a survival benefit in those who came into the trial on ICS because they have the greatest risk for exacerbations and thus the greatest risk for death (9). We believe that the most likely cause of the observed survival benefit was the reduction in recurrent exacerbations, especially those leading to hospitalization, demonstrating the benefit of ICS in this patient population.

It is important to recognize that IMPACT was not an ICS withdrawal study. Although ~77% of patients entered the trial on ICS, because of the 2:2:1 randomization, only approximately 15% of the overall population underwent withdrawal of ICS. The vast majority of the population (85%) did not experience ICS removal. In addition, deaths occurred in all arms throughout the trial, indicating no "surge" in deaths caused by abrupt withdrawal of ICS. Overall mortality on the long-acting muscarinic antagonist–long-acting β_2 agonist arm was actually lower than what has been previously observed in similar patients with advanced COPD (10, 11), also strongly suggesting that abrupt ICS withdrawal was not the cause of the findings.

Even if we were to believe Dr. Suissa's argument that ICS withdrawal was harmful, we would then have to conclude that the addition of ICS was beneficial for these patients in the first place.

What is clear is that most patients who met the IMPACT inclusion criteria benefited from triple therapy compared with dual therapy. Patients with symptomatic COPD and a history of exacerbation who received triple therapy with fluticasone furoate/umeclidinium/vilanterol experienced clinically relevant improvements in lung function and health-related quality of life, reduction in exacerbations and hospitalizations, and now a confirmed additional benefit of improved survival compared with patients randomized to umeclidinium/vilanterol. ■

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David A. Lipson, M.D.*
GlaxoSmithKline
Collegeville, Pennsylvania
and
University of Pennsylvania
Philadelphia, Pennsylvania

Mark T. Dransfield, M.D.
University of Alabama at Birmingham
Birmingham, Alabama

MeiLan K. Han, M.D.‡
University of Michigan
Ann Arbor, Michigan

On behalf of all the authors

ORCID ID: 0000-0001-6732-4593 (D.A.L.).

*Corresponding author (e-mail: david.a.lipson@gsk.com).
‡M.K.H. is Deputy Editor of *AJRCCM*. Her participation complies with American Thoracic Society requirements for recusal from review and decisions for authored works.

References

1. Lipson DA, Crim C, Criner GJ, Day NC, Dransfield MT, Halpin DMG, *et al.*; IMPACT Investigators. Reduction in all-cause mortality with fluticasone furoate/umeclidinium/vilanterol in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2020;201:1508–1516.
2. Pascoe SJ, Lipson DA, Locantore N, Barnacle H, Brealey N, Mohindra R, *et al*. A phase III randomised controlled trial of single-dose triple therapy in COPD: the IMPACT protocol. *Eur Respir J* 2016;48: 320–330.
3. Martinez FJ, Han MK, Allinson JP, Barr RG, Boucher RC, Calverley PMA, *et al*. At the root: defining and halting progression of early chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2018;197: 1540–1551. [Published erratum appears in *Am J Respir Crit Care Med* 198:1463.]
4. Lipson DA, Barnhart F, Brealey N, Brooks J, Criner GJ, Day NC, *et al.*; IMPACT Investigators. Once-daily single-inhaler triple versus dual therapy in patients with COPD. *N Engl J Med* 2018;378:1671–1680.
5. Wedzicha JA, Banerji D, Chapman KR, Vestbo J, Roche N, Ayers RT, *et al.*; FLAME Investigators. Indacaterol-glycopyrronium versus salmeterol-fluticasone for COPD. *N Engl J Med* 2016;374: 2222–2234.
6. Ferguson GT, Rabe KF, Martinez FJ, Fabbri LM, Wang C, Ichinose M, *et al*. Triple therapy with budesonide/glycopyrrolate/formoterol fumarate with co-suspension delivery technology versus dual therapies in chronic obstructive pulmonary disease (KRONOS): a double-blind, parallel-group, multicentre, phase 3 randomised controlled trial. *Lancet Respir Med* 2018;6:747–758.
7. Rabe KF, Martinez FJ, Ferguson GT, Wang C, Singh D, Wedzicha JA, *et al*. A phase III study of triple therapy with budesonide/ glycopyrrolate/formoterol fumarate metered dose inhaler 320/18/9.6 μg and 160/18/9.6 μg using co-suspension delivery technology in moderate-to-very severe COPD: the ETHOS study protocol. *Respir Med* 2019;158:59–66.
8. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: 2020 report. [accessed 2020 Apr 21]. Available from: https://goldcopd.org.
9. Rothnie KJ, Müllerová H, Smeeth L, Quint JK. Natural history of chronic obstructive pulmonary disease exacerbations in a general practice-based population with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2018;198:464–471.
10. Lange P, Marott JL, Vestbo J, Olsen KR, Ingebrigtsen TS, Dahl M, *et al*. Prediction of the clinical course of chronic obstructive pulmonary disease, using the new GOLD classification: a study of the general population. *Am J Respir Crit Care Med* 2012;186:975–981.
11. Soriano JB, Lamprecht B, Ramírez AS, Martinez-Camblor P, Kaiser B, Alfageme I, *et al*. Mortality prediction in chronic obstructive pulmonary disease comparing the GOLD 2007 and 2011 staging systems: a pooled analysis of individual patient data. *Lancet Respir Med* 2015;3:443–450.

