Adoption of Antifibrotic Medications: A Closer Look at the Data

To the Editor:

We read with great interest the paper by Dempsey and colleagues entitled “Adoption of the Anti-Fibrotic Medications Pirfenidone and Nintedanib for Patients with Idiopathic Pulmonary Fibrosis” (1). This is an area of great importance as we seek to better understand the uptake of novel therapeutics within the United States in a disease in which no prior approved therapies were available. Understanding adoption rates of such therapies helps to inform researchers in academic settings, clinical practice, and industry as we attempt to improve the lives of our patients with these diseases.

In this article, the authors demonstrate a relatively low rate of antifibrotic medication adoption since it was first approved in the United States for idiopathic pulmonary fibrosis (IPF) in 2014. We have no reason to doubt the veracity of the data but suggest that the time interval examined underestimates the true rate of adoption of these therapeutic agents. Per Rogers’ diffusion of innovation theory (2), adoption of innovation is a process that occurs over time as more people are willing to do something they had not done previously. In the current study, the authors identified an adoption rate of both nintedanib and pirfenidone of approximately 13.2% each, which is reported as the average adoption rate over the study period (October 1, 2014, to July 31, 2019). However, a closer look at the data by our team suggests a different pattern. Using the same OptumLabs data of commercial and Medicare Advantage members with IPF, we found a similar adoption rate of nintedanib as reported by Dempsey and colleagues (1). However, breaking down the observed time period into annual calendar year intervals, we observed a different trend. In fact, we found that the proportion of patients being treated with antifibrotic therapy ranges from 2.6% (for the 3 months encompassing October–December 2014) to 36.8% (for the first 6 months of 2019), and we believe this provides a more representative picture of antifibrotic adoption as well as the trend.

The reason(s) for the early slower uptake are unclear. One factor of potential importance is patient access to pulmonologists. Approximately half of the untreated patients with IPF in this data set had a visit to a pulmonologist during the baseline period, whereas this rate was significantly higher for treated patients (76%). For IPF, which is primarily specialist managed, access to a pulmonary specialist likely regulates the implementation of a new IPF treatment. Whether this is due to geographical limitations, insurance benefits, or other contributing factors is unknown, but it also likely contributes to the discrepancy in adoption of antifibrotics the authors noted.

We urge the authors to reconsider their results in light of these points, as it may result in drawing more comprehensive conclusions about the findings. We also note that both antifibrotics are accompanied by robust patient-assistance programs, which mitigate the out-of-pocket costs to many patients unable to afford them; thus, the conclusion that low adoption of antifibrotics “may be associated with the high out-of-pocket cost” appears premature and perhaps incomplete.

Author disclosures are available with the text of this letter at www.atsjournals.org.

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Reply: Adoption of Antifibrotic Medications: A Closer Look at the Data

From the Authors:

We would like to thank Dr. White and colleagues from Boehringer Ingelheim Pharmaceuticals for their suggestions to strengthen our recent publication in AnnalsATS (1). We agree that understanding the real-world adoption rates of novel medications such as antifibrotics is an important undertaking.

Dr. White and colleagues offer a different way of reporting the adoption of the antifibrotics using the same administrative database we did to run our study. As with our data (and the Rogers diffusion of innovation theory cited), they demonstrate an increase in antifibrotic prescriptions over time; however, instead of using a quarterly adoption rate as we did in our analysis, a semiannual calendar year adoption rate is used in theirs. This method leads to the finding that in the first 6 months of 2019, more than a third of patients with idiopathic pulmonary fibrosis (IPF) received a prescription for one of the antifibrotic medications. We appreciate the reevaluation of the data by Dr. White and colleagues. However, as their methods are unclear to us (specifically how they defined their IPF cohort, coverage requirements, and denominator) and only a snapshot of data is offered, it is difficult for us to comment on whether their way of reporting truly provides a “more representative picture” of the antifibrotic landscape. It is possible that their adoption rate is inflated by only capturing patients seen during the first 6 months of 2019 (and therefore those more likely to receive a prescription) or by patients with fibrotic interstitial lung diseases other than IPF. We did our best to avoid such confounding variables in our study by carefully constructing the cohort to only include patients with IPF based on prior local validation work. Thus, it is our continued belief that the rate observed in our study among a cohort of patients with IPF provides a reasonably accurate picture of the adoption of the medications in everyday clinical practice since their approval in 2014.

As discussed in the manuscript, we are in agreement with Dr. White and colleagues that referral to a pulmonary physician (and ideally a multidisciplinary group including chest radiologists, pulmonary pathologists, rheumatologists, and thoracic surgeons) is critical for the management of a complex disease like IPF and that the observed lack of referrals in our study may have contributed to the lower-than-expected adoption rate. This finding likely also explains the significant difference in adoption found in our analysis and those of various U.S. IPF registries where involvement of a pulmonary consultant and multidisciplinary group is an essential component of care (2, 3).

Finally, it is appreciated that pharmaceutical companies such as Boehringer Ingelheim provide generous subsidies for some of their therapies, including the antifibrotics. These prescription-assistance programs provide free or low-cost medications and have undoubtedly had a significant impact for eligible patients. However, these programs also often have complex application processes and strict income requirements and are meant almost exclusively for patients who are uninsured or underinsured (4). As our study included only patients with Medicare Advantage and private insurance prescription drug coverage, the majority of our cohort would likely not qualify to receive financial assistance for the antifibrotics. Thus, we stand by our observation that the out-of-pocket costs for the medications are high and could contribute to the low adoption rate of the drugs. Although data supporting the efficacy of these important medications continue to grow, we remain concerned about the out-of-pocket cost of the antifibrotics observed in our study (and in clinical practice) and believe further cost analyses are needed. □

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2 Rogers EM. Diffusion of innovations. 5th ed. New York, NY: Free Press; 2003.