Incidence of acute exacerbations of chronic respiratory disease during pulmonary rehabilitation delivered at home or hospital

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To the Editor:

Pulmonary rehabilitation is an important treatment for people with chronic respiratory disease [1]. Alternative models of pulmonary rehabilitation, including telerehabilitation, have demonstrated comparable improvements in outcomes such as quality of life and exercise capacity to traditional centre-based (hospital or community) models, but higher completion rates [2]. People with chronic respiratory disease are susceptible to viral infections that are a major cause of acute exacerbations of symptoms, and ultimately impact on quality of life and disease burden [3, 4]. Exacerbations may occur during centre-based pulmonary rehabilitation and can be a barrier to attendance [5, 6]. Infection control measures, such as physical distancing and shielding in at-risk populations, can have an important role in the prevention of exacerbations, as evidenced by the substantial reduction in the number of exacerbations of chronic respiratory disease during the COVID-19 pandemic [7–9]. Compared to centre-based rehabilitation models that are conventionally delivered *via* face-to-face group settings, telerehabilitation models delivered remotely into the home may allow greater attainment of infection control measures such as physical distancing or avoidance of group gatherings and thus potentially reduce exposure to major causes of exacerbations (*e.g.* virus transmission). However, whether the likelihood of an exacerbation in people with chronic respiratory disease is lower when undertaking telerehabilitation within the home environment compared to centre-based pulmonary rehabilitation is not clear.

The REACH (Rehabilitation Exercise At Home) trial [10] was a multicentre, randomised controlled equivalence trial conducted between 2016 and 2020 that compared the clinical equivalence of 8 weeks of telerehabilitation (at home) and centre-based pulmonary rehabilitation (hospital outpatient) in chronic respiratory disease. The aim of the present secondary analysis was to compare the incidence of exacerbations in people with chronic respiratory diseases undertaking pulmonary rehabilitation remotely at home (telerehabilitation) to people having conventional in-person group classes of centre-based pulmonary rehabilitation. We hypothesised that number of exacerbations may be lower in telerehabilitation participants who received pulmonary rehabilitation at home. An additional aim was to identify clinical characteristics associated with exacerbations during rehabilitation.

The trial (ACTRN12616000360415) methods [11] and primary analyses have been published [10]. Briefly, people were included if they had a primary diagnosis of COPD, asthma, interstitial lung disease or bronchiectasis, were aged ⩾40 years, and were able to read and speak English and provide informed consent. People were excluded if they: had attended pulmonary rehabilitation within the previous 18 months, unless they had experienced an exacerbation requiring hospitalisation since completion; were unable to complete cardiopulmonary exercise testing; experienced an emergency department presentation or hospitalisation due to brittle or unstable asthma within the previous 3 months; or had comorbidities that precluded exercise training.

All participants attended a centre for comprehensive baseline assessment and collection of demographic information including comorbidities, long-term oxygen use, previous pulmonary rehabilitation and hospitalisation history. Participants in both groups received an 8-week programme of twice-weekly supervised (aerobic and resistance) exercise training and standardised education and self-management interventions including recognising and managing exacerbations. The centre-based participants undertook

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In people with chronic respiratory disease undertaking pulmonary rehabilitation, approximately 1/3 developed an exacerbation; however, there was no difference between telerehabilitation and centre-based group settings, and no effect on programme completion https://bit.ly/4bXe2dy

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sessions at their local centre in groups of 8–16 people. Following a home visit, the telerehabilitation participants undertook sessions remotely in virtual groups of 4–6 people.

To quantify exacerbations, data corresponding to each participant's rehabilitation period were sourced from hospital medical records and the government-funded Pharmaceutical Benefits Scheme, which details all prescribed and subsidised medications including antibiotics and oral corticosteroids. An exacerbation was classified as moderate when an antibiotics and/or oral corticosteroids prescription was filled, or severe if an emergency department presentation or hospitalisation occurred. The research team were blinded to group allocation during data extraction and analyses. Data were analysed using SPSS V.28.0 (IBM). Between-group comparisons for exacerbations were compared using a Chi-squared test. Associations of clinical characteristics (including sex, history of hospitalisation, type of lung disease, 6-min walk test distance, chronic respiratory disease questionnaire dyspnoea score and time in moderate-to-vigorous physical activity) with exacerbations during pulmonary rehabilitation were tested *via* logistic regression. The number of programme sessions attended in those who did or did not experience exacerbations during pulmonary rehabilitation were compared using the Mann–Whitney U-test. Statistical significance was set at $p<0.05$.

