2023

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10.1183/23120541.00209-2023

Lopez, P., Fitzgerald, D. B., McVeigh, J. A., Badiei, A., Muruganandan, S., Newton, R. U., . . . Peddle-McIntyre, C. J. (2023). Associations of physical activity and quality of life in parapneumonic effusion patients. ERJ Open Research, 9(5), article 00209-2023. https://doi.org/10.1183/23120541.00209-2023

# Associations of physical activity and quality of life in parapneumonic effusion patients

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Shareable abstract (@ERSpublications)
**Patients with parapneumonic pleural effusion are mostly sedentary and present poor quality of life. Increasing moderate-to-vigorous physical activity following discharge from hospital may provide meaningful improvements in quality of life.** https://bit.ly/473QCSQ

Cite this article as: Lopez P, Fitzgerald DB, McVeigh JA, *et al*. Associations of physical activity and quality of life in parapneumonic effusion patients. *ERJ Open Res* 2023; 9: 00209-2023 [DOI: 10.1183/23120541.00209-2023].



Received: 4 April 2023
Accepted: 17 July 2023

## Abstract

*Introduction* Little is known about activity behaviours and quality of life (QoL) of patients with parapneumonic pleural effusions (PPE) after hospital discharge. This study is a secondary analysis of a randomised trial (dexamethasone *versus* placebo) for hospitalised patients with PPE. We: 1) described the patients' activity behaviour patterns and QoL measured at discharge and at 30 days post-discharge; and 2) examined the association between activity behaviours and QoL scores.

*Methods* Activity behaviour (7-day accelerometry; Actigraph GT3X+) and QoL (Medical Outcomes Study Short-Form 36) were assessed. Repeated measures analysis of covariance controlling for baseline values and a series of linear regression models were undertaken.

*Results* 36 out of 53 eligible participants completed accelerometry assessments. Despite modest increases in light physical activity (+7.5%) and some domains of QoL (>2 points) from discharge to 30 days post-discharge, patients had persistently high levels of sedentary behaviour (>65% of waking wear time) and poor QoL (⩽50 out of 100 points) irrespective of treatment group (p=0.135–0.903). Increasing moderate-to-vigorous physical activity was associated with higher scores on most QoL domains (p=0.006–0.037). Linear regression indicates that a clinically important difference of 5 points in physical composite QoL score can be achieved by reallocating 16.1 min·day$^{-1}$ of sedentary time to moderate-to-vigorous physical activity.

*Conclusion* Patients with PPE had low levels of physical activity and QoL at discharge and 30 days post-discharge irrespective of treatment. Moderate-to-vigorous physical activity participation was associated with higher QoL scores. Increasing moderate-to-vigorous physical activity following discharge from the hospital may be associated with improvements in QoL.

## Introduction

Pneumonia is one of the leading causes of hospitalisation, morbidity and mortality worldwide [1, 2]. Parapneumonic pleural effusions (PPEs), which complicate up to 50% of patients with pneumonia [3], represent a significant healthcare burden and are associated with a worse prognosis [1–5]. Parapneumonic effusions typically exhibit a significant pleural inflammatory response, with all-cause mortality of pleural infections remaining unacceptably high (~15% in hospital; ~25% at 3 months) [6]. Furthermore, the

economic burden associated with managing these infections surpasses USD 100 million annually [7]. The goals of PPEs management are to eradicate the infection, alleviate symptoms and quickly return patients to their normal daily living activities.

Treating PPE involves systemic antibiotic therapy and drainage of the infected pleural fluid and often requires hospital stays. Chest pain and dyspnoea are common symptoms [8], often impacting the patient's well-being and quality of life (QoL). In addition, pre-existing comorbidity is very common in these patients [9]. Up to 40% of patients with PPE [9] are affected by various conditions such as asthma, COPD, type II diabetes and chronic kidney disease, which further impede early mobilisation and overall recovery, including physical activity. In previous studies [10, 11], patients with PPE walked a range of 926 to 1356 daily steps and spent ∼95% of their awake hours being sedentary following a median of 4 to 7 days after hospital admission. Importantly, greater mean daily steps during hospitalisation were associated with a ∼10% reduced length of hospital stay [10], while every additional 500-step increase in daily steps after discharge was associated with a ∼24% reduced 30-day mortality [11].

Advances in the field of activity behaviour quantification through accelerometry now allow assessment of patients' daily activity behaviours [10–12]. In malignant pleural effusion (MPE), it is already known that: 1) patients can adhere to accelerometry protocols [13]; 2) accelerometer-derived information such as number of steps per day reflect different performance status and survival groups [13]; and 3) accelerometry has the sensitivity to detect differences between MPE procedures [14]. However, information on activity behaviours such as sedentary, light, moderate and vigorous physical activity time and QoL is lacking in patients with PPE. Such data may help inform supportive care strategies to facilitate a faster recovery during and after hospitalisation.

Our recent multicentre randomised STOPPE trial [15, 16] demonstrated the feasibility and safety of administering intravenous dexamethasone for 48 h. However, the administration of adjunct systemic corticosteroid therapy did not have an impact on clinical parameters and outcomes, such as the need for pleural drainage, duration of hospitalisation, antibiotic therapy and QoL. In this study, we present the accelerometry assessment of participants from the STOPPE trial [15, 16]. The primary outcome was to describe sedentary and physical activity behaviour patterns and QoL in PPE patients treated with dexamethasone, or placebo, at the time of discharge and at 30 days after. Secondary outcomes were to examine the association of physical activity behaviour with QoL assessment scores in these patients. Because differences were not identified in any outcomes between intravenous dexamethasone and placebo in the main trial [15, 16], our hypotheses are that patients receiving intravenous dexamethasone would not present better activity behaviour or QoL compared to placebo. Our secondary hypothesis is that physical activity components would be associated with higher QoL levels in PPE patients.

