahawa median kelewatan diagnosis adalah antara 12 hingga 25 bulan. Beberapa kajian menunjukkan purata kelewatan diagnosis adalah antara 18 hingga 24 bulan. Faktor-faktor biasa yang menyebabkan kelewatan diagnosis DPLD boleh dikategorikan kepada tiga kategori, iaitu faktor berkaitan dengan pesakit, pegawai perubatan dan sektor penjagaan kesihatan. Penemuan utama menunjukkan bahawa faktor yang paling ketara adalah disebabkan oleh kekurangan kesedaran dan pendidikan, yang memanjangkan masa mendiagnosis penyakit ini. Peningkatan kesedaran dan pendidikan di kalangan pesakit dan pegawai perubatan, serta mempunyai indikator yang jelas untuk tujuan mengutamakan rujukan, dapat mempercepatkan proses mendiagnosis DPLD. Pemahaman faktor-faktor yang menyumbang kepada kelewatan diagnosis dapat memastikan pelaksanaan dan penilaian pelbagai strategi bagi tujuan mengurangkan kelewatan serta meningkatkan prognosis pesakit.

Kata kunci: *Kelewatan diagnosis; penyakit diffuse parenchymal lung disease; ulasan skop*

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ABSTRACT

Diffuse parenchymal lung disease (DPLDs) has posed significant challenges to physicians, with diagnostic delay being among the most common issues. This study aims to comprehensively review the literature on the average time durations and reasons for the delay in diagnosis. A systematic literature search was conducted using the MEDLINE and Web of Sciences databases to identify relevant studies. A total of 13 studies were included in this scoping review. Most studies indicated that the median total diagnostic delay ranged from approximately 12 to 25 months. Several studies revealed a mean diagnostic delay ranging from 18 to 24 months. The common factors causing diagnosis delay in DPLDs can be categorised into three groups: patient, health provider and healthcare sector. Key findings reveal that diagnostic delays are most pronounced due to a lack of awareness and education, leading to prolonged time from symptom onset to definitive diagnosis and treatment. Increasing awareness and education among patients and healthcare providers, along with clear indicators that facilitate priority referrals, may expedite DPLDs diagnosis. By understanding the factors contributing to diagnostic delay, different strategies can be implemented and evaluated to further reduce the delay and improve patient prognosis.

Keywords: Diagnosis delay; diffuse parenchymal lung disease; scoping review

INTRODUCTION

Diffuse parenchymal lung diseases (DPLDs) is also known as interstitial lung diseases (ILD), encompasses a broad spectrum of lung disorders characterised by non-infectious infiltrates. These infiltrates typically affect the pulmonary interstitium and alveoli, leading to architectural distortion and irreversible fibrosis.

Types of DPLDs

Idiopathic pulmonary fibrosis (IPF) is the predominant, severe and advancing form of DPLDs. There are additional subtypes that also exhibit progressive fibrosing characteristics, including connective tissue disease-associated ILD (CTD-ILD), fibrotic hypersensitivity pneumonitis (HP), unclassifiable ILD, idiopathic non-specific interstitial pneumonia (NSIP), sarcoidosis and organising pneumonia.

A recent systematic review by Gupta et al. (2023) shows that the prevalence of IPF ranges from 7 to 1,650 per 100,000 person. This review assessed data from 39 incidences and 78 prevalence studies published between 2015 and 2021, covering all major world regions, with a predominant focus on Asia (30%). Musellim et al. (2013) investigated rates of DPLDs across 31 centers, reporting an incidence of 25.6 cases per 100,000 person. Sarcoidosis was the most frequent subtype (37.6%), followed by IPF (19.9%).

A registry from India by Collins et al. (2016) identified 1,084 patients with DPLDs, with 14% diagnosed with IPF and another 14% with CTD-ILD, most commonly cause by rheumatoid arthritis. Similarly, study by Alhamad (2013) showed that among 330 cases, the highest number of subtypes was CTD-ILD (34.8%), followed by IPF (23.3%), sarcoidosis (20%) and HP (6.3%). In Malaysia, the Sirol Aflah et al. (2019) conducted in a single center identified 54 cases of IPF. Another study by Ong et al. (2022) found 54 patients with rheumatoid arthritis-associated interstitial lung disease. These studies highlighted the global prevalence and subtype distribution of DPLDs, emphasising the need for region-specific

research and targeted healthcare strategies.

