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Reply to Prieto-Centurion *et al.*

From the Authors:

We would like to thank Drs. Prieto-Centurion, Artis, and Coultas for their interest in our article (1). We wholly agree with the points raised with respect to the need to support the sustained adoption of healthy lifestyle behaviors. The focus of our article was to explore alternative approaches to pulmonary rehabilitation (PR) that would increase its availability and uptake while not diluting its effectiveness. However, as the authors point out, the challenge of maintaining the benefits of rehabilitation, irrespective of the mode of delivery, should not be overlooked.

The benefits of rehabilitation are well described, but outcomes of this intervention are usually assessed shortly after completion of the program (2). The seminal study by Griffiths and colleagues clearly demonstrated that in the absence of any maintenance strategy, the gains from rehabilitation tend to subside at 12 months (3). Many efforts have been made to identify an effective and acceptable program to support graduates of rehabilitation to maintain benefits. The evidence about the best format to use is inconclusive (4, 5). Maintenance strategies commonly describe the frequency and method of contact (e.g., once-a-month drop-in sessions [6] and regular telephone contact [7]) rather than the content and nature of the behavioral intervention to support effective self-management. A taxonomy of behavior-change techniques, first described by Michie and colleagues in 2013 (8), has the potential to unravel which techniques may be most effective in supporting and sustaining healthy behaviors. The authors identified 93 distinct behavior-change techniques that were clustered into 16 groups. It would not be unreasonable for us to consider using this taxonomy to describe approaches used as part of rehabilitation and maintenance trials.

It might be speculated that home-based programs would have a longer-lasting effect than center-based programs, given that the participants engage in self-directed exercise behaviors in their home environment. The current literature does not entirely support this assumption, as the three noninferiority trials of home- versus center-based PR cited in our review had differing results. The Canadian study (9) demonstrated retention of some improvements in health-related quality of life and cycle endurance training at 12 months for both home- and center-based groups. These improvements were not at the level of the gains seen immediately after completion of the program but were significant when compared within group. In that study, there was some follow-up contact with healthcare professionals, but it was minimal. The Australian and UK studies (10, 11) offered a more independently managed form of rehabilitation; however, the data from these studies are difficult to compare because the follow-up periods were 6 and 12 months, respectively. The longer follow-up in the Australian study (9) yielded data similar to those reported by Griffiths and colleagues (3): by and large, both groups had returned to baseline at 12 months with respect to their 6-minute walking distance and health-related quality of life. The UK-based study reported that at 6 months there was some retention of exercise capacity above baseline levels (on endurance shuttle walking test), but health-related quality of life had reverted to baseline in the home-based group, with some benefits retained in the center-based group. It is worth noting that in the absence of any interventions, on average, the decline in walk distance is in the region of 20 m/yr (12).

We would wholeheartedly agree that packages of PR should be embedded in an integrated system of care to support the maintenance of benefits. The specific details of these packages of care will depend on the healthcare system, the context of the package, and the acceptability of these modes of support to the individual.

Fine-tuning PR to address the above challenges and opportunities is still a work in progress, and these areas are fertile ground for research. ■

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Inhaled Corticosteroids and Adult Asthma

To the Editor:

We read with interest the concise review by Beasley and colleagues on inhaled corticosteroids (ICS) in adult asthma (1). We agree that the definition of low, moderate, and high doses of ICS is arbitrary, as stated in the Global Initiative for Asthma report, although the Global Initiative for Asthma makes clear that it is simply an assessment of estimated clinical comparability based on available studies and product information, and that a large number of patients with asthma need only a low dose of ICS (www.ginasthma.org).

However, with regard to the statement that the maximum obtainable patient benefit is with low-dose ICS, we would like to emphasize that the evidence provided to support this statement is from studies on nonphenotyped asthma, a significant proportion of which probably have no or low levels of airway eosinophilia. The main therapeutic target of ICS is the eosinophil, and the degree of airway eosinophilia varies significantly from one patient to another, so that the dose of ICS needed to reduce such eosinophilia significantly varies greatly. It is likely that the "classical" benefit/systemic effects curve differs significantly in eosinophilic asthma, and that the observed plateau is shifted to the right in this population. The reason for the reported lack of efficacy of doubling and quadrupling of doses of ICS is likely that the nature of airway inflammation was not considered in those clinical trials. Furthermore, studies that have looked at sputum eosinophils have demonstrated that high doses of corticosteroids are as effective as prednisone in moderate to severe exacerbations (2, 3). Another study showed that high-dose ICS is also effective in treating exacerbations of asthma (4).

The best way to show an ICS dose response and compare ICS products is therefore not to use unselected patients but, rather, to choose patients with either high sputum eosinophils or high F_{ENO} and then perform dose escalation studies (5). Furthermore, ICS dose response also depends on the outcome measured, with airway hyperresponsiveness showing the best dose-dependent improvement over time (6).

As stated in all guidelines, we should always consider using the lowest possible dose of ICS (or oral corticosteroids [OCS], and ideally no OCS) to control asthma while avoiding the risks for

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