## Methods

### *Settings and participants*

The present study is a follow-up analysis using data from our published multicentre randomised trial in adults with PPE (STOPPE trial, ACTRN12618000947202) [15, 16]. Participants recruited at the lead site (Sir Charles Gairdner Hospital, Western Australia) were offered accelerometry assessment. The study was approved by the Human Research and Ethics Committee of Sir Charles Gairdner and Osborne Park Healthcare Group (RGS840). All patients provided written informed consent.

### *Procedures*

Details of inclusion criteria and recruitment have been previously reported [15, 16]. Briefly, patients hospitalised for community-acquired pneumonia and with evidence of a pleural effusion were randomly assigned (2:1) to the dexamethasone or placebo group, with minimisation for Chalmers predictive score, known diabetes mellitus and size of the pleural effusion, to ensure equal representation in each group. Participants received 4 mg of intravenous dexamethasone, or saline (placebo), every 12 h for 48 h to a total of four doses. Participants were asked to complete a QoL questionnaire at discharge and 30 days post discharge and asked to wear the accelerometry device on their hip for 7 consecutive days following hospital discharge (*i.e.* days 1 to 7 following discharge) and following their 30-day post-discharge assessment (*i.e.* days ∼30 to 36 post-discharge). Patients were followed up on alternate days until hospital discharge and at 30 days post-discharge. Demographic and clinical data such as age, sex, smoking status, Eastern Cooperative Oncology Group (ECOG) performance status, comorbidities and primary malignancy were collected by self-report and medical records, respectively.

### Outcome measures

Device-assessed activity behaviours were measured by Actigraph GT3X+ accelerometers (Actigraph, Pensacola, FL, USA) and the data were processed in SAS (version 9.4, Cary, NC, USA) using an established algorithm [17]. Accelerometers were programmed to record raw data at a frequency of 30 Hz. Using 60-s epoch data of counts of the vertical axis, the proportion of time spent in sedentary behaviour, light physical activity and moderate-to-vigorous physical activity were determined as <100 counts·min$^{-1}$, ⩾100 and <1951 counts·min$^{-1}$, and ⩾1951 counts·min$^{-1}$, respectively [18, 19]. Daily steps were also recorded. Patients with at least 2 valid days of 8 h of waking wear time were included for analysis [20, 21]. Data assessors were blinded to group assignments. All variables were calculated per day and then averaged across all valid days for each patient. Data are also presented as per cent of waking wear time (*i.e.* relative sedentary time, relative light physical activity, relative moderate-to-vigorous physical activity). While there is no established minimum clinically important difference (MCID) for daily steps in patients with PPE, in drawing on other clinical populations, a MCID of 600–1000 steps has been reported in patients with COPD [22].

QoL was assessed using the 36-Item Short-Form Survey (SF-36) version 2 [23], which includes physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional and mental health domains [23], and a physical (PCS) and a mental (MCS) composite score. SF-36 scores range from 0 to 100, with higher scores representing better QoL. The MCID for components of the SF-36 PCS and the SF-36 MCS has been reported as 5 points in a range of populations [24].

### Statistical analysis

Data were analysed using SPSS Statistics (v.27; IBM Corp., Armonk, NY, USA). Normality of the distribution was assessed using Kolmogorov–Smirnov test. Data are presented as mean±SD or median (IQR) as appropriate. Changes over the follow-up period were assessed using two-way (group × time) repeated measures analysis of covariance (ANCOVA) controlling for baseline values to account for potential differences between the dexamethasone and placebo groups over time (discharge *versus* 30-day post-discharge). Bonferroni *post hoc* tests were performed when the main effect for time was significant. Data not normally distributed were log transformed (ln) for analysis. Statistical significance was set at an $\alpha$ of 0.05.

Single-activity, partition and isotemporal substitution models were undertaken, as previously described [25–28], using linear regression to estimate the association of sedentary, physical activity and total wear time with the SF-36 domains with the physical and mental composite scores at 30 days following discharge. Accelerometer variables were scaled to 10-min increments to standardise each activity and because of its importance for health outcome improvement [29, 30]. In the single-activity model, each accelerometer variable was assessed individually without accounting for the other activities to examine the association with SF-36 domains. For the partition model, the accelerometer variables were included in the model to examine their independent association with SF-36 domains. The isotemporal substitution model was applied to examine the impact of reallocating 10 min of sedentary time to 10 min of either light or moderate-to-vigorous physical activity. In this model, light and moderate-to-vigorous physical activity time and total time were held constant, while the variable being replaced (*i.e.* sedentary time) was not included. All the models were adjusted by age (continuous variable) and group (*i.e.* dexamethasone, placebo). Only complete cases were included in the analyses. Results are presented as unstandardised coefficients (B) and standard errors (SE). A comprehensive description of the models can be found in the supplementary material.

## Results

### Sample characteristics

Of the 53 participants enrolled in the lead site, 36 participants (47.2% male; age 64.6±16.6 years) completed at least 2 days of assessment (mean±SD 6.3±1.4 days) and were included for further analyses (figure 1). Most participants (80.6%) had an ECOG performance status of 0. Comorbidities, especially cardiac (63.9%) and pulmonary (44.4%) diseases, were common (table 1).

### Sedentary and physical activity behaviour and QoL at discharge and 30 days

The median waking wear time for the entire sample over 7 days following discharge and at 30 days post-discharge were 14.4 (IQR 13.1–16.0) hours and 13.9 (IQR 12.6–15.3) hours, respectively, representing a median difference of 35.6 (IQR 30.3–91.3) min·day$^{-1}$ (p=0.030). No significant differences in waking wear time were observed between groups (table 2).