Associated Risk Factors

Many factors have been associated with DPLDs. Studies have identified several risk factors, including age, gender, smoking, drug-induced causes, environmental/occupational exposures and autoimmune disease. Older age is a well-established risk factor, with higher incidence rates observed particularly among those over 60 years of age. This increased susceptibility is due to biological changes in the lungs that occur with aging, making them more prone to illness (Leuschner et al. 2020; Salisbury et al. 2016). Males are more commonly affected by DPLDs compared to females and tend to have a worse prognosis, with an increased risk of disease progression and higher mortality rates compared to female patients (Kawano-Dourado et al. 2021). Inhaled tobacco smoke causes inflammation, destruction, remodeling, and repair of respiratory system compartments - from airways to alveolar walls - leading to pathological changes and pulmonary fibrosis. Both animal and human studies have shown that cigarette smoke triggers mechanisms of interstitial damage, leading to alveolar wall fibrosis with increased elasticity and collagen content over time and with greater exposure intensity (Franks & Galvin 2014; Serrano Gotarredona et al. 2022).

A temporal association between lung infiltration and drug exposure needs to be identified to suspect drug-induced DPLDs. These conditions usually show a variety of clinical patterns, starting from mild breathing symptoms to progressive respiratory failure, which ultimately leads to mortality. Among the medications that may trigger drug-induced DPLDs are chemotherapeutic agents, antibiotics, antiarrhythmic agents and immunosuppressants (Spagnolo et al. 2022; Yoo et al. 2022). Studies of environmental and occupational exposures have been prevalent across all DPLDs subtypes compared to other chronic respiratory diseases. For instance, there is substantial evidence that metals, wood, asbestos, silica and coal dust are significant contributors to DPLDs (Lee et al. 2022; Reynolds et al. 2020; Rivera-Ortega & Molina-Molina 2019). DPLDs are also frequently related to autoimmune diseases. Patients with CTDs have a higher risk of developing DPLDs compared to patients without CTDs. Studies have shown that ILD is most associated with rheumatoid arthritis (58%), SLE (13%), Sjogren syndrome (27%), inflammatory myopathies (80%), systemic scleroderma (91%) and mixed CTD (67%) (Jeganathan & Sathananthan 2020; Yoo et al. 2022).

Long-term exposure to the causes leads to progressive inflammation and direct damage to the lung epithelium. Over time, this will inevitably progress to pulmonary fibrosis and result in respiratory failure. Ultimately, patients will face premature mortality, disrupting their daily lives and leading to a poor quality of life and shortened survival prospect (Lee et al. 2022; Reynolds et al. 2020; Rivera-Ortega & Molina-Molina 2019; Serrano Gotarredona et al. 2022). The delay in diagnosis accelerates this process by prolonging the time before initiation of treatment. This review aims to provide an updated and comprehensive synthesis of the evidence on the time to diagnose DPLDs and the reasons for delays in diagnosis.

MATERIALS AND METHODS

Study Design

The study design followed the methodological framework for scoping reviews by Arksey and O'Malley (2005), which was further enhanced by the Joanna Briggs Institute. The stages of

the scoping review framework included (i) research question identification; (ii) relevant study identification; (iii) study selection; (iv) data charting; and (v) collation, summarisation and report of results. The checklist for Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) extension for Scoping Reviews was followed to ensure the comprehensiveness of the review.

Search Strategy

A systematic literature search was conducted across several databases to identify relevant studies. Articles were screened and assessed for eligibility. Data were extracted from eligible studies to summarise, collate, appraise the quality and create a narrative account of the findings.

Published studies were identified from electronic literature databases including PubMed and Web of Sciences. The literature search included medical subject headings (MeSH) headings and related text and keyword searches. The keywords used are "interstitial lung disease", "diffuse parenchymal lung disease", "diagnosis" and "delay". The population of included literature was patients with DPLDs, irrespective of subtype. To ensure recency, only articles published from 1 January 2017, to the last date of search (28 February 2023) were considered eligible. English language restrictions were applied. All the search results were imported into EndNote version 20 (Clarivate, Pennsylvania, United States of America) and later used to generate the reference list for the review.

Inclusion Criteria

The review included studies that met several criteria. These studies were required to be published in peer-reviewed journals and accessible through electronic databases. Only research conducted in acute or chronic clinical care settings was considered. Additionally, studies were included if they described variables related to diagnostic delays, such as the delay itself, the time duration and reasons for the delay, the factors responsible for it, or the specific context of diagnostic delays in DPLDs. Furthermore, only articles available in the English language were eligible for inclusion.

Exclusion Criteria

Conference abstracts, books, and grey literature were excluded from the review. This is because it is difficult to assess the quality, validity, and reproducibility of the findings, as they often lack rigorous peer review and methodological information.

