2. Redl H, Schlag G, Bahrami S, Schade U, Ceska M, Stütz P. Plasma neutrophil-activating peptide-1/interleukin-8 and neutrophil elastase in a primate bacteremia model. *J Infect Dis* 1991;164:383–388.
3. Diez-Ruiz A, Tilz GP, Zangerle R, Baier-Bitterlich G, Wachter H, Fuchs D. Soluble receptors for tumour necrosis factor in clinical laboratory diagnosis. *Eur J Haematol* 1995;54:1–8.
4. Azevedo ZM, Moore DB, Lima FC, Cardoso CC, Bougleux R, Matos GI, Luz RA, Xavier-Elsas P, Sampaio EP, Gaspar-Elsas MI, *et al*. Tumor necrosis factor (TNF) and lymphotoxin-alpha (LTA) single nucleotide polymorphisms: importance in ARDS in septic pediatric critically ill patients. *Hum Immunol* 2012;73:661–667.
5. Kangelaris KN, Sapru A, Calfee CS, Liu KD, Pawlikowska L, Witte JS, Vittinghoff E, Zhuo H, Auerbach AD, Ziv E, *et al*.; National Heart, Lung, and Blood Institute ARDS Network. The association between a Darc gene polymorphism and clinical outcomes in African American patients with acute lung injury. *Chest* 2012;141:1160–1169.
6. Wei Y, Tejera P, Wang Z, Zhang R, Chen F, Su L, Lin X, Bajwa EK, Thompson BT, Christiani DC. A missense genetic variant in LRRC16A/CARMIL1 improves acute respiratory distress syndrome survival by attenuating platelet count decline. *Am J Respir Crit Care Med* 2017;195:1353–1361.

Reply

From the Authors:

We appreciate the interest in our recent publication (1) from Dr. Shimatani and colleagues and thank them for their letter. With regard to the idea that the temporal evolution of acute respiratory distress syndrome (ARDS) may influence subphenotype assignment, we note that all subjects in the FACTT (Fluid and Catheter Treatment Trial) study were enrolled within the first 48 hours of ARDS, but the precise time elapsed between meeting ARDS criteria and plasma sampling for each patient is not available in this data set. In our previous work on ARDS subphenotypes (2), patients were enrolled within the first 36 hours of meeting ARDS criteria, thus narrowing the window further, but again the precise interval between meeting criteria and enrollment for each patient was not available. We agree with the authors that the evolution and stability of ARDS subphenotypes over time is a critically important topic for further study, and we are currently preparing a manuscript on this very topic. We also agree with the letter's point regarding the potential influence of genotype on ARDS subphenotype and plan to address this topic in our future research as well. We appreciate the authors' interest and their thoughtful questions regarding our work. ■

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

Carolyn S. Calfee, M.D., M.A.S.
Kevin Delucchi, Ph.D.
University of California San Francisco
San Francisco, California

Katie R. Famous, M.D., Ph.D.
Kaiser Permanente
Oakland, California

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Reference

1. Famous KR, Delucchi K, Ware LB, Kangelaris KN, Liu KD, Thompson BT, Calfee CS; ARDS Network. Acute respiratory distress syndrome subphenotypes respond differently to randomized fluid management strategy. *Am J Respir Crit Care Med* 2017;195:331–338.
2. Calfee CS, Delucchi K, Parsons PE, Thompson BT, Ware LB, Matthay MA; NHLBI ARDS Network. Subphenotypes in acute respiratory distress syndrome: latent class analysis of data from two randomised controlled trials. *Lancet Respir Med* 2014;2:611–620.

Controlled Clinical Trials and Real-Life Experience with Pulmonary Rehabilitation

To the Editor:

We read with great interest the study by Güell and colleagues, which provides compelling evidence that providing a maintenance program after an initial intensive program of pulmonary rehabilitation (PR) leads to improvements in functional capacity and the BODE (body mass index, airflow obstruction, dyspnea, and exercise capacity) index, a strong predictor of mortality in chronic obstructive pulmonary disease (COPD) (1). Güell and colleagues' study reinforces the importance of PR programs and shows that continued participation in PR could maintain improved patient outcomes. Once enrolled, 66% of the patients were adherent to the maintenance program at 3 years, suggesting that patients who get enrolled in PR are likely to understand and experience the benefits, and thus continue to participate in the program. The study adds to the growing body of literature that reports on the salutary effects of pulmonary rehabilitation on physiological parameters in the context of well-designed clinical trials (2, 3).

One could raise doubt, however, about whether the results of the study are applicable to real-world practice. The study population had a 96.5% PR completion rate, which to our knowledge has not been reported outside of clinical trials. For instance, Jones and colleagues reported that less than 10% of all hospital discharges for acute exacerbation of COPD completed postdischarge pulmonary rehabilitation, although such services were fully commissioned and available (4). In that study, only 32% of the eligible subjects received referrals, which appeared to be a major barrier to inclusion. In our tertiary academic center, Cleveland Clinic Main Campus Hospital, patients are seen at the COPD exacerbation clinic after discharge from the hospital. In a recent survey of 172 patients who attended the clinic, 72 patients could not be referred to pulmonary rehabilitation. Of the 72 patients, 29 patients could not be referred because they had attended pulmonary rehabilitation before and no reimbursement was available for the maintenance program by insurers. Of the eligible patients, 96% were referred for pulmonary rehabilitation. Despite this, 68% of patients with referral did not attend rehabilitation for a variety of reasons such as patient refusal, transportation issues, full-time employment, financial issues, and nursing home placement. These barriers we encountered were similar to those previously published (5, 6). We found that patients who attended the COPD exacerbation clinic in the

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