No significant group × time interactions were observed for relative sedentary time (p=0.307), relative light physical activity time (p=0.370) and relative moderate-to-vigorous physical activity time (p=0.205)

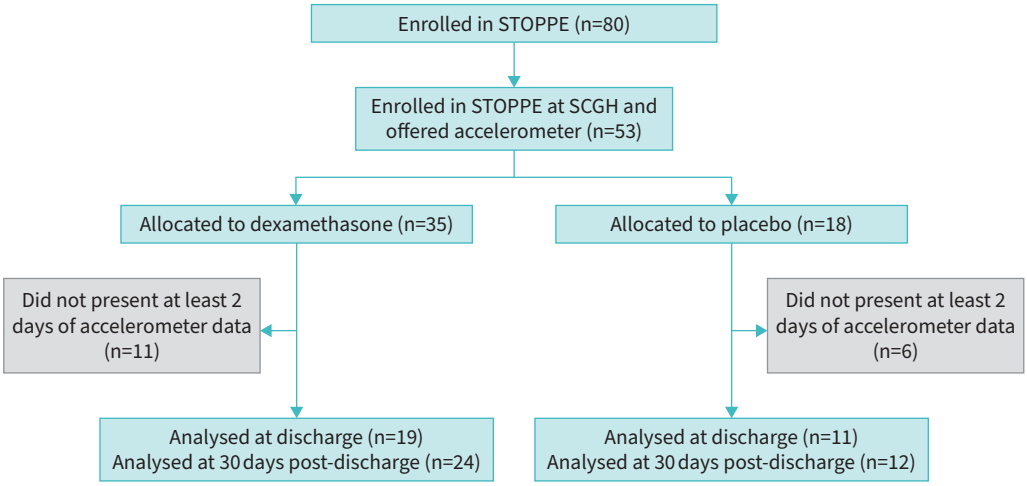


FIGURE 1 Participants' flow through the trial assessments. SCGH: Sir Charles Gairdner Hospital.

(table 2). At discharge, participants spent 11.0 (IQR 9.7–11.4) hours (73.6±10.1%) of waking wear time in sedentary behaviour, 3.9±1.9 hours (25.5±9.9%) in light physical activity and only 3.4 (IQR 1.3–9.1) min (0.4%, IQR 0.2%–0.8%) in moderate-to-vigorous physical activity. Physical activity levels increased between discharge and the 30-day assessment. As a result, sedentary time was reduced by 8.2% to 65.4±10.3% of the waking wear time while light physical activity was increased by 7.5% to 33.0±10.0% of waking wear time ($p<0.001$). No significant changes were observed in moderate-to-vigorous physical activity relative to waking wear time ($p=0.179$). The mean steps walked per day rose from 6368±3840 to

TABLE 1 Baseline demographic and clinical characteristics

| | Total | Dexamethasone | Placebo |
|---|---|---|---|
| **Participants n** | 36 | 24 | 12 |
| **Age years, mean±SD** | 64.6±16.6 | 63.5±18.5 | 66.8±12.6 |
| **Sex, male, n (%)** | 17 (47.2) | 11 (45.8) | 6 (50.0) |
| **Smoking status, n (%)** | | | |
| Current | 2 (5.6) | 2 (8.3) | 0 (0.0) |
| Former | 17 (47.2) | 9 (37.5) | 8 (66.7) |
| Nonsmoker | 17 (47.2) | 13 (54.2) | 4 (33.3) |
| **ECOG performance status scale, n (%)** | | | |
| 0 | 29 (80.6) | 20 (83.3) | 9 (75.0) |
| 1 | 4 (11.1) | 2 (8.3) | 2 (16.7) |
| 2 | 3 (8.3) | 2 (8.3) | 1 (8.3) |
| **Comorbidities, n (%)** | | | |
| Pulmonary[#] | 16 (44.4) | 13 (54.2) | 3 (25.0) |
| Cardiac[¶] | 23 (63.9) | 16 (66.7) | 7 (58.3) |
| Renal | 3 (8.3) | 2 (8.3) | 1 (8.3) |
| Diabetes mellitus | 8 (22.2) | 4 (16.7) | 4 (33.3) |
| Liver cirrhosis | 1 (2.8) | 0 (0.0) | 1 (8.3) |
| Depression/anxiety | 11 (30.6) | 7 (29.2) | 4 (33.3) |
| **Type of primary malignancy, n (%)** | | | |
| Breast | 3 (8.3) | 1 (4.2) | 2 (16.7) |
| Skin | 2 (5.6) | 1 (4.2) | 1 (8.3) |
| Lymphoma | 1 (2.8) | 1 (4.2) | 0 (0.0) |
| Prostate | 1 (2.8) | 0 (0.0) | 1 (8.3) |
| Uterine | 1 (2.8) | 0 (0.0) | 1 (8.3) |

ECOG: Eastern Cooperative Oncology Group. [#]: COPD, asthma, interstitial lung disease, pulmonary embolism, pulmonary hypertension and others; [¶]: hypertension, ischaemic heart disease, congestive cardiac failure, atrial fibrillation, pericardial effusion and others.

