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Works in Progress: Using Administrative Data to Estimate the Prevalence of Progressive Fibrosing Interstitial Lung Disease

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The world of interstitial lung disease (ILD) is undergoing a paradigm shift in the way it conceptualizes and treats patients with progressive fibrosing ILD (1). Rather than focusing solely on the underlying etiology of a patient's ILD, recent evidence highlights the importance of also considering the shared pathophysiology across the progressive fibrotic disease spectrum (2), as well as the common benefits provided by antifibrotic therapy when used in patients with varying causes of pulmonary fibrosis (3, 4). Yet, in part because progressive fibrosing ILD is a novel concept for which treatment was only recently approved, and also because it is a phenotype that can affect any of a heterogeneous group of distinct lung diseases, data regarding the prevalence of progressive fibrotic ILD (outside of idiopathic pulmonary fibrosis [IPF]) are scarce and highly variable (5).

In this issue of *AnnalsATS*, Singer and colleagues (pp. 1112–1121) report the observations of a retrospective review of administrative claims data that attempts to provide a real-world estimate of the prevalence of non-IPF fibrosing ILD (6). The authors assumed the great challenge of identifying patients with progressive fibrosis using *International Classification of Diseases, Tenth Revision* (ICD-10) codes that are based on specific ILD diagnoses rather than disease behavior. To do this, they designed a multistep algorithm to characterize patients as having chronic fibrosing ILD using ICD-10 codes and then used procedural and pharmacy claims to identify several proxies for disease progression, such as pulmonary function testing claims within 3 months, computed tomography chest claims in a year, and oral corticosteroid prescriptions. The authors methodically included multiple definitions of disease progression that provide differing degrees of diagnostic stringency to account for the variation in estimating fibrosing ILD prevalence on the basis of administrative claims. After applying their carefully crafted algorithm, Singer and colleagues estimated a prevalence range for non-IPF progressive fibrosing ILD of 12.14–29.05 per 10,000 among Medicare Part D enrollees between 2015 and 2019. This estimate is significantly higher than those obtained in previous analyses in Europe and the United States (1.94–7.8 per 10,000) (5) and

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estimates of 0.89–2.36 per 10,000 among commercial insurance enrollees found in this study (6).

The authors deserve praise for their creative approach to using administrative claims data to estimate prevalence. They have plausibly identified patients with non-IPF progressive fibrotic ILD, even though there existed no specific diagnostic code to describe this phenotype during the period studied. In addition, there was no approved disease-directed treatment for non-IPF progressive fibrosing ILD until after the INBUILD (Nintedanib in Progressive Fibrosing Interstitial Lung Diseases) trial, the results of which were published at the end of the study's identification period (4). Lacking direct access to pulmonary function testing, radiographic images, or symptom information, the authors have sensibly included numerous claims-based surrogates for disease progression and provided multiple definitions of progressive disease that offer a range of likely prevalence, an appropriate strategy for inferring clinical worsening from claims-based data.

Despite the authors' best efforts, the study has several limitations that should be recognized. Because nintedanib had yet to be approved for non-IPF progressive fibrosing ILD, the analysis was conducted at a time when little incentive existed for physicians to accurately differentiate fibrotic from nonfibrotic ILD using diagnostic codes. Therefore, the study algorithm may have missed patients labeled with nonspecific ICD-10 codes that were not included in the algorithm, such as J84.9 (ILD, unspecified). Next, corticosteroids and immunosuppression prescription claims are an imperfect surrogate for disease progression. Many inflammatory ILDs (especially those related to connective tissue disease) stabilize after appropriate pharmacologic treatment of the underlying inflammatory state (7, 8). Because corticosteroid use was the single most commonly identified proxy for disease progression in the study, caution should be taken in interpreting the estimated prevalence associated with steroid use. Finally, the authors note that 85% of subjects identified as having fibrotic ILD were included on the basis of the ICD-10 code J84.10 (other interstitial pulmonary diseases with fibrosis). In a chart-review study examining the utility of the closest equivalent *International Classification of Diseases, Ninth Revision* code, 515 (postinflammatory pulmonary fibrosis), Vu and colleagues determined that 90% of patients receiving this designation lacked a diagnosis of ILD (9). Although ICD-10 code J84.10 is not exactly equivalent to *International Classification of Diseases, Ninth Revision* code 515 (the postinflammatory fibrosis code was split in two with the implementation of ICD-10 to include J84.10 and J84.89), this casts some doubt on the validity of the authors' observations.

