



Home spirometry for idiopathic pulmonary fibrosis: ready for prime time?

Toby M. Maher^{1,2}

Affiliations: ¹NIHR Respiratory Biomedical Research Unit, Royal Brompton Hospital, London, UK. ²Fibrosis Research Group, National Heart and Lung Institute, Imperial College, London, UK.

Correspondence: Toby M. Maher, Fibrosis Research Group, Inflammation, Repair & Development Section, NHLI, Sir Alexander Fleming Building, Imperial College, London, SW7 2AZ. E-mail: t.maher@imperial.ac.uk

 @ERSpublications

Home spirometry in IPF can be used to shorten clinical trials and may enable patient self-management in the future <http://ow.ly/Jqft30dGiaB>

Cite this article as: Maher TM. Home spirometry for idiopathic pulmonary fibrosis: ready for prime time?. *Eur Respir J* 2017; 50: 1701403 [<https://doi.org/10.1183/13993003.01403-2017>].

The treatment of idiopathic pulmonary fibrosis (IPF) has been transformed with the advent of effective anti-fibrotic therapy [1]. Despite this there remain many challenges confronting those providing day-to-day care to individuals with IPF. Although IPF inevitably progresses over time, the rate at which it does so varies between individuals and is frequently punctuated by life-threatening acute exacerbations or episodes of infection. Additionally, there is currently a lack of measures for determining efficacy of anti-fibrotic treatment for individual patients, which makes decisions to change or persist with therapy difficult. From a clinical trial perspective, the successes of pirfenidone and nintedanib make the development of the next generation of treatments harder. With all future trials expected to be performed on background anti-fibrotic therapy, the rate of decline in FVC seen in trials will be less, thus reducing the window for determining the efficacy of any additional drug [2].

Such challenges require innovative solutions. Technological developments in the past decade have seen a huge explosion in home health monitoring. These new technologies combined with the capacity of smartphones to store data and track change over time have empowered individuals with conditions such as diabetes and cardiovascular disease to monitor and better self-manage their illnesses, with consequent reductions in hospitalisation and improved survival [3, 4]. In respiratory clinics, it is no longer unusual for patients to bring data from personal oxygen saturation monitors or activity trackers with them to their consultation. These developments provide an opportunity for changing current clinical paradigms and raise the question of how home disease monitoring might best be performed in chronic progressive respiratory diseases such as IPF.

Spirometry has been one of the mainstays in the clinical monitoring of IPF [5]. The landmark phase-three trials confirming the anti-fibrotic effects of pirfenidone and nintedanib also corroborated the value of serial change in forced vital capacity (FVC) as a measure of disease progression [6–8]. RUSSELL *et al.* [9] have recently demonstrated that daily home spirometry can be reliably and feasibly undertaken by individuals with IPF. Furthermore, their study demonstrated the value of domiciliary monitoring of FVC as a means for detecting acute exacerbations and for providing early identification of individuals with rapidly progressive disease.

In the current issue of the *ERJ*, JOHANNSON *et al.* [10] build on this previous work and report on the utility of weekly, home spirometry, undertaken in 25 individuals with IPF, as a way of reducing the numbers needed to power future clinical trials [10]. In addition to recording weekly FVC, subjects were also asked to complete the University of California San Diego shortness of breath questionnaire (UCSD SOBQ) and

Received: July 12 2017 | Accepted: July 13 2017

Conflict of interest: Disclosures can be found alongside this article at erj.ersjournals.com

Copyright ©ERS 2017

to estimate dyspnoea severity *via* a visual analogue scale (VAS). As with the previous work by RUSSELL *et al.* [9], JOHANSSON *et al.* [10] found home spirometry to be feasible for subjects to undertake, with good 24-week compliance, and the data generated compared favourably with clinic-based readings. The authors then used their data to model power equations for a 6-month clinical trial performed in subjects with IPF receiving standard anti-fibrotic therapy. Assumptions were tested across a range of FVC changes and possible drug effect-sizes and compared to the historic IPF clinical trial approach of measuring baseline and end-of-study FVC. Irrespective of the assumptions made and despite the greater variability of home readings, the effect of having a larger available data set for each subject was to reduce the number of required trial participants four-fold. Although not mentioned by the authors, an additional benefit of calculating rate of FVC change from multiple readings is that it minimises the inaccuracy introduced into endpoint analysis by missing data arising from trial dropouts and deaths.