Screening

Firstly, titles were read and screened for their relevance to the topic. After that, the reviewers read and screened the relevant titles' abstracts. Subsequently, the full texts of the screened abstracts were read. The reviewers did the screening processes at both abstract and full text levels independently according to the inclusion criteria. One author performed a search of the electronic database for literature in September 2022 and a final update in February 2023. Two authors independently reviewed and screened the abstracts of the search articles for inclusion.

Data Extraction

Data were extracted from the screened studies using Microsoft Excel 365, version 16.97 (Microsoft Corporation, Washington, United States of America). The spreadsheet included the following domains: (i) study identification

details (article title, authors, country of study, publication year, host institution); (ii) methodological characteristics (study design, study objective, sample characteristics); (iii) main findings; and (iv) conclusions. Study eligibility was reverified at the start of and during data extraction. Any discrepancies in the extracted data between the two reviewers were resolved through discussion. Details regarding publication, methodology, and results were extracted and recorded.

Data Analysis

All findings were narratively summarised and reported based on themes that emerged from the charted evidence. To ensure data accuracy, two public health specialists verified the findings as an additional step in the data analysis.

RESULTS

Search Strategy

The study search and selection process were outlined in the PRISMA flow diagram in Figure 1. Following abstract screening and exclusion of ineligible articles, 13 articles were selected for data extraction. These articles were included in this scoping review, focusing on diagnosis delay, average time duration and factors responsible for the delay. All articles were published in English and were reviewed

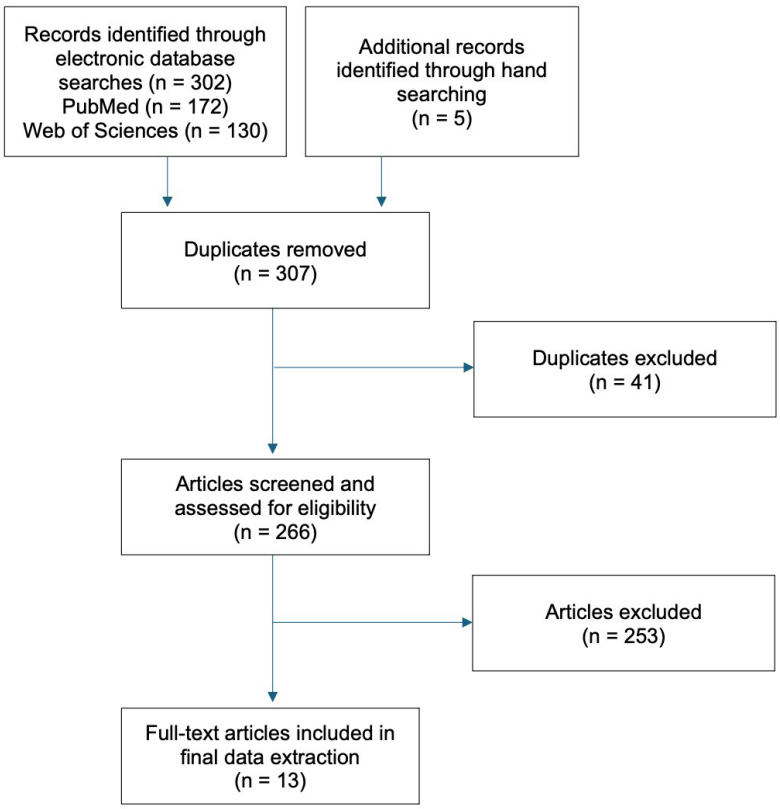

FIGURE 1: PRISMA flowchart of the study selection process

in detail to identify factors causing delay in the diagnosis of DPLDs. Due to the heterogeneity of the included studies, a scoping review was performed.

Studies Included

Of the 13 reviewed articles, three are multinational studies, and ten are single-country studies. Among the multinational studies, one involved thirteen countries (Spain, Belgium, United Kingdom, Italy, Germany, Netherlands, Bulgaria, France, Poland, Austria, Ireland, Norway, and Romania), another involved four countries (France, Germany, United States and Japan) and the third involved two countries (United Kingdom and Ireland). Out of the ten single-country studies, four were conducted in United States, one in Pakistan, one in Sweden, one in Finland, one in Denmark, one in Netherlands and one in Saudi Arabia. The sample sizes of these studies ranged from 46 - 7306.

