Early versus delayed pulmonary rehabilitation: A randomized controlled trial – Can we do it?

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Introduction
Providing outpatient pulmonary rehabilitation (PR) following hospitalization for an acute exacerbation of chronic obstructive pulmonary disease (AECOPD) has been found to improve exercise capacity, quality of life and a reduction in unplanned hospital admissions and mortality.¹ These positive effects, although studied in the short term, have led to national and international guidelines supporting the provision of post-exacerbation PR (PEPR).²,³ However, uptake is poor with less than 10% of hospital discharges for AECOPD completing PEPR.⁴ We therefore considered whether it would be effective to delay PR for patients who have recently been hospitalized for their AECOPD.

Methods
We conducted a randomized controlled trial (RCT) at Glenfield Hospital, University Hospitals of Leicester, United Kingdom over a period of approximately 2 years. Ethical approval was sought and granted (08/H0406.133). Patients were referred to PR following their admission for an exacerbation of COPD and attended an outpatient assessment and were offered the study. Inclusion criteria were confirmed diagnosis of COPD prior to current admission and an increase in self-reported breathlessness on exertion. Exclusion criteria were inability to provide informed consent; acute cardiac event; and the presence of musculoskeletal, neurological and psychiatric co-morbidities that would prevent the delivery of PR. Written consent was gained and patients were randomized by the sealed envelope technique to either PEPR which occurred within 4 weeks of hospital discharge or delayed PEPR (D-PEPR) which commenced 7 weeks after a control period of no intervention. The PR intervention was identical for both groups. Outcome measures included the incremental shuttle walking test (ISWT) and the endurance shuttle walk test (ESWT). These were repeated at discharge. Health-related quality of life measures were gathered, but on analysis, there were insufficient complete data sets to enable accurate analysis so this has not been reported. PR was delivered twice weekly for 6 weeks, with each session being 2 hours. It consisted of individualized aerobic and resistance exercises and education which covered topics including chest clearance and energy conservation.

Results
Fifty-seven patients were referred to PR by a variety of healthcare professionals following an AECOPD that required a hospitalization. It was initially intended to recruit n = 120 to this study. However, recruitment was problematic throughout the study with only 57 patients referred and of those 36 patients

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were consented and assessed. Figure 1 shows the flow of eligibility, randomization and follow-up in the study. As a result of the original sample number not being met in the allocated time and lower than anticipated uptake and retention issues, the trial was terminated prematurely and was deemed a failed trial. Randomization was not equal across both arms with $n = 24$ in the early PR group and $n = 12$ in the D-PEPR group. Baseline characteristics are outlined in Table 1. Both groups were well matched for age, lung function and exercise capacity ($p > 0.05$). Previous admissions and hospitalization data were not collected.

However, consistent with the literature, we did document some important improvements in the PEPR group detailed in Table 2 which shows the mean
### Table 1. Baseline characteristics for all patients across both groups.

|                         | PEPR (n = 24; mean (SD)) | D-PEPR (n = 12; mean (SD)) |
|-------------------------|--------------------------|----------------------------|
| Age (years)             | 64.32 (7.37)             | 65.8 (7.24)                |
| FEV₁ (l)                | 1.10 (0.44)              | 1.34 (0.54)                |
| FEV₁ (% pred)           | 51.04 (20.46)            | 52.33 (17.53)              |
| FEV₁/FVC ratio          | 0.46 (12.99)             | 45.45 (9.48)               |
| ISWT (m)                | 250.80 (170.41)          | 173.33 (128.44)            |
| ESWT (s)                | 239.17 (154.64)          | 186.91 (143.86)            |

PEPR: post-exacerbation pulmonary rehabilitation; D-PEPR: delayed post-exacerbation pulmonary rehabilitation; FEV₁: forced expiratory volume in one second; FVC: forced vital capacity; ISWT: incremental shuttle walking test; ESWT: endurance shuttle walk test.

### Table 2. Mean changes with 95% CI for patients who completed pulmonary rehabilitation in both groups.

|                         | Early PR (n = 14) | D-PEPR at 7 weeks after the control period of no intervention (n = 6) | Post D-PEPR (n = 3) following completion of D-PEPR |
|-------------------------|-------------------|-----------------------------------------------------------------------|-----------------------------------------------|
| ISWT (m)                | 250.10 (92.16–407.98)* | 13.33 (−52.97 to 26.31)                                              | 40.00 (−139.37 to 59.37)                       |
| ESWT (s)                | 239.17 (154.64) | 23.20 (−259.87 to 213.47)                                            | 283.33 (−736.23 to 1302.90)                    |

CI: confidence interval; PR: pulmonary rehabilitation; D-PEPR: delayed post-exacerbation pulmonary rehabilitation; ISWT: incremental shuttle walking test; ESWT: endurance shuttle walk test

* *p < 0.05.

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**Figure 2.** Patient flow through study at time points of outcome measures.
changes after early PR in the first column, repeated outcome measures after a control period for the D-PEPR group and the post D-PEPR mean changes. Figure 2 outlines the flow of patients through the study and the time points of the outcome measures.

Statistically significant improvements were found in both walking tests for PEPR which is in keeping with other literature and no natural recovery was observed. However, conclusions were difficult to draw due to the low sample in D-PEPR.

Conclusion
In summary, there is strong evidence that demonstrates the benefits of PEPR.\(^1\) However, referral rate and uptake rate are low for PEPR and the benefits are only reaching a small number of those patients.\(^4\) In relation to this study, we found recruitment and retention of patients problematic. This may be due to the unstable nature of the condition following an exacerbation or due to patient reluctance to partake in a structured programme soon after hospitalization. Although our results suggested that those patients who attended PR sooner after an AECOPD showed better improvements than the delayed group, it is problematic to draw any firm conclusions due to the significantly small sample number.

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