**TABLE 2** Sedentary and physical activity behaviour at discharge and 30 days following discharge from hospital

| Outcome | Discharge | 30 days | Time | Group×Time |
|---|---|---|---|---|
| **Steps per day** | | | | |
| Both groups | 6368±3840 | 8345±3727¶ | F=16.9 | F=0.3 |
| Dexamethasone | 6524±4210 | 8286±4167 | p<0.001 | p=0.619 |
| Placebo | 6099±3276 | 8448±3003 | | |
| **Waking wear time per day, h#** | | | | |
| Both groups | 14.4 (13.1–16.0) | 13.9 (12.6–15.3)¶ | F=13.9 | F=1.1 |
| Dexamethasone | 14.5 (13.1–16.0) | 14.1 (12.7–15.4) | p<0.001 | p=0.294 |
| Placebo | 14.0 (12.6–18.0) | 13.5 (12.1–13.9) | | |
| **Sedentary time per day, h#** | | | | |
| Both groups | 11.0 (9.7–11.4) | 9.1 (7.8–10.4) | F=1.7 | F=2.4 |
| Dexamethasone | 10.8 (9.4–11.4) | 9.3 (7.9–10.6) | p=0.208 | p=0.135 |
| Placebo | 11.0 (10.5–11.2) | 8.3 (7.5–10.1) | | |
| **Light physical activity time per day, h** | | | | |
| Both groups | 3.9±1.9 | 4.6±1.5¶ | F=26.6 | F=0.0 |
| Dexamethasone | 3.8±1.8 | 4.5±1.6 | p<0.001 | p=0.903 |
| Placebo | 4.0±2.1 | 4.7±1.4 | | |
| **Moderate-to-vigorous physical activity time per day, min#** | | | | |
| Both groups | 3.4 (1.3–9.1) | 6.1 (1.4–24.1) | F=1.6 | F=0.8 |
| Dexamethasone | 2.6 (0.8–11.8) | 5.5 (1.3–21.6) | p=0.218 | p=0.388 |
| Placebo | 3.9 (1.8–8.7) | 6.8 (1.8–29.0) | | |
| **Relative sedentary time per day, %** | | | | |
| Both groups | 73.6±10.1 | 65.4±10.3 | F=3.5 | F=1.1 |
| Dexamethasone | 73.4±11.1 | 66.5±10.8 | p=0.072 | p=0.307 |
| Placebo | 73.8±8.6 | 63.3±9.5 | | |
| **Relative light physical activity time per day, %** | | | | |
| Both groups | 25.5±9.9 | 33.0±10.0 | F=19.2 | F=0.8 |
| Dexamethasone | 25.5±10.7 | 31.9±10.2 | p<0.001 | p=0.370 |
| Placebo | 25.6±8.8 | 34.9±9.8 | | |
| **Relative moderate-to-vigorous physical activity time per day, %#** | | | | |
| Both groups | 0.4 (0.2–0.8) | 0.7 (0.2–2.7) | F=1.9 | F=1.7 |
| Dexamethasone | 0.3 (0.1–1.3) | 0.7 (0.2–2.4) | p=0.179 | p=0.205 |
| Placebo | 0.5 (0.2–0.8) | 0.8 (0.3–3.8) | | |

Data are presented as mean±SD, unless otherwise indicated. #: statistical analysis based on log transformed data and presented as median (IQR); ¶: p-value <0.05 derived from pairwise comparison between discharge and 30 days following discharge from hospital.

8345±3727, representing a mean increase of 31.0% or 2041 steps per day (95% CI 1070–3012 steps; p<0.001).

35 participants completed the SF-36 questionnaires at both time points (table 3). No significant group × time interactions were observed for SF-36 domains. A significant improvement in bodily pain from 38.2 (IQR 30.6–46.7) to 46.7 (IQR 38.2–62.0) points (p<0.001) and physical composite score from 35.6 (IQR 28.8–41.6) to 44.2 (IQR 32.9–50.0) points (p=0.003) was observed from discharge to 30-day assessment in the overall cohort.

### *Single-activity, partition and isotemporal substitution model*

Results from single-activity and partition models were similar and are presented in table 4. In summary, 10 min of moderate-to-vigorous physical activity per day was associated with higher scores of physical functioning, role physical, general health, social functioning, role emotional, mental health and physical composite scores, with scores ranging from 2.1 to 4.3 points (p=<0.001–0.034). No consistent relationship was observed between QoL domains and 10 min of sedentary or light physical activity.

Results from the isotemporal substitution model are presented in table 5. Based on this hypothetical model, if an individual replaces 10 min of sedentary time with moderate-to-vigorous physical activity, this would result in higher scores on physical functioning, role physical, general health, social functioning, mental health and physical composite score at 30 days post-discharge, with values ranging from 2.2 to 3.8 points (p=0.006–0.037). To meet a MCID of 5 points for SF-36 physical composite score, adults with PPE would need to reallocate 16.1 min of sedentary time per day to moderate-to-vigorous physical activity. No

