



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

MAM reports grants from the US National Heart, Lung, and Blood Institute and the US National Institutes of Health, the US Department of Defense, the California Institute of Regenerative Medicine, and Roche-Genentech; and consultancy fees from Citius Pharmaceuticals and Novartis, outside of the submitted work. BTT reports consulting fees for Bayer, Thetis, and Novartis, outside of the submitted work.

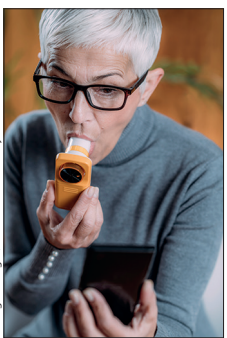
*Michael A Matthay, B Taylor Thompson
 michael.matthay@ucsf.edu

Cardiovascular Research Institute, Departments of Medicine and Anesthesia, University of California, San Francisco, CA 94143, USA (MAM); and Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA (BTT)

- 1 The Recovery Collaborative Group, Horby P, Lim WS, et al. Dexamethasone in hospitalized patients with Covid-19—preliminary report. *N Engl J Med* 2020; published online July 17. <https://doi.org/10.1056/NEJMoa2021436>.
- 2 Lamontagne F, Agoritsas T, Macdonald H, et al. A living WHO guideline on drugs for covid-19. *BMJ* 2020; **370**: m3379.
- 3 Dequin PF, Heming N, Meziani F, et al. Effect of hydrocortisone on 21-day mortality or respiratory support among critically ill patients with COVID-19: a randomized clinical trial. *JAMA* 2020; **324**: 1298–306.
- 4 Tomazini BM, Maia IS, Cavalcanti AB, et al. Effect of dexamethasone on days alive and ventilator-free in patients with moderate or severe acute respiratory distress syndrome and COVID-19: the CoDEX randomized clinical trial. *JAMA* 2020; **324**: 1307–16.
- 5 Angus DC, Derde L, Al-Beidh F, et al. Effect of hydrocortisone on mortality and organ support in patients with severe COVID-19: the REMAP-CAP COVID-19 corticosteroid domain randomized clinical trial. *JAMA* 2020; **324**: 1317–29.
- 6 The WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACT) Working Group. Association between administration of systemic corticosteroids and mortality among critically ill patients with COVID-19: a meta-analysis. *JAMA* 2020; **324**: 1330–41.
- 7 Beigel JH, Tomashek KM, Dodd LE, et al. Remdesivir for the treatment of Covid-19—final report. *N Engl J Med* 2020; published online Oct 8. <https://doi.org/10.1056/NEJMoa2007764>.
- 8 WHO SOLIDARITY Trial Consortium, Pan H, Peto R, et al. Repurposed antiviral drugs for COVID-19—interim WHO SOLIDARITY trial results. *medRxiv* 2020; published online Oct 15. <https://doi.org/10.1101/2020.10.15.20209817> (preprint).
- 9 Matthay MA, Wick KD. Corticosteroids, COVID-19 pneumonia and acute respiratory distress syndrome. *J Clin Invest* 2020; published online Sept 25. <https://doi.org/10.1172/JCI143331>.
- 10 Lane HC, Fauci AS. Research in the context of a pandemic. *N Engl J Med* 2020; published online July 17. <https://doi.org/10.1056/NEJMe2024638>.
- 11 Kuri-Cervantes L, Pampena MB, Meng W, et al. Comprehensive mapping of immune perturbations associated with severe COVID-19. *Sci Immunol* 2020; **5**: eabd7114.
- 12 Hadjadji J, Yatim N, Barnabei L, et al. Impaired type I interferon activity and inflammatory responses in severe COVID-19 patients. *Science* 2020; **369**: 718–24.
- 13 Antcliffe DB, Burnham KL, Al-Beidh F, et al. Transcriptomic signatures in sepsis and a differential response to steroids. *Am J Respir Crit Care Med* 2019; **199**: 980–86.
- 14 Villar J, Ferrando C, Martínez D, et al. Dexamethasone treatment for the acute respiratory distress syndrome: a multicentre, randomised controlled trial. *Lancet Respir Med* 2020; **8**: 267–76.
- 15 Harhay MO, Casey JD, Clement M, et al. Contemporary strategies to improve clinical trial design for critical care research: insights from the First Critical Care Clinical Trialists Workshop. *Intensive Care Med* 2020; **46**: 930–42.