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One Step at a Time: A Phased Approach to Behavioral Treatment Development in Pulmonary Rehabilitation

To the Editor:

We have read with great interest the article by Barker and colleagues (1). We want to congratulate the authors for their publication and hope to contribute to this important discussion.

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Despite evidence and consensus across international guidelines (2) that patients who have experienced an acute exacerbation of chronic obstructive pulmonary disease (AECOPD) should participate in pulmonary rehabilitation (PR) within 4 weeks after hospital discharge, the uptake of this treatment remains low (3). This is of concern, as PR has been shown to improve dyspnea, quality of life, and exercise capacity, and reduces hospital readmissions among patients with AECOPD (2). The authors rightly indicate that to date, very few studies have investigated the effects of interventions that aim to increase uptake of PR after an AECOPD (4). None of the existing published studies used a randomized controlled trial (RCT) design.

Barker and colleagues conducted an RCT to investigate the effects of an intervention, an educational video about PR, as an adjunct to usual care (1). Their primary outcome was uptake of PR within 28 days of hospital discharge. They concluded that a video delivered at hospital discharge did not improve uptake of PR. Although their RCT was well conducted, it does not appear that the authors applied behavioral theory to guide the key messages included in the video, nor was there a progressive and systematic framework guiding the development of their behavior-change intervention as suggested by the Obesity-related Behavioral Intervention Trials (ORBIT) model (5). The ORBIT model encourages investigators to complete a series of studies to define and refine the intervention (phase I) and to preliminarily test it (phase II) before conducting efficacy (phase III) and effectiveness (phase IV) trials, akin to the usual practice of pharmaceutical studies. These suggested steps for behavioral intervention development ensure that the treatment package includes essential components offered in an efficient way and, importantly, helps to ensure a clinically significant effect on the behavioral risk factor (5). Although this process can be long and laborious, it is a critical step to prevent a potential waste of resources—for example, by conducting a large RCT for a treatment that cannot impact the target clinical outcomes (5).

It seems that Barker and colleagues designed their RCT before they determined whether their video intervention included the essential components (e.g., a motivational communication style and the optimal frequency, duration, and timing of contacts to show the video). The video was only shown once at hospital discharge, a time that can be very overwhelming for patients and family members, and thus is not the best time to make such a decision (6). Indeed, 6 out of the 15 participants interviewed did not recall even watching the video at hospital discharge. Furthermore, at the outset of the RCT, the potential effect on behavioral risk factors (such as knowledge about PR, and self-efficacy/readiness for commencing PR) was not known, as no preliminary testing of these important mediate outcomes was performed. Finally, the rationale for their secondary outcomes is not clear. It is unlikely that an educational video shown once at hospital discharge would have an impact on PR completion rates and adherence, physical performance, or health-related quality of life.

The present study by Barker and colleagues addresses a very important question and was well conducted for an RCT. However, if the authors had used a theoretical framework such as the ORBIT model, they would have had the opportunity to strengthen their behavioral intervention and make it as effective as possible before conducting an RCT. It is important to emphasize the value of using a systematic, phased approach to develop a behavioral treatment before testing it in rigorous effectiveness trials. ■

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Tania Janaudis-Ferreira, P.T., Ph.D.*
McGill University
Montreal, Quebec, Canada
and
McGill University Health Centre
Montreal, Quebec, Canada

Bryan Ross, M.D., M.Sc.
Jean Bourbeau, M.D., M.Sc.
McGill University Health Centre
Montreal, Quebec, Canada

ORCID ID: 0000-0003-0944-3791 (T.J.-F.).

*Corresponding author (e-mail: tania.janaudis-ferreira@mcgill.ca).

References

1. Barker RE, Jones SE, Banya W, Fleming S, Kon SSC, Clarke SF, *et al*. The effects of a video intervention on posthospitalization pulmonary rehabilitation uptake: a randomized controlled trial. *Am J Respir Crit Care Med* 2020;201:1517–1524.
2. Puhan MA, Gimeno-Santos E, Cates CJ, Troosters T. Pulmonary rehabilitation following exacerbations of chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2016;12:CD005305.
3. Spitzer KA, Stefan MS, Priya A, Pack QR, Pekow PS, Lagu T, *et al*. Participation in pulmonary rehabilitation after hospitalization for chronic obstructive pulmonary disease among Medicare beneficiaries. *Ann Am Thorac Soc* 2019;16:99–106.
4. Early F, Wellwood I, Kuhn I, Deaton C, Fuld J. Interventions to increase referral and uptake to pulmonary rehabilitation in people with COPD: a systematic review. *Int J Chron Obstruct Pulmon Dis* 2018;13:3571–3586.
5. Czajkowski SM, Powell LH, Adler N, Naar-King S, Reynolds KD, Hunter CM, *et al*. From ideas to efficacy: the ORBIT model for developing behavioral treatments for chronic diseases. *Health Psychol* 2015;34:971–982.
6. Janaudis-Ferreira T, Tansey CM, Harrison SL, Beaurepaire CE, Goodridge D, Bourbeau J, *et al*. A qualitative study to inform a more acceptable pulmonary rehabilitation program after acute exacerbation of chronic obstructive pulmonary disease. *Ann Am Thorac Soc* 2019;16:1158–1164.

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Reply to Janaudis-Ferreira *et al.*

From the Authors:

We thank Janaudis-Ferreira and colleagues for their interest in our randomized controlled trial (1) and their important contribution to the debate surrounding strategies to improve uptake of

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