Among the 13 studies, four were conducted prospectively (one cohort and three surveys), while the remaining nine used retrospectively collected data (seven cross-sectional and two cohort). Most of the studies assessed diagnostic events, timeliness and intervals based on patient medical records. Two of these studies used a combination of patient reports obtained from questionnaires and interviews, alongside diagnostic information derived from facility-based medical records. Another two studies assessed diagnostic events and intervals based on questionnaires or interviews, mainly relying on participants' memory. The remaining studies utilised claim data from insurance beneficiaries. Table 1 provided a summary of each of the reviewed studies.

Diagnostic Delays

Our analysis revealed the complexity of defining diagnostic delay, as each study employed different measurements for assessing this delay. The most frequently used time frame measured the interval from the onset of symptoms to the final diagnosis. Other time intervals examined include the period from symptom presentation to the first visit to a healthcare professional, from symptom presentation to referral, from radiological imaging evidence to final diagnosis and from initial misdiagnosis to final diagnosis. Among the 13 studies reviewed, only one did not explicitly define the term "diagnostic delay".

The studies employed various statistical methods to compare the duration of diagnostic delay, including mean, median and percentage. Mean and median are the most used statistics to describe the duration of diagnosis delay, with accompanying measures of accuracy such as standard deviation or interquartile range, respectively. Four studies reported time intervals using the median, while three studies reported using the mean. Percentage was used in cases when the study described delays beyond a specific period (e.g. < 1 year, > 1 year, > 3 years), with a common cut-off point of 1 year. Two studies reported delays as a percentage, categorising delays beyond 1 year. One prospective study used a combination of mean and median to measure the time interval, while three studies combined median and percentage. Additionally, the units of time varied between studies (days, months and years). To standardise and allow for comparability of data, months were selected as the unit of measurement for diagnostic delay.

TABLE 1: Articles exploring diagnosis delay in DPLDs

No	Study	Country	Year	Study type	Sample size (total)	Measurement method	Time interval measured
1	Hoffman et al.	Netherlands	2022	Retrospective	409	Median	Time from start of symptoms to first visit with pulmonologist
						Median	Time from first visit with pulmonologist to start of symptoms
						Median	Time from start of symptoms to diagnosis
2	Waseem et al.	Pakistan	2022	Retrospective	70	Mean	Time of delay in diagnosis
3	Lancaster et al.	France, Germany, Japan, United States	2021	Prospective	1249	Mean	Time from diagnosis to the first prescription
						Mean	Patient age at symptom onset
						Mean	Patient age at diagnosis
						Median	Time from symptom onset to seeking medical care
						Median	Time from the first physician visit to diagnosis
4	van der Sar et al.	United States, France, Germany, Italy, Spain, United Kingdom, Australia, Brazil, Canada, and Japan.	2021	Prospective	273	Percentage	First appointment with a primary care physician within 3 months of symptom onset
						Percentage	Time to diagnosis of 1 year or less
						Percentage	Patient referred to a pulmonologist within three primary care visits
						Percentage	First visit within 3 months after referral to a pulmonary specialist
5	Alhamad et al.	Saudi Arabia	2020	Retrospective	212	Mean	Time between the onset of symptoms and diagnosis
6	Snyder et al.	United States	2020	Retrospective	801	Median	Time from symptom onset to diagnosis
						Percentage	Time from symptom onset to diagnosis of >1 year
						Median	Time from first imaging evidence of pulmonary fibrosis to diagnosis
						Percentage	Patient had imaging evidence of pulmonary fibrosis ≤1 year prior to diagnosis

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7	Brereton et al.	United Kingdom Ireland	2020	Retrospective	247	Median	Time from primary care referral to secondary care respiratory clinic review
						Median	Time from primary care referral to ILD clinic
						Median	Time from primary care referral to antifibrotic commencement
8	Hoyer et al.	Denmark	2019	Prospective	204	Median	Total diagnostic delay
						Median	Time from onset of symptoms until the first healthcare contact
						Median	Time from first contact with a general practitioner until referral to secondary healthcare
						Median	Time from first visit due to the current respiratory symptoms until referral to an ILD center
						Median	Time from referral to an ILD center until the first patient visit at this hospital
						Median	Time from first visit at the ILD center until the final diagnosis
						Median	Time from the HRCT scan until the final diagnosis
9	Mooney et al.	United States	2019	Retrospective	7306	Percentage	Patient had at least one diagnostic test of interest during the 5-year pre-diagnosis period
						Percentage	Pulmonologist visit within 5 years before final diagnosis
						Percentage	Initial pulmonologist visit more than 3 years before diagnosis
10	Pritchard et al.	United States	2019	Retrospective	146	Percentage	Chest CT with ILD features obtained prior to pulmonology referral
						Median	Time from chest CT to pulmonology referral
						Percentage	PFT with ILD features obtained by PCP prior to chest CT and pulmonology referral
						Median	Time from PFT to chest CT when ILD reported by pulmonologist
						Median	Time from PFT to pulmonology referral when ILD reported

