Interventional lifestyle and self-management trials: A double-edged sword. Is it time to mandate formal data and safety monitoring?

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Worldwide, the number of individuals living with chronic respiratory disease is increasing, because of both new diagnoses but also because people are living longer with their condition.1 Irrespective of the cause of their underlying respiratory condition, those with advanced disease have common physical limitations, psychological comorbidities and complex care needs. Support and care at home is commonly provided by family members, often at significant personal cost,2 and the role these informal caregivers play in patient care is often overlooked. Traditional interventions focus on disease sufferers, however targeting those providing care is a potentially complementary treatment, particularly when trying to improve factors such as adherence to medication, smoking cessation and physical activity.3

In this issue of the journal, Frith and colleagues present the results of their large randomised controlled trial of a personalised intervention targeting the both patients and their caregivers of people with advanced chronic respiratory disease.4 Inclusion criteria were not based on a specific disease but instead a marker of advanced disease; individuals with respiratory failure receiving home oxygen treatment. Caregivers in the intervention group received two nurse-led, home-based personalised educational sessions based upon developing action plans for exacerbations, motivating patients to participate in their care, developing a partnership between patient and caregiver, and ensuring that the health and well-being of the caregiver was not neglected. No difference in the composite primary end point (survival to hospitalisation, residential care admission or death) was found. Improvements in the intervention group were seen in important patient-focused measures including fatigue, mastery, vitality and general health.

Somewhat unexpectedly, the authors found an excess mortality for patients in the intervention group.

While unexpected there are now several trials in chronic respiratory disease to have reported adverse outcome for ‘lifestyle or self-management’ interventions.4–7 It is difficult to appreciate a potential causal mechanism in these various trials, especially when adverse signals were temporally separate from the interventional period.4,6 However, with several published reports potential safety concerns cannot be ignored.

One similarity of all the trials is that they are in high-risk populations, for example, respiratory failure or post-hospitalisation where adverse events are common. However, none of these trials were powered to detect a difference in mortality, and therefore, a type 1 error may account for the results. Adverse events will be more likely in these trials as follow-up in all trials was a minimum of 6 months, longer than many other reported interventional trials.

Imbalances in disease severity may also help explain worse outcomes in intervention groups, with significantly worse functional impairment,4 respiratory failure and cardiac co-morbidity,7 and lung function8 reported, respectively. None of these trials stratified their randomisation on any markers of disease severity.

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Frith et al. highlight the importance of instituting data and safety monitoring boards in all trials of therapeutic interventions. We would support this, and indeed would suggest that lifestyle and self-management trials should be required to (1) have a minimum follow-up ‘washout’ period, (2) stratify for disease severity prior to randomisation in high-risk populations and (3) ensure the same robust governance of clinical trials of Investigational Medicinal Products are in place.

This study highlights the complex interaction between patient and caregiver involving a balance of positive and negative aspects impacting on the physical and mental health of both parties. Disease-specific education is a key part in the management of any chronic disease, however, should be viewed as double-edged, potentially (and hopefully) of benefit, but are not without risk.

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