Interestingly, the improvements in precision seen with weekly spirometry were not observed when it came to the weekly measurement of breathlessness by either VAS score or UCSD-SOBQ. The authors attribute this to the underlying structure of the data generated and the fact that FVC decline is essentially linear whilst the week-by-week change in breathlessness score is less predictable, especially when readings are compared many weeks apart. This observation highlights the importance of prospective observational studies when it comes to validating or refuting observations derived from historical retrospective studies.

JOHANSSON *et al.* [10] have made an important contribution to the future development of IPF clinical trials. Their data build on previous observations and further confirm the feasibility of home FVC measurement by individuals with IPF. A question remains as to the optimum frequency for measuring home spirometry. RUSSELL *et al.* [9] asked subjects to undertake daily measurements as compared to the weekly measurements performed by JOHANSSON *et al.* [10]. It remains to be tested whether the extra data provided by daily measurements further reduce trial numbers. It should also be noted that a proportion of subjects examined by JOHANSSON *et al.* [10] were either on anti-fibrotic medication at entry in to the study or else commenced treatment at some point during their participation in the home monitoring programme. The authors did not examine the effect background treatment had on their assumptions regarding temporal change in FVC during the 24-week observation period.

Home spirometry is already being introduced into clinical trials for individuals with fibrotic lung disease and is even being used as a primary endpoint in a recently initiated trial of pirfenidone in individuals with unclassifiable interstitial lung disease (NCT 03099187). The next step for home monitoring is for studies to examine the value of such an approach for improving outcomes in clinical practice. This will require the development and testing of algorithms for detecting individuals with rapidly progressive disease and those experiencing acute deterioration. It also remains to be examined whether home monitoring can be used to determine response to anti-fibrotic therapy and therefore be used as a tool to decide when to switch therapies. A further area for research is to determine whether integration of other monitoring modalities (oximetry, pulse and blood pressure measurements, actigraphy, *etc.*) better identifies change in health status in individuals with IPF. The work by JOHANSSON *et al.* [10] provides an important foundation for changing the delivery of care for individuals with IPF and hopefully represents a stepping stone towards empowering disease sufferers to better participate in the management of their condition.

Acknowledgements

T.M. Maher is supported by an NIHR Clinician Scientist Fellowship (NIHR Ref.: CS-2013-13-017).

References

- 1 Richeldi L, Collard HR, Jones MG. Idiopathic pulmonary fibrosis. *Lancet* 2017; 389: 1941–1952.
- 2 Maher TM. Precision medicine in idiopathic pulmonary fibrosis. *QJM* 2016; 109: 585–587.
- 3 Lin MH, Yuan WL, Huang TC, *et al.* The clinical effectiveness of telemedicine for chronic heart failure: A systematic review and meta-analysis. *Minerva Med* 2016; in press.
- 4 Bonoto BC, de Araújo VE, Godói IP, *et al.* Efficacy of mobile apps to support the care of patients with diabetes mellitus: a systematic review and meta-analysis of randomized controlled trials. *JMIR Mhealth Uhealth* 2017; 5: e4.
- 5 Zappala CJ, Latsi PI, Nicholson AG, *et al.* Marginal decline in forced vital capacity is associated with a poor outcome in idiopathic pulmonary fibrosis. *Eur Respir J* 2010; 35: 830–836.
- 6 Richeldi L, du Bois RM, Raghu G, *et al.* Efficacy and safety of nintedanib in idiopathic pulmonary fibrosis. *N Engl J Med* 2014; 370: 2071–2082.
- 7 King TE Jr, Bradford WZ, Castro-Bernardini S, *et al.* A phase 3 trial of pirfenidone in patients with idiopathic pulmonary fibrosis. *N Engl J Med* 2014; 370: 2083–2092.
- 8 Karimi-Shah BA, Chowdhury BA. Forced vital capacity in idiopathic pulmonary fibrosis—FDA review of pirfenidone and nintedanib. *N Engl J Med* 2015; 372: 1189–1191.
- 9 Russell AM, Adamali H, Molyneaux PL, *et al.* Daily home spirometry: an effective tool for detecting progression in idiopathic pulmonary fibrosis. *Am J Respir Crit Care Med* 2016; 194: 989–997.
- 10 Johannson KA, Vittinghoff E, Morisset J, *et al.* Home monitoring improves endpoint efficiency in idiopathic pulmonary fibrosis. *Eur Respir J* 2017; 50: 1602406.