We believe that lung function should be incorporated into this type of analysis to allow an assessment of how the respiratory system is working. A recent meta-analysis has shown that altered diffusion persists in 36% of patients with nonsevere COVID-19 and 66% of patients with severe COVID-19 between 1 and 3 months after infection (4). A recent study has reported a reduced diffusion capacity in 22% of patients without oxygen requirements and in 56% of patients with ICU requirements 6 months after the infection (5). These results reinforce the picture of greater functional respiratory compromise in the most severe patients. Without lung function assessment, it is particularly difficult to establish a strong relationship between respiratory complications and poor post–COVID-19 health.

One of the most relevant assessments in the follow-up of patients after COVID-19 is physical capacity, and the 6MWT is a useful instrument that is widely used in healthy subjects and for studying many diseases (6). This test provides useful information not only about physical capacity but also about exertional desaturation (6). The authors used this test, but only 71% of the subjects were able to perform it (1). One wonders what happened to those who could not perform the test, whether they suffered the most severe cases, and how many of them were in the ICU. This information is relevant as recent studies of patients after COVID-19 have reported a significant reduction in the distance walked in the 6MWT and a significant connection between the number of patients with scores less than the lower limit and the severity of the disease (5). It would also be useful to see the score as a percentage of the recommended reference values (6).

Finally, the common characteristic of the studies described above is that they have a significant number of patients across the entire spectrum of severity (3–5). In Townsend and colleagues, of the 487 patients who were offered a follow-up appointment, only 153 (31.4%) accepted, of whom only 19 (3.9%) had been in the ICU. It is difficult to establish how representative this group is of the COVID-19 population, which represents the clear possibility of selection bias.

The study by Townsend and colleagues is an important step in investigating the possible causes of the persistence of symptoms and the functional sequelae after COVID-19, but future investigations should incorporate lung function or CT and use a more representative sample so that the consequences after COVID-19 infection can be analyzed while minimizing the risk of misinterpretation.

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Reply: The Relation between Persistent Poor Health after COVID-19 and Respiratory Complications or Initial Disease Severity

From the Authors:

We appreciate the comments of Torres-Castro and colleagues and welcome the opportunity to provide further details on respiratory follow up and ill-health in our post–coronavirus disease (COVID-19) cohort (1). Our study was a pragmatic approach to the follow up of COVID-19 survivors, in line with current published recommendations (2). This approach allowed for the entire spectrum of acute COVID-19 infections to be evaluated, from those managed in the community to those admitted to the intensive care unit (ICU). We included all patients attending the clinic in our analysis, regardless of completion of all assessments, to

reduce bias. Overall, 44 patients (29%) did not undergo a 6-minute-walk testing (6MWT). The reasons were poor baseline mobility ($n = 3$); patient preference ($n = 36$), most commonly because of the patient's time constraints; and lack of access to testing ($n = 5$). Of these 44 patients, 38 (86%) were managed in the community during their primary illness, with 6 admitted. Of the 44 patients, 2 (4.5%) were admitted to the ICU during their acute illness. There is no difference in initial illness severity between those who underwent 6MWT and those who did not ($t = 1.44$, $P = 0.15$).

The generation of normal reference ranges for 6MWT is difficult. There is no clear consensus as to which formula should be used, resulting in large differences between predicted normal ranges among studies (3). Therefore, we contextualize the distance covered in our study in the setting of established cutoffs associated with adverse clinical outcomes. Seven (7/109, 6%) patients recorded a 6MWT distance of less than 350 m, which has previously been associated with an increased risk of hospitalization in patients with lung disease (4).

An important difference between our study and those published thus far is the inclusion of patients both hospitalized and nonhospitalized during acute infection. This provides a more complete assessment of respiratory sequalae and a more robust assessment of the impact of initial disease severity. This may explain our finding that initial illness severity does not predict ongoing ill health, contrary to studies focusing solely on hospitalized survivors.

As suggested by Torres-Castro and colleagues, there is a role for pulmonary function tests (PFTs) and cross-sectional imaging in the follow up of these patients. Current guidelines suggest that all patients undergo chest X-ray, with cross-sectional imaging recommended in the setting of an abnormal chest X-ray (2). PFTs should be considered in patients deemed to have severe pneumonia during initial infection. In line with these guidelines, we performed cross-sectional imaging on those with abnormal chest X-rays (5/115, 4%), whereas 20 patients (20/153, 13%) underwent PFTs. The indications for PFTs were distance covered at 6WMT <350 m ($n = 10$, 50%), significant desaturations on 6MWT ($n = 2$, 10%), and maximal Borg score ≥ 8 ($n = 8$, 40%). Forced expiratory volume in 1 second (mean percentage predicted, 96; standard deviation [SD], 19) and forced vital capacity (mean percentage predicted, 100; SD, 25) were within normal limits, whereas diffusing capacity of the lung for carbon monoxide was mildly reduced (mean percentage predicted, 79; SD, 16).

Our approach focused on clinically significant respiratory consequences of COVID-19. It was to this end that the pragmatic approach to assessment, in line with guidelines, was implemented. The combination of chest X-ray and 6MWT demonstrates a low rate of objective clinically significant results, with a high burden of subjective symptoms reported. It adds to the growing body of evidence suggesting that so-called long COVID-19 symptoms can be seen in all patient groups (5). We agree with Torres-Castro and colleagues that complete respiratory evaluation with cross-sectional imaging and PFTs are required to fully describe the respiratory recovery in these patients for research purposes. We agree that further studies are required to investigate the consequences of COVID-19 infection across all systems and not merely respiratory recovery.

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