**TABLE 3** SF-36 domains at discharge and 30 days following discharge from hospital

| Outcome | Discharge | 30 days | Time | Group×Time |
|---|---|---|---|---|
| **SF-36: Physical functioning**[#] | | | | |
| Both groups | 36.5 (28.8–48.9) | 46.1 (29.8–51.8) | F=7.9 | F=0.1 |
| Dexamethasone | 36.5 (28.8–48.0) | 38.4 (30.8–53.7) | p=0.008 | p=0.723 |
| Placebo | 39.4 (26.0–52.8) | 46.1 (28.8–49.9) | | |
| **SF-36: Role physical** | | | | |
| Both groups | 35.2±11.5 | 36.6±9.8 | F=34.2 | F=0.2 |
| Dexamethasone | 34.7±11.2 | 36.1±10.2 | p<0.001 | p=0.674 |
| Placebo | 36.2±12.6 | 37.8±9.1 | | |
| **SF-36: Bodily pain**[#] | | | | |
| Both groups | 38.2 (30.6–46.7) | 46.7 (38.2–62.0)[¶] | F=26.1 | F=0.2 |
| Dexamethasone | 38.2 (30.6–46.7) | 46.7 (38.2–55.6) | p<0.001 | p=0.631 |
| Placebo | 32.4 (25.3–47.9) | 50.7 (37.2–62.0) | | |
| **SF-36: General health** | | | | |
| Both groups | 42.5±9.7 | 44.4±10.1 | F=9.2 | F=1.0 |
| Dexamethasone | 40.5±9.3 | 42.3±10.1 | p=0.004 | p=0.335 |
| Placebo | 46.8±9.5 | 48.9±8.7 | | |
| **SF-36: Vitality** | | | | |
| Both groups | 41.8±10.8 | 42.9±10.3 | F=13.7 | F=1.6 |
| Dexamethasone | 40.4±10.3 | 43.3±11.1 | p<0.001 | p=0.210 |
| Placebo | 45.0±11.7 | 42.0±8.3 | | |
| **SF-36: Social functioning**[#] | | | | |
| Both groups | 37.3 (27.3–47.3) | 42.3 (27.3–49.8) | F=15.9 | F=0.1 |
| Dexamethasone | 32.3 (27.3–42.3) | 37.3 (27.3–52.3) | p<0.001 | p=0.742 |
| Placebo | 42.3 (27.3–53.6) | 44.8 (29.8–48.6) | | |
| **SF-36: Role emotional**[#] | | | | |
| Both groups | 45.7 (26.6–56.2) | 45.7 (31.8–52.7) | F=6.9 | F=0.3 |
| Dexamethasone | 42.2 (24.8–56.2) | 45.7 (31.8–56.2) | p=0.012 | p=0.585 |
| Placebo | 45.7 (27.4–56.2) | 44.0 (27.4–50.1) | | |
| **SF-36: Mental health** | | | | |
| Both groups | 46.5±10.7 | 47.7±9.9 | F=17.9 | F=1.7 |
| Dexamethasone | 45.9±10.2 | 46.3±9.6 | p<0.001 | p=0.195 |
| Placebo | 47.7±12.1 | 50.7±10.4 | | |
| **SF-36: Physical composite score**[#] | | | | |
| Both groups | 35.6 (28.8–41.6) | 44.2 (32.9–50.0)[¶] | F=10.3 | F=0.4 |
| Dexamethasone | 35.6 (30.5–39.9) | 40.3 (32.8–49.3) | p=0.003 | p=0.530 |
| Placebo | 35.1 (28.4–46.3) | 46.7 (33.0–50.5) | | |
| **SF-36: Mental composite score** | | | | |
| Both groups | 44.8±11.9 | 44.6±10.8 | F=11.6 | F=0.3 |
| Dexamethasone | 43.7±11.6 | 44.4±10.9 | p=0.001 | p=0.614 |
| Placebo | 47.2±12.6 | 45.2±11.0 | | |

Data are presented as mean±SD, unless otherwise indicated. SF-36: Medical Outcomes Study Short-Form 36. [#]: statistical analysis based on log transformed data and presented as median (IQR); [¶]: p-value <0.05 derived from pairwise comparison between discharge and 30 days following discharge from hospital.

significant associations of SF-36 domains were observed when reallocating 10 min of sedentary time to light physical activity (p=0.347–0.828).

## Discussion

This sub-analysis of the STOPPE trial presented important data showing a low level of physical activity and QoL scores in patients with PPE both at the time of hospital discharge and after 30 days, despite some interval improvement. Dexamethasone did not improve these parameters. Although a significant improvement was observed in light physical activity time, we did not observe increases in moderate-to-vigorous physical activity. Exploratory modelling suggested that significant improvements in QoL scores may be hypothetically achievable if patients spend ∼16 min a day in moderate-to-vigorous physical activity instead of being sedentary. Thus, we highlight a neglected area in the management of PPE and the need to understand the reasons underlying the poor physical activity levels and QoL in order to develop therapeutic interventions.

**TABLE 4** Associations of 10 min of sedentary time, light physical activity, moderate-to-vigorous physical activity and total time with SF-36 domains and physical and mental composite scores in the single-activity and partition models in adults with pneumonia-related pleural effusion at 30 days following discharge (n=36)