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11	Sköld et al.	Sweden	2019	Retrospective	3503	Median	Time from the appearance of the first early symptoms to the final diagnosis
12	Cosgrove et al.	United States	2018	Prospective	600	Median	Time from initial onset of symptoms to the first doctor visit
						Median	Time from initial onset of symptoms to final diagnosis
						Median	Time between the initial misdiagnosis and the final diagnosis
						Percentage	Time from symptom onset to the final diagnosis of >1 year
						Percentage	Time from symptom onset to the final diagnosis of >3 years
13	Purokivi et al.	Finland	2017	Retrospective	91	Mean	Time from symptom onset to referral
						Mean	Time from referral to the first visit in the tertiary center

Duration from Symptom Onset to Final Diagnosis

The studies employed various definitions to measure the duration of diagnostic delay. Six studies assessed the duration from symptom presentation to diagnosis confirmation as the measurer of diagnostic delay. Among these, four studies reported median values, with the median total diagnostic delay ranging from approximately 12 to 25 months (Hoffman et al. 2022; Hoyer et al. 2019; Snyder et al. 2020; Sköld et al. 2019). However, Cosgrove et al. (2018) reported a shorter median duration of seven months. Only one study by Alhamad et al. (2020) provided the mean delay, which was approximately 11 months.

Three studies reported the duration of diagnostic delay in percentage terms, using a cutoff point of one year. These studies further categorised the duration into less than three months, between one to two years, between two to three years and more than three years. The findings indicated that approximately 40 to 49% of patients experienced a diagnostic delay of more than one year from symptom onset to final diagnosis (Cosgrove et al. 2018; Snyder et al. 2020; van der Sar et al. 2021), with 20% being diagnosed within three years (Cosgrove et al. 2018**)**. Additionally, some studies found that 30% of patients were diagnosed within three months (van der Sar et al. 2021), 26% within one to two years, approximately 13% within two to three years and nearly 24% took more than three years (Snyder et al. 2020**).**

Symptoms prior to diagnosis

Eight studies documented the frequency of symptoms reported by patients prior to diagnosis. The most frequently reported symptoms were dyspnea and dry cough, as noted in eight studies (Cosgrove et al. 2018;

Hoffman et al. 2022; Lancaster et al. 2021; Pritchard et al. 2019; Purokivi et al. 2017; Sköld et al. 2019; Snyder et al. 2020; van der Sar et al. 2021). Fatigue was the next most common symptom, recorded in five studies (Cosgrove et al. 2018; Lancaster et al. 2021; Sköld et al. 2019; Snyder et al. 2020; van der Sar et al. 2021). Patients also experienced productive cough hemoptysis (Lancaster et al. 2021; Purokivi et al. 2017), swollen fingers (Lancaster et al. 2021; van der Sar et al. 2021) and weight loss (Snyder et al. 2020; van der Sar et al. 2021). Additional symptoms observed in patients with DPLDs included chest tightness, wheezing (Lancaster et al. 2021), arthralgia and gastroesophageal reflux disease (GERD) (van der Sar et al. 2021).

The review also found that patients presenting with multiple symptoms were more likely to have a shorter diagnostic time (less than 1 year). The median diagnostic time for patients experiencing multiple symptoms was approximately 11 months. For patients with a single symptom, they are less likely to receive a diagnosis within a year if the presenting symptom is cough compared to those presenting with dyspnea (Sköld et al. 2019**).** This is because dyspnea is frequently associated with acute exacerbation of DPLDs and usually presents at the later stages of the disease. On the other hand, physicians commonly attribute cough to other respiratory diseases such as chronic obstructive pulmonary disease (COPD). Dyspnea also disrupts the daily life of patients with DPLDs, leading to a lower quality of life.