Home monitoring for patients with ILD during the COVID-19 pandemic and beyond



Microgen Images/Science Photo Library

The current COVID-19 pandemic has challenged the continuity of health care and research. Health-care providers around the world are required to deal with social distancing and quarantine measures, while simultaneously ensuring quality of care for their patients. Consequently, eHealth applications, such as home monitoring, have gained increasing interest during the past months. For the vulnerable population of patients with interstitial lung diseases, home monitoring could be particularly relevant. We describe experiences with home monitoring in interstitial lung diseases, the effect of COVID-19 on its use, and opportunities for more hybrid forms of monitoring.

Interstitial lung diseases are a heterogeneous group of often progressive and deadly diseases. Treatment generally consists of immunosuppression or antifibrotic treatment, and supportive measures. Regular hospital visits are required for comprehensive patient support, including monitoring disease course and response to treatment. Lung function (ie, forced vital capacity) is

the most used outcome measure to guide treatment decisions, and the accepted primary outcome for clinical trials in interstitial lung disease. Hospital visits can be challenging for patients because of dyspnoea, supplemental oxygen needs, and dependency on caregivers. Furthermore, travel distances can be considerable because in many countries, care for interstitial lung disease is centralised in specialist centres. Hence, monitoring physiological parameters and symptoms at home could have advantages for both clinical practice and research.¹

During the past 5 years, the feasibility and reliability of home monitoring and home spirometry in interstitial lung disease have been increasingly studied. Studies in idiopathic pulmonary fibrosis showed that home spirometry yielded reliable results, predicted disease progression better than did hospital spirometry, and could possibly decrease sample sizes for future trials.^{2,3} A 24-week randomised controlled trial suggested that a home monitoring program tended to improve

Published Online
 October 16, 2020
[https://doi.org/10.1016/S2213-2600\(20\)30452-5](https://doi.org/10.1016/S2213-2600(20)30452-5)

psychological wellbeing, allowed for individually tailored treatment decisions, and yielded reliable home spirometry results over time.⁴ Patient satisfaction with home monitoring was high in this study.⁴

Although these results are promising, other studies struggled with home spirometry. A study⁵ published this year in patients with unclassifiable interstitial lung disease used home spirometry (ie, forced vital capacity) as the primary endpoint. However, the planned statistical analysis could not be applied due to highly variable home-based forced vital capacity measurements.⁵ In the multinational INMARK study,⁶ a strong correlation between home and hospital spirometry was found at different timepoints, but changes in lung function over time were only weakly correlated. Another study⁷ that used home spirometry and accelerometry to assess disease behaviour in the peri-diagnostic period encountered high measurement variability and some technical issues.

These studies were pioneers in this field and have generated valuable insights on how to improve the use of home monitoring in care and research (appendix). One of the main problems has been the measurement variability encountered in some studies. Probable reasons for this variability are insufficiently thorough patient instruction and technical issues with the spirometers. Furthermore, in most studies, patients were masked for their home spirometry results and there was no real-time data transmission to the research team. These factors hampered direct feedback and quality control, causing increasing measurement variation and decreasing adherence over time. An online home monitoring application with technical support in the native language and direct feedback to patients and health-care providers could help to overcome these challenges. Moreover, the role of the patient is crucial. Co-development of home monitoring systems with patients might lead to higher adherence and patient satisfaction with home monitoring.^{8,9} The identified statistical analysis challenges could be tackled by predefining the minimum number of measurements that are needed for reliable longitudinal analysis, and unifying the way that missing data and outliers are handled.

The COVID-19 outbreak will force the interstitial lung disease community to move further towards digital care, both in clinical practice and for

research purposes.¹⁰ Because many patients with interstitial lung disease are older, have impaired lung function, and might be using immunosuppressive drugs, they wisely strive to minimise their risk of exposure to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and stay at home. On top of this, travel and hospital access restrictions exist in many countries.¹⁰ Together, these factors lead to numerous missed clinic visits, affecting care and research. Ongoing trials are facing important protocol deviations as scheduled study visits are cancelled, and enrollment of new patients has paused. As a consequence, the development of novel drug compounds might be considerably slowed down.