| Variables | Sedentary time | | Light physical activity | | Moderate-to-vigorous physical activity | | Total time | |
|---|---|---|---|---|---|---|---|---|
| | B±SE | p-value | B±SE | p-value | B±SE | p-value | B±SE | p-value |
| **Single-activity model** | | | | | | | | |
| SF-36: Physical functioning | −0.1±0.2 | 0.620 | 0.4±0.2 | 0.064 | 4.3±1.2 | **<0.001** | 0.2±0.2 | 0.162 |
| SF-36: Role physical | −0.1±0.1 | 0.471 | 0.1±0.2 | 0.406 | 2.5±1.0 | **0.019** | 0.0±0.1 | 0.763 |
| SF-36: Bodily pain | 0.0±0.2 | 0.963 | −0.0±0.2 | 0.921 | 2.4±1.4 | 0.088 | 0.0±0.2 | 0.920 |
| SF-36: General health | −0.2±0.2 | 0.226 | 0.2±0.2 | 0.222 | 3.0±1.1 | **0.011** | 0.0±0.2 | 0.916 |
| SF-36: Vitality | −0.1±0.2 | 0.637 | 0.3±0.2 | 0.117 | 2.5±1.1 | **0.032** | 0.2±0.2 | 0.282 |
| SF-36: Social functioning | −0.2±0.2 | 0.183 | 0.1±0.2 | 0.522 | 3.2±1.3 | **0.022** | −0.1±0.2 | 0.611 |
| SF-36: Role emotional | −0.3±0.2 | 0.122 | 0.2±0.2 | 0.455 | 2.3±1.3 | 0.083 | −0.1±0.2 | 0.530 |
| SF-36: Mental health | −0.1±0.1 | 0.554 | 0.3±0.2 | 0.097 | 2.6±1.0 | **0.012** | 0.2±0.1 | 0.274 |
| SF-36: Physical composite score | −0.1±0.2 | 0.764 | 0.2±0.2 | 0.354 | 3.2±1.2 | **0.011** | 0.1±0.2 | 0.455 |
| SF-36: Mental composite score | −0.2±0.2 | 0.206 | 0.2±0.2 | 0.317 | 2.1±1.2 | 0.084 | −0.0±0.2 | 0.863 |
| **Partition model** | | | | | | | | |
| SF-36: Physical functioning | 0.1±0.2 | 0.737 | 0.3±0.2 | 0.237 | 3.8±1.3 | **0.005** | - | - |
| SF-36: Role physical | −0.1±0.2 | 0.656 | 0.0±0.2 | 0.999 | 2.5±1.1 | **0.033** | - | - |
| SF-36: Bodily pain | −0.0±0.2 | 0.990 | −0.1±0.2 | 0.574 | 2.6±1.5 | 0.079 | - | - |
| SF-36: General health | −0.1±0.2 | 0.403 | 0.0±0.2 | 0.857 | 2.9±1.2 | **0.023** | - | - |
| SF-36: Vitality | 0.0±0.2 | 0.837 | 0.2±0.2 | 0.305 | 2.2±1.2 | 0.080 | - | - |
| SF-36: Social functioning | −0.2±0.2 | 0.213 | −0.1±0.2 | 0.606 | 3.2±1.4 | **0.029** | - | - |
| SF-36: Role emotional | −0.3±0.2 | 0.166 | −0.1±0.2 | 0.743 | 2.2±1.4 | 0.110 | - | - |
| SF-36: Mental health | 0.0±0.1 | 0.911 | 0.2±0.2 | 0.313 | 2.2±1.0 | **0.034** | - | - |
| SF-36: Physical composite score | 0.0±0.2 | 0.927 | 0.1±0.2 | 0.790 | 3.2±1.3 | **0.020** | - | - |
| SF-36: Mental composite score | −0.2±0.2 | 0.343 | 0.0±0.2 | 0.920 | 2.0±1.3 | 0.135 | - | - |

p-values given in bold are statistically significant. SF-36: Medical Outcomes Study Short-Form 36; B: non-standardised coefficient; SE: standard error.

Patients with pleural infection are often elderly, have high symptom burden, significant morbidity, and require lengthy hospitalisations for systemic antibiotics and invasive drainage procedures (and/or surgery) [9]. These, coupled with high incidences of baseline cardiopulmonary comorbidity, could result in deconditioning and poor physical activity. Over the following 30 days, light physical activity levels were modestly improved, and any increase in moderate-to-vigorous physical activity observed was trivial in our

**TABLE 5** Association between replacing 10 min of sedentary time and either light physical activity or moderate-to-vigorous physical activity on SF-36 domains using the isotemporal substitution model in adults with pneumonia-related pleural effusion at 30 days following discharge (n=36)

| Variables | Sedentary time | | Light physical activity | | Moderate-to-vigorous physical activity | | Total time | |
|---|---|---|---|---|---|---|---|---|
| | B±SE | p-value | B±SE | p-value | B±SE | p-value | B±SE | p-value |
| **Isotemporal model** | | | | | | | | |
| SF-36: Physical functioning | - | - | 0.2±0.2 | 0.347 | 3.8±1.3 | **0.006** | 0.1±0.2 | 0.762 |
| SF-36: Role physical | - | - | 0.1±0.2 | 0.725 | 2.5±1.1 | **0.031** | −0.1±0.2 | 0.677 |
| SF-36: Bodily pain | - | - | -0.1±0.2 | 0.604 | 2.7±1.5 | 0.079 | −0.0±0.2 | 0.909 |
| SF-36: General health | - | - | 0.2±0.2 | 0.377 | 3.0±1.2 | **0.018** | −0.2±0.2 | 0.376 |
| SF-36: Vitality | - | - | 0.2±0.2 | 0.379 | 2.1±1.2 | 0.088 | 0.0±0.2 | 0.853 |
| SF-36: Social functioning | - | - | 0.1±0.2 | 0.597 | 3.5±1.4 | **0.020** | −0.3±0.2 | 0.195 |
| SF-36: Role emotional | - | - | 0.2±0.2 | 0.423 | 2.5±1.4 | 0.078 | −0.3±0.2 | 0.175 |
| SF-36: Mental health | - | - | 0.2±0.2 | 0.353 | 2.2±1.0 | **0.037** | 0.0±0.1 | 0.911 |
| SF-36: Physical composite score | - | - | 0.1±0.2 | 0.828 | 3.1±1.3 | **0.022** | 0.0±0.1 | 0.973 |
| SF-36: Mental composite score | - | - | 0.2±0.2 | 0.382 | 2.1±1.3 | 0.108 | −0.2±0.2 | 0.348 |

p-values given in bold are statistically significant. SF-36: Medical Outcomes Study Short-Form 36; B: non-standardised coefficient; SE: standard error.

cohort. Similar results have been reported in patients with acute exacerbations of COPD following hospitalisation, where time spent in moderate physical activity did not improve between week 1 and week 6 following discharge from hospital [31]. Although information on MCID does not exist for patients with PPE, increases in daily number of steps (+2041 steps) were above the MCID of 600–1000 steps observed in patients with COPD [22]. We observed that moderate-to-vigorous physical activity time was well below that observed in older adults (~3 min·day$^{-1}$ *versus* 26–52 min·day$^{-1}$ [32, 33]) and those levels reported in patients following hospitalisations for acute exacerbations of COPD (32–35 min·day$^{-1}$) [31], and ultimately well below recommended levels of physical activity (150 min·week$^{-1}$) [34]. Not surprisingly, we found that QoL scores, specifically the SF-36 PCS, was low at discharge from the hospital, with values substantially below normative values in older adults without the disease (46 to 49 points [35–37]). Despite improvements above the MCID of 5 points in SF-36 PCS, values remained below normative values [35–37] at 30 days.