Duration from Symptom Onset to First Doctor Visit

Four studies reported the median time from symptom onset to the first doctor visit, ranging from approximately one to six months (Cosgrove et al. 2018; Hoyer et al. 2019; Hoffman et al. 2022; Lancaster et al. 2021). van der Sar et al. (2021) also presented the results in percentages, showing that 52% of patients sought treatment within three months, while 30% took more than six months. In certain areas, patients are referred from primary care to specialists for further assessment. The mean time taken for this referral was 18 months (Purokivi et al. 2017), whereas the median time was around five months (Hoyer et al. 2019). Additionally, approximately 77% of patients referred to a pulmonary specialist had their first visit within three months (van der Sar et al. 2021). Within five years before their diagnosis, nearly 71% of patients saw a specialist, and among these, 34.7% sought treatment from a specialist for more than three years (Mooney et al. 2019). The majority of patients were referred to a specialist within three visits to primary care, but some required more than four primary care visits before being referred to a specialist (Cosgrove et al. 2018; Hoyer et al. 2019; van der Sar et al. 2021)**.**

Duration of from Diagnostic Workup to Referral and Final Diagnosis

Two studies measured the time interval from diagnostic workup to final diagnosis. The most common tests conducted were chest computed tomography (CT) scan (100%), chest X-rays (99%) and pulmonary function test (75%) (Mooney et al. 2019). The studies also showed that at least one diagnostic test was performed during the five years preceding the diagnosis. The median waiting time from a pulmonary function test showing ILD features to referral was approximately four months, and from a chest CT scan with ILD features to referral was approximately one month. The median waiting time from a pulmonary function test to a chest CT scan was approximately three months. The reported median time from imaging evidence

of pulmonary fibrosis to diagnosis was approximately six months (Hoyer et al. 2019; Snyder et al. 2020). Nearly 9% of patients were diagnosed between one to two years after having imaging evidence, 4% took between two to three years, and 10% required more than three years to receive a final diagnosis (Snyder et al. 2020**).** Additionally, 58% of patients had a chest CT scan over a year before their final diagnosis, 33% over three years prior, and another 33% over four years prior (Mooney et al. 2019**).**

Factors Behind the Delay in Diagnosis

In general, the factors that cause diagnosis delay in DPLDs can be categorised into three groups: patient-related factors, health provider-related factors and healthcare sector-related factors. Each of these groups included numerous reasons.

(i) Patient-related factors

Sociodemographic factors are frequently associated with diagnostic delays. Some studies have demonstrated a significant association between gender (male) and longer delays in DPLDs diagnosis (Hoyer et al. 2019; Waseem et al. 2022). Age is also related to longer diagnosis duration, as shown by one study conducted in 2019 (Sköld et al. 2019). Older patients are likely to remain undiagnosed within one year of symptom onset. The probability of diagnosing DPLDs decreases by nearly 1% each year with increasing age. Diagnosis delays are more common among illiterate patients, belong to rural areas, and have lower socio-economic status (Waseem et al. 2022). Family history is also a significant factor associated with the time of diagnosis (Hoffman et al. 2022). Longer diagnostic delays are reported among patients with a history of medication use, including commonly prescribed medications respiratory, cardiovascular and nervous system issues (Hoyer et al. 2019; Sköld et al. 2019).

The common and non-specific nature of symptoms often leads patients to dismiss initial symptoms and not seek medical attention immediately (Cosgrove et al. 2018; Sköld et al. 2019; van der Sar et al. 2021). Patients attribute the symptoms to other causes such as colds, smoking, stress, aging and other established diseases. They seek primary care visits due to the impact of symptoms on their daily activities, such as shortness of breath, cough and fatigue. Some pursue further investigation following suggestions from family members, friends or other physicians (van der Sar et al. 2021).

(ii) Health provider factor

Diagnosis delays can also be attributed to unfamiliarity with DPLDs among physicians. The presenting symptoms of DPLDs mimic other common chronic conditions, leading to deferred suspicion of DPLDs or misdiagnosis of other diseases. Commonly reported initial misdiagnoses include asthma, COPD and pneumonia (Lancaster et al. 2021; van der Sar et al. 2021). Additionally, there are shortcomings in the content of referral letters from primary care physicians to specialists. Inadequate information includes anamnesis content, such as smoking history, occupational history and previous medication information. Crucial clinical examination results such as lung auscultation, are also often missing in the letters (Purokivi et al 2017). The inability to fulfil diagnostic criteria listed under the 2011 ATS/ERS/JRS/ALAT guidelines in the early disease stages is also recognised as a cause of diagnosis delays (Hoyer et al. 2019).