We currently use our previously developed home monitoring programme, integrated with a video consultation option, to replace face-to-face consultations. Our experience is that home monitoring of lung function, symptoms, and adverse events can secure patient safety from both a care and clinical trial perspective. At the same time, patients are more actively involved in their disease, enhancing self-management. The incremental use of home monitoring and video consultations for patients with interstitial lung disease during the COVID-19 pandemic will provide further valuable information about feasibility, experiences, and the satisfaction of patients and health-care providers. Nevertheless, structured studies are needed to provide more data on long-term safety and the effects of replacing face-to-face consultations with home monitoring in this patient population. Home monitoring can also be used to facilitate international interstitial lung disease registries, with patients taking the lead and collecting most registry data at home. This practice will facilitate meaningful collaboration between patients, doctors, researchers, and other stakeholders to improve insights into disease behaviour and response to therapy across diseases and borders. In addition, it could provide a more definite answer to questions about the reliability of (online) home spirometry in a diverse population and the feasibility of eHealth applications in a multinational setting. Whether home spirometry can be optimised to the extent that it can be used as a primary endpoint in future clinical trials is yet to be seen, but will hopefully become clearer.

Given that the COVID-19 pandemic is expected to last longer, clinicians and researchers should team up with different stakeholders to provide high-quality,

See Online for appendix

durable eHealth solutions. By involving patients in the development and evaluation of digital care, eHealth applications can be better adapted to patients' needs and wishes. Moreover, policy makers and insurance companies should be motivated to stimulate research and support further development, optimisation, and up-scaling of digital care. To allow for wide-scale implementation, organisational, legislative, ethical, and reimbursement issues also need to be taken into account. Altogether, the challenges faced in COVID-19 times have also created opportunities to expand novel ways of monitoring in order to improve quality and access of care and research for patients with interstitial lung disease.

MSW reports grants and speaker and consultancy fees from Boehringer-Ingelheim, Hoffman la Roche, and consultancy fees from Galapagos and Respivant, outside of the submitted work; all grants and fees are paid to her institution. CCM reports grants and consultancy fees from Boehringer-Ingelheim, outside of the submitted work; all grants and fees are paid to her institution. GN declares no competing interests.

G Nakshbandi, C C Moor, *M S Wijzenbeek
m.wijzenbeek-lourens@erasmusmc.nl

Department of Respiratory Medicine, Erasmus Medical Center, Rotterdam, Netherlands, 3015 GD, Rotterdam

- 1 Wijzenbeek M, Cottin V. Spectrum of fibrotic lung diseases. *N Engl J Med* 2020; **383**: 958–68.
- 2 Johansson KA, Vittinghoff E, Morisset J, Lee JS, Balmes JR, Collard HR. Home monitoring improves endpoint efficiency in idiopathic pulmonary fibrosis. *Eur Respir J* 2017; **50**: 1602406.
- 3 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**: 989–97.
- 4 Moor CC, Mostard RLM, Grutters JC, et al. Home monitoring in patients with idiopathic pulmonary fibrosis. A randomized controlled trial. *Am J Respir Crit Care Med* 2020; **202**: 393–401.
- 5 Maher TM, Corte TJ, Fischer A, et al. Pirfenidone in patients with unclassifiable progressive fibrosing interstitial lung disease: a double-blind, randomised, placebo-controlled, phase 2 trial. *Lancet Respir Med* 2020; **8**: 147–57.
- 6 Maher T, Cottin V, Russell A-M, et al. Correlation between home and clinic spirometry in subjects with IPF: results from the INMARK trial. *Eur Respir J* 2019; **54** (suppl 63): PA1318.
- 7 Wijzenbeek M, Bendstrup E, Valenzuela C, et al. Design of a study assessing disease behaviour during the peri-diagnostic period in patients with interstitial lung disease: the STARLINER study. *Adv Ther* 2019; **36**: 232–43.
- 8 Moor CC, Wapenaar M, Miedema JR, Geelhoed JJM, Chandoesing PP, Wijzenbeek MS. A home monitoring program including real-time wireless home spirometry in idiopathic pulmonary fibrosis: a pilot study on experiences and barriers. *Respir Res* 2018; **19**: 105.
- 9 Johansson KA. Remote monitoring in idiopathic pulmonary fibrosis: home is where the bluetooth-enabled spirometer is. *Am J Respir Crit Care Med* 2020; **202**: 316–17.
- 10 Wong AW, Fidler L, Marcoux V, et al. Practical considerations for the diagnosis and treatment of fibrotic interstitial lung disease during the coronavirus disease 2019 pandemic. *Chest* 2020; **158**: 1069–78.