The causes of the insufficient moderate-to-vigorous physical activity in patients with PPE are likely multi-factorial. Slow recovery from respiratory limitations (*e.g.* hypoxaemia) because of the pneumonia and PPE [38], chest pain from the infection or drainage interventions [8], deconditioning from long hospitalisation [39], low mood and exacerbations of underlying cardiopulmonary comorbidities may all contribute [40]. Potentially, we also speculate that psychological elements, such as the misconception of a need for bedrest and/or fear of "over-doing" activities after a major illness, may be important.

The clinical impact of the physical activity profile is an interesting and important area to explore in patients with parapneumonic effusion. We found that low levels of moderate-to-vigorous rather than light physical activity correlated with low QoL scores. Our finding concurs with previous studies in adults [41, 42] that indicates a significant correlation between higher moderate-to-vigorous physical activity and better QoL scores. It is expected that hospitalised patients will present lower levels of physical activity and increase their levels following discharge from hospital [43], although not substantially (~8%) as we observed in our cohort. Engaging in moderate-to-vigorous physical activity rather than light physical activity is still important to overcome hospitalisation's detrimental effects [44] given several benefits in cardiometabolic health [45–47], independent living [48] and cognition [49], leading to an enhanced QoL. This is an interesting finding in patients with PPE as it supports that interventions targeting physical activity levels could enhance QoL in patients with PPE. However, additional intervention studies are required to determine if this relationship is causal.

Our hypothesis-generating modelling suggested an interesting scenario – that reallocating ~16 min·day$^{-1}$ of sedentary time to moderate-to-vigorous physical activity could be associated with meaningful improvements in QoL. While these data indicate a relationship, it does not imply causation of poor QoL. Nonetheless, other studies have successfully reallocated 10 to 30 min of sedentary time to moderate-to-vigorous activity and improved physical function performance, metabolic and cardiovascular health outcomes in a variety of clinical populations (*e.g.* cancer and stroke) [45–47]. Whether such intervention is feasible and will benefit PPE patients deserves further investigations.

A previous meta-analysis comprising more than one million participants showed that regular physical activity was associated with a ~20% reduced risk of pneumonia and ~35% reduced risk of pneumonia-related mortality [50]. However, changing physical activity behaviour is challenging. Strategies comprising time-efficient workouts (*i.e.* short bouts of physical activity) may be more tolerable for patients with several comorbidities or following discharge from hospital. Even several bouts of <1 min of moderate-to-vigorous exercise were found to be feasible, well-tolerated and time-efficient to break prolonged sedentary activities and improve cardiorespiratory fitness and metabolic health in healthy adults [51, 52]. Vigorous-intensity physical activity (or vigorous intermittent lifestyle physical activity) [53], such as suggesting the patient taking the stairs on a normal day, may offer a promising opportunity to increase moderate-to-vigorous physical activity in this group of patients.

Our study has limitations. First, PPE patients present with different underlying causes (*i.e.* bacterial, viral, fungal), clinical presentation (*i.e.* age, immune status, symptoms) and radiographic findings (*i.e.* small localised *versus* large multiloculated), and our findings require confirmation in larger cohorts. Second, our observational data preclude determining the causality of physical activity behaviours on measures of QoL, which will require an intervention study. Third, we utilised the SF-36, a set of generic quality-of-life measures, rather than a disease-specific questionnaire. Although specific QoL questionnaires do not exist for pleural effusion, the SF-36 has been utilised in previous pneumonia studies [54, 55] and may be valuable to capture aspects of QoL in this population. Fourth, our data were limited to patients' activity

behaviour at 30 days post-discharge. The long-term follow-up of physical activity levels and QoL in this population will be informative to design future intervention strategies for promoting exercise.

In summary, this is the first report on poor physical activity levels and QoL scores in pneumonia patients with pleural effusion, and the abnormalities persisting following discharge from the hospital. From this research we provide a platform for urgent investigation of this important but neglected aspect of post-pneumonia care. Uncovering the drivers for the poor physical activity levels to design therapeutic interventions to increase especially moderate-to-vigorous activities warrants further research.

Provenance: Submitted article, peer reviewed.

Acknowledgements: The authors thank Emily Jeffery (School of Population Health, Curtin University, Perth, WA, Australia) for assistance with accelerometer data assessment.

This study is registered at www.anzctr.org.au with identifier number ACTRN12618000947202. Data used will be made available upon reasonable request to the corresponding author.

The study was approved by the Human Research and Ethics Committee of Sir Charles Gairdner and Osborne Park Health Care Group (RGS840).

Conflict of interest: All authors have nothing to disclose.

Support statement: The STOPPE trial has received support from Sir Charles Gairdner Research Advisory Committee project grants and Northern Health Foundation. The funding body was not involved in the study design, collection, analysis, and interpretation of data, writing of the report or the decision to submit for publication.