Overall, the study adds meaningful value to the field by demonstrating another method by which claims-based algorithms might offer useful information on disease prevalence. Although imperfect, claims data can provide valuable information related to prevalence, disease activity, and outcomes research, especially for entities such as progressive fibrosing ILDs. Such rare and deadly diseases make the conduct of large clinical trials designed to meet clinically meaningful endpoints incredibly difficult (10, 11). And although multicenter cohort or registry studies offer a way to include larger populations over time, their patient makeup limits generalizability outside of the large referral centers from which they typically come. It is worth emphasizing that the utility of claims data depends on whether the proposed analytic algorithm produces an accurate reflection of real patient diagnoses and outcomes. Because of the challenges inherent in the analysis of claims data, algorithms used for this purpose should ideally be validated prospectively using actual chart review of a subset of patients comparing coded diagnoses with those reached by clinical expert review of history, imaging, and biopsy results when available. The performance of this type of validation study will serve as an important next step in the use of claims-based data to define progressive fibrotic ILD, especially given that a "specific" ICD-10 code (J84.170) now exists for these diseases.

In summary, the study by Singer and colleagues is an admirable demonstration of the potential for creative analysis using administrative data to estimate the real-world prevalence of non-IPF forms of progressive fibrotic ILD. Accurate estimates of the prevalence of progressive fibrotic diseases are urgently needed to improve prognostic counseling for patients and to allow fair allocation of resources given the association of progressive fibrosing ILDs with significantly higher healthcare resource usage (5). Validation of the algorithm designed for this study would certainly strengthen the authors' inferences, but this should not detract from the importance of such research using large administrative claims data sets to study ILD epidemiology and outcomes, for which clinical trials and cohort studies are ill suited. Much about the natural history and progression of non-IPF forms of fibrotic ILD remains unknown, and observational studies of high quality and sound methodology will play an important role in better informing clinicians, researchers, and policy makers about this group of diseases. ■

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Let's Talk about Sex: Sexual Health in Pulmonary Arterial Hypertension

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Pulmonary arterial hypertension (PAH) is a progressive pulmonary vasculopathy that leads to right ventricular dysfunction and right heart failure. Despite advances in therapy, patients with PAH experience severe impairment in health-related quality of life (HRQOL) (1). Individuals with PAH experience fatigue, shortness of breath, palpitations, and chest pain that limit even usual activity, and these patients are sedentary most of the day (2, 3). Patients with PAH not only manage the physical burden of the disease and complex medical regimens that can include continuous parenteral infusions, but they also experience anxiety and depressive symptoms that can negatively affect social relationships (3, 4).

Sexual health includes a sense of self-esteem, personal attractiveness and competence, and freedom from sexual dysfunction (5). Although an important dimension of quality of life, little is known about sexual health and sexual health–related quality of life (SHRQOL) in PAH. Sexual health may not be adequately discussed during routine follow-up visits. This may be attributable to a lack of confidence or specialized training among healthcare professionals, clinicians' or patients' lack of comfort discussing sensitive topics, patients' reluctance to share intimate details of their relationships and sex lives, cultural sensitivities that make sexual activity taboo, or time constraints. One study showed that nearly all patients with PAH and a majority of their partners (72%) reported that their sex lives were severely affected by the diagnosis of PAH (6). Partners of individuals with PAH also began to view themselves as caregivers rather than intimate partners, especially as the disease progressed (7). Moreover, a small study of women with PAH found that participants had low SHRQOL and endorsed symptoms at degrees comparable to those among individuals with clinically diagnosed sexual dysfunction (8).

In this issue of *AnnalsATS*, Yee and colleagues (pp. 1122–1129) have published their data from semistructured in-depth interviews with 13 self-identified women with PAH who attended the Pulmonary Hypertension Association (PHA) International Pulmonary Hypertension Conference and Scientific Sessions (9). A trained clinical psychologist and a pulmonologist who self-identified as women performed the interviews. Albeit with a small sample size, focused on women, the study was conducted using rigorous qualitative methods. All patients reported experiencing dyspnea during sex and a decrease in the frequency of intimate encounters. Participants distinguished between having unaffected sexual desire and the physical limitations to sexual activity as their symptom burden increased. Patients reported avoiding sexual intercourse for fear of eliciting symptoms. Participants noted that side effects such as vaginal dryness in those on diuretics and heavy and/or prolonged menstrual bleeding in those on anticoagulants negatively affected sexual activity.

Parenteral therapies posed additional challenges in terms of patient (and sexual partner) concerns about catheter dislodgment, treatment interruption, and pump displacement. Participants expressed guilt about the impact of their disease on their sexual partners and their relationships. They also noted that their sexual partners expressed fear of exacerbating patients' symptoms. Finally, participants expressed low self-esteem because of changing body image related to wearing a pump or oxygen tubing or weight gain. A recent study of women with PAH in Italy identified similar themes regarding sexuality and intimate relationships (10).

A clear message from this study is that women (and likely persons of all genders) with PAH need more information, support communities, and counseling from

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