A total of 140 participants participated in this trial (telerehabilitation n=70; centre-based rehabilitation n=70). A total of 52 participants experienced an exacerbation across both intervention groups. No statistically significant differences were observed in the number of participants with moderate exacerbations (telerehabilitation n=26 *versus* centre-based n=22; p=0.476) or severe exacerbations (telerehabilitation n=4 *versus* centre-based n=2; p=0.404), or both (telerehabilitation n=28 *versus* centre-based n=24; p=0.484). There were also no significant differences in the number of participants with filled prescriptions of antibiotics only (telerehabilitation n=17 *versus* centre-based n=15; p=0.687) or oral corticosteroids only (telerehabilitation n=4 *versus* centre-based n=7; p=0.346), or both (telerehabilitation n=10 *versus* centre-based n=5; p=0.172). Analysis comparing the number of participants who experienced an exacerbation (n=52) with those who did not (n=88) demonstrated that significantly more females than males experienced an exacerbation during their rehabilitation period (p=0.004) but no other between-group differences in clinical characteristics including programme completion and number of sessions attended (table 1). A binary logistic regression model demonstrated that females were 3.6 (95% CI 1.5–9.4) times

TABLE 1 Characteristics of participants with or without an exacerbation during the rehabilitation period

	Participants with ⩾1 exacerbation (n=52)	Participants with no exacerbation (n=88)	Between-group difference, p-value
Age, years	67 (62–73)	70 (63–73)	0.413
Male	16 (31)	49 (56)	0.004*
Diagnosis			
COPD	36 (69)	63 (72)	0.678
Bronchiectasis	8 (15)	10 (11)	
Asthma	3 (6)	9 (10)	
ILD	5 (10)	6 (7)	
Number of comorbidities	3 (2–5)	4 (2–5)	0.984
FEV_1, % predicted, mean±SD	62±4	61±3	0.728
Long-term oxygen therapy	7 (14)	5 (6)	0.117
Smoking status			
Current smoker	6 (12)	12 (14)	0.761
Ex-smoker	40 (77)	62 (71)	
Never smoker	6 (12)	13 (15)	
HADS score			
Anxiety	5 (2–10)	6 (3–10)	0.416
Depression	5 (3–7)	4 (3–8)	0.690
mMRC scale score, n (0/1/2/3/4)	1/26/15/10/0	2/34/31/16/5	0.357
Hospitalisation in previous 12 months	13 (25)	13 (15)	0.150
Previous pulmonary rehabilitation attendance	15 (29)	15 (17)	0.100
Programme completion	42 (81)	73 (82)	0.877
Number of programme sessions attended			
Telerehabilitation	13 (11–15)	14 (12–15)	0.240
Centre-based rehabilitation	15 (11–16)	15 (10–16)	0.435

Data are presented as median (interquartile range) or n (%) participants, unless otherwise stated. FEV_1: forced expiratory volume in 1 s; HADS: Hospital Anxiety and Depression Scale; ILD: interstitial lung disease; mMRC: modified Medical Research Council. *: p<0.05.

more likely to experience an exacerbation than males. Participants with a hospitalisation in the previous 12 months were 2.2 (95% CI 0.8–5.9) times more likely to experience an exacerbation (than those without hospitalisation in the previous 12 months); however, this was not statistically significant.

This secondary analysis of a randomised controlled trial demonstrated that: 1) approximately a third (37%) of people with chronic respiratory disease experienced a moderate-to-severe exacerbation during 8 weeks of pulmonary rehabilitation; 2) the incidence of exacerbation was similar between programmes delivered at home or at a centre; 3) programme completion rates were similar in people who did and did not experience an exacerbation during the programme; and 4) females were more likely to experience an exacerbation during rehabilitation.

The incidence of exacerbations was comparable to participants with COPD reporting exacerbations in 8 weeks of outpatient rehabilitation (21%) [6] or inpatient rehabilitation before and during the COVID-19 pandemic (31–54%) [12]. Although this study was completed prior to the COVID-19 pandemic, the findings provide reassurance that people with chronic respiratory disease are not more likely to experience exacerbations during rehabilitation delivered in group settings compared to remote delivery. Like previous work in COPD, albeit not in a pulmonary rehabilitation context, females were more likely to experience an exacerbation [13]. Although not statistically significant, the two-fold greater odds of exacerbations in people who experienced a hospitalisation in the previous 12 months is in line with previous estimates in COPD [14] that had measured exacerbations over a longer duration and with larger sample sizes.

Limitations of note for the current study are that it was a secondary analysis of a trial; it was not powered for analysis of exacerbations during pulmonary rehabilitation nor designed to investigate all potential risk factors and triggers associated with exacerbations (*e.g.* seasonality and indoor/outdoor air quality). We did not have ethics approval to collect retrospective data on history of hospitalisation at baseline, which may have impacted the assessed associations. However, our previous work has shown that in COPD, self-reporting of hospitalisations is reasonably accurate [15]. Whilst our definitions of exacerbations are well accepted, we did not ascertain the cause of exacerbations and cannot be entirely certain that all antibiotics or corticosteroid prescriptions were for managing exacerbations. Participants with brittle or uncontrolled asthma who had an emergency department presentation or hospitalisation in the 3 months prior to the study were excluded, which may have affected the prevalence of exacerbations in the subgroup of asthma participants.

In conclusion, this study suggests the incidence of exacerbations of chronic respiratory disease is similar during pulmonary rehabilitation delivered at home or at a centre. Females are at a greater risk of exacerbation during rehabilitation, and further work is required to elucidate the pathophysiological, biological and social determinants that underlie this sex-related difference.

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