(iii) Healthcare sector factor

The diagnosis of DPLDs highly depends on resource availability. Due to the complexity of the disease, patients are scheduled to undergo diagnostic procedures/investigations such as radiology imaging and specific serological tests. The availability of DPLDs experts and facilities to conduct investigations/procedures is not readily available in every healthcare facility (Alhamad et al. 2020). Accessibility to these healthcare facilities and specialists may hinder and cause delays in diagnosis (Graney et al. 2021). The waiting time related to scheduling and availability, and the need to repeat tests/ procedures, also contribute to diagnosis delays (Cosgrove et al. 2018). A year of diagnostic delay is associated with approximately a 2% increase in fibrosis extent on chest CT scans. Underreporting of lung abnormalities in CT scans is associated with delays in pulmonary referrals possibly due to a lack of thoracic radiologists (Pritchard et al. 2019). Geographical disparities may affect the time it takes to access medical services for DPLDs. Enhancements in conducting investigations/imaging and correctly interpreting them for early referral to specialised centres may minimise potential delays and accelerate appropriate treatment for patients.

The above factors create a complex network that contributes to the deferment of DPLDs diagnosis. Table 2 provided factors contributing to DPLDs diagnosis delay. These barriers should be the focus of future initiatives to shorten the diagnostic delay.

DISCUSSION

This is the first scoping review to investigate delays in DPLDs diagnosis. A scoping review is regarded as the optimal approach for

TABLE 2: Factors contributing to diagnosis delay in DPLDs

Categories	Factors	References
Patient-related	Age: elderly	Sköld et al. (2019)
	Gender: male	Hoyer et al. (2019); Waseem et al. (2022)
	Literacy: illiterate	Waseem et al. (2022)
	Socio-economic status: low	Waseem et al. (2022)
	Non-specific symptoms/ Lack of awareness about DPLDs	van der Sar et al. (2021); Cosgrove et al. (2018); Sköld et al. (2019)
	Delay with doctor appointment	van der Sar et al. (2021)
	Family history	Hoffman et al. (2022)
	History of medication usage	Sköld et al. (2019); Hoyer et al. (2019)
Health provider	Misdiagnosis	Lancaster et al. (2021); van der Sar et al. (2021); Hoyer et al. (2019)
	Unfamiliarity with DPLDs	Lancaster et al. (2021); van der Sar et al. (2021)
	Inadequate content in referral letter	Purokivi et al. (2017)
	Delay in writing referral to specialist	van der Sar et al. 2021; Hoyer et al. (2019)
Healthcare sector	Scheduling and availability of diagnostics tests and procedures	Alhamad et al. (2020); Cosgrove et al. (2018)
	Limited access or proximity to tertiary care-level expertise	Alhamad et al. (2020)

systematically mapping existing evidence, pinpointing knowledge gaps, and offering comprehensive guidance for potential research on diagnostic delay and their associated factors. This review identified 13 studies published between 2017 and 2022 that investigated diagnosis delay duration and its causes among patients with DPLDs. Each study differed in the measurement of time intervals.

Existing data suggest that the diagnostic process of DPLDs is complex, involving multiple and repeated physician visits, diagnostic tests, and referrals, leading to delays in diagnosis and initiation of treatment. Addressing the barriers to early diagnosis of DPLDs requires an understanding of diagnostic timeliness, intervals, delays and the factors associated with them. Among the studies, potential predictors of delay were investigated, including patient, healthcare provider and healthcare system perspectives. Previous research shows that a lengthy diagnostic process adversely affects the quality of life, leading to disease progression, reduces lung function by 5-10% over six months, significantly impacts patient well-being and increases mortality. Delays are also associated with poorer outcomes among IPF patients. Longer referral times to tertiary centers correlate with higher mortality risk in DPLD patients (Cosgrove et al. 2018; Lamas et al. 2011; Pritchard et al. 2019). Patients with delayed diagnoses incur higher costs for inpatient care, emergency hospital visits, and pulmonologists visits, with threefold higher costs for diagnostic testing and 4-5 times higher costs for cardiologist and general practitioner visits compared to timely diagnosed patients (Shetty et al. 2024). Thus, early diagnosis helps arrest irreversible lung function deterioration, improve patient survival and reduces costs.

Initiatives to shorten diagnosis delays should focus on the three main factors. Prompt diagnosis is crucial because various therapies are available to slow down DPLD progression, enhance quality of life and potentially increase life expectancy. The irreversible lung damage caused by the disease highlights the importance of early treatment. Studies have shown that using antifibrotic medication significantly improves survival rates (Alhamad et al. 2020; Hoffmann et al. 2022). Increased waiting time for diagnosis confirmation also delays assessment for treatment such as lung transplantation (Lamas et al. 2011).

To address the diagnostic delays identified in this review, several key strategies can be implemented to improve the timeliness of diagnosis and patient outcomes. A primary factor contributing to delays is a lack of awareness about DPLDs among patients (Cosgrove et al. 2018; Sköld et al. 2019; van der Sar et al. 2021). To combat this, first, enhancing public awareness and patient education is crucial. Targeted campaigns should focus on educating the general population about key symptoms of DPLDs, such as persistent cough, dyspnea and fatigue. By improving symptom recognition, patients are more likely to seek medical attention early, which can help to reduce delays and support earlier detection. In addition to public education, strengthening family support can play a crucial role in encouraging patients to pursue timely medical evaluation. Families can provide emotional support and motivation for patients to seek a proper diagnosis and follow-up care.

Secondly, improving healthcare providers' education and referral practices is essential. Training programs should emphasise the latest diagnostic criteria and guidelines and address common misdiagnoses. Regular updates and training sessions on these guidelines can prevent delays caused by outdated practices (Hoyer et al. 2019). Additionally, healthcare providers should be encouraged to use symptom-based algorithms to decide when to

refer patients with suspected DPLDs (Thickett et al. 2014). These approaches will help to ensure timely referrals and reduce the risk of missed diagnoses.

To further enhance diagnostic efficiency, standardised criteria for referrals and imaging should be implemented. Developing and using a clear list of criteria on when to refer patients for specialist evaluation or imaging can help to reduce waiting times and ensure timely diagnosis (Lamas et al. 2011; van der Sar et al. 2021). Establishing a clinical pathway or protocol for diagnosing DPLDs includes a step-by-step process from initial symptom assessment to multidisciplinary team discussions. This pathway will standardise, expedite and streamline the diagnostic process.

Fostering regular communication between pulmonologists and primary care physicians is necessary to facilitate an efficient diagnostic process. Scheduled meetings can improve collaboration, reduce inappropriate referrals, and ensure that all necessary information is included in referrals to specialists (Purokivi et al. 2017). By implementing these strategies, healthcare providers can minimise diagnostic delays, improve patient outcomes and enhance overall care for individuals with DPLDs.

Additionally, improving accessibility to specialised centers is fundamental. This involves enhancing physical infrastructure, ensuring the availability of adequate diagnostic equipment such as CT machines, and recruiting qualified pulmonologists, thoracic radiologists and rheumatologists. Collaboration between the public and private sectors is essential to create a sustainable system that supports early diagnosis and reduces the disease burden on patients, families and the healthcare system (Graney et al. 2021).

Moreover, establishing voluntary coalitions and partnerships can help to address budget limitations and resource constraints. These coalitions can facilitate the sharing of resources, knowledge, and expertise, improving patient access to high-quality care. Integrated care models that consider the physical and psychological burdens of travel can also enhance patient compliance and ensure timely diagnosis and treatment (Graney et al. 2021).

Efforts should focus on streamlining the referral process and improving the availability of diagnostic and therapeutic resources within healthcare facilities. By addressing these factors, the healthcare system can better support the early diagnosis and management of DPLDs, ultimately improving patient outcomes and reducing the overall impact of the disease.

Study Limitations

This scoping review is small, with only 13 studies meeting our inclusion criteria, and lacks a comprehensive quality assessment of the included studies (Munn et al. 2018). Pinpointing the time intervals for patients with DPLDs is also challenging. Patients' responses to survey questions rely on memory recollection, making the data susceptible to inaccuracies due to recall bias (Gupta et al. 2023; Hoffman et al. 2022; Hoyer et al. 2019). According to the latest recommendations by the American Thoracic Society (ATS) and European Respiratory Society (ERS) (2002), DPLDs confirmation requires a thorough review of all clinical and investigation results obtained from the patient by a team of experts. The role of multidisciplinary team discussions for disease confirmation is not widely discussed in the studies. These factors need to be recognised and addressed to encourage early diagnosis and initiation of treatment. Unfortunately, it is difficult to infer and compare findings across studies due to variations in how diagnostic times, events, intervals, and delays were conceptualised and

assessed.

CONCLUSION

In conclusion, this scoping review of 13 articles has examined the duration of diagnostic delays and identified contributing factors. These delays can be categorised into three main groups: (i) patient-related factors; (ii) healthcare provider-related factors; and (iii) systemic factors within the healthcare sector. The review underscores the urgency for implementing new quality improvement strategies aimed at minimising the time between symptom onset and confirmation of DPLDs. Achieving an early diagnosis of DPLDs requires collaborative efforts from all stakeholders, particularly patients and physicians. Patients play a crucial role by recognising symptoms promptly and seeking timely medical advice, while physicians' expertise and responsiveness are essential for achieving a patient-centered diagnosis without delay.

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