## References

1 File TM. Community-acquired pneumonia. *Lancet* 2003; 362: 1991–2001.
2 Musher DM, Thorner AR. Community-acquired pneumonia. *N Engl J Med* 2014; 371: 1619–1628.
3 Dean NC, Griffith PP, Sorensen JS, *et al.* Pleural effusions at first ED encounter predict worse clinical outcomes in patients with pneumonia. *Chest* 2016; 149: 1509–1515.
4 Taryle DA, Potts DE, Sahn SA. The incidence and clinical correlates of parapneumonic effusions in pneumococcal pneumonia. *Chest* 1978; 74: 170–173.
5 Falguera M, Carratalà J, Bielsa S, *et al.* Predictive factors, microbiology and outcome of patients with parapneumonic effusion. *Eur Respir J* 2011; 38: 1173–1179.
6 Brims F, Popowicz N, Rosenstengel A, *et al.* Bacteriology and clinical outcomes of patients with culture-positive pleural infection in Western Australia: a 6-year analysis. *Respirology* 2019; 24: 171–178.
7 Gupta I, Eid SM, Gillaspie EA, *et al.* Epidemiologic trends in pleural infection. A nationwide analysis. *Ann Am Thorac Soc* 2021; 18: 452–459.
8 Light RW, Lee YG. Textbook of Pleural Diseases. 2nd Edn. Boca Raton, CRC Press, 2008.
9 Cargill TN, Hassan M, Corcoran JP, *et al.* A systematic review of comorbidities and outcomes of adult patients with pleural infection. *Eur Respir J* 2019; 54: 1900541.
10 Rice H, Hill K, Fowler R, *et al.* Reduced step count and clinical frailty in hospitalized adults with community-acquired pneumonia. *Respir Care* 2020; 65: 455–463.
11 Ryrsø CK, Dungu AM, Hegelund MH, *et al.* Physical inactivity and sedentarism during and after admission with community-acquired pneumonia and the risk of readmission and mortality: a prospective cohort study. *J Clin Med* 2022; 11: 5923.
12 Woo H, Aoki H, Kataoka H, *et al.* Early walking time is associated with recovery of activities of daily living during hospitalization in older patients with community-acquired pneumonia: a single-center prospective study. *Geriatr Gerontol Int* 2021; 21: 1099–1104.
13 Jeffery E, Lee YG, McVeigh J, *et al.* Feasibility of objectively measured physical activity and sedentary behavior in patients with malignant pleural effusion. *Support Care Cancer* 2017; 25: 3133–3141.
14 Peddle-McIntyre CJ, Muruganandan S, McVeigh J, *et al.* Device assessed activity behaviours in patients with indwelling pleural catheter: a sub-study of the Australasian Malignant PLeural Effusion (AMPLE)-2 randomized trial. *Respirology* 2023; 28: 561–570.
15 Fitzgerald DB, Waterer GW, Read CA, *et al.* Steroid therapy and outcome of parapneumonic pleural effusions (STOPPE): study protocol for a multicenter, double-blinded, placebo-controlled randomized clinical trial. *Medicine (Baltimore)* 2019; 98: e17397.
16 Fitzgerald DB, Waterer GW, Budgeon C, *et al.* Steroid therapy and outcome of parapneumonic pleural effusions (STOPPE): a pilot randomized clinical trial. *Am J Respir Crit Care Med* 2022; 205: 1093–1101.

17 McVeigh JA, Winkler EA, Healy GN, *et al.* Validity of an automated algorithm to identify waking and in-bed wear time in hip-worn accelerometer data collected with a 24 h wear protocol in young adults. *Physiol Meas* 2016; 37: 1636–1652.
18 Freedson PS, Melanson E, Sirard J. Calibration of the Computer Science and Applications, Inc. accelerometer. *Med Sci Sports Exerc* 1998; 30: 777–781.
19 Matthews CE, Chen KY, Freedson PS, *et al.* Amount of time spent in sedentary behaviors in the United States, 2003-2004. *Am J Epidemiol* 2008; 167: 875–881.
20 Evenson KR, Wen F, Metzger JS, *et al.* Physical activity and sedentary behavior patterns using accelerometry from a national sample of United States adults. *Int J Behav Nutr Phys Act* 2015; 12: 20.
21 Demeyer H, Mohan D, Burtin C, *et al.* Objectively measured physical activity in patients with COPD: recommendations from an international task force on physical activity. *Chronic Obstr Pulm Dis* 2021; 8: 528–550.
22 Demeyer H, Burtin C, Hornikx M, *et al.* The minimal important difference in physical activity in patients with COPD. *PLoS One* 2016; 11: e0154587.
23 Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care* 1992; 30: 473–483.
24 Samsa G, Edelman D, Rothman ML, *et al.* Determining clinically important differences in health status measures: a general approach with illustration to the Health Utilities Index Mark II. *Pharmacoeconomics* 1999; 15: 141–155.
25 Mekary RA, Willett WC, Hu FB, *et al.* Isotemporal substitution paradigm for physical activity epidemiology and weight change. *Am J Epidemiol* 2009; 170: 519–527.
26 van Roekel EH, Bours MJ, Breedveld-Peters JJ, *et al.* Modeling how substitution of sedentary behavior with standing or physical activity is associated with health-related quality of life in colorectal cancer survivors. *Cancer Causes Control* 2016; 27: 513–525.
27 Welch WA, Ehlers D, Gavin KL, *et al.* Effects of reallocating sedentary time with physical activity on quality of life indicators in breast cancer survivors. *Psychooncology* 2019; 28: 1430–1437.
28 Tabaczynski A, Courneya KS, Trinh L. Replacing sedentary time with physical activity and sleep: associations with quality of life in kidney cancer survivors. *Cancer Causes Control* 2020; 31: 669–681.
29 Glazer NL, Lyass A, Esliger DW, *et al.* Sustained and shorter bouts of physical activity are related to cardiovascular health. *Med Sci Sports Exerc* 2013; 45: 109–115.
30 Clarke J, Janssen I. Sporadic and bouted physical activity and the metabolic syndrome in adults. *Med Sci Sports Exerc* 2014; 46: 76–83.
31 Tsai LL, Alison JA, McKenzie DK, *et al.* Physical activity levels improve following discharge in people admitted to hospital with an acute exacerbation of chronic obstructive pulmonary disease. *Chron Respir Dis* 2016; 13: 23–32.
32 Roe LS, Harrison S, Cawthon PM, *et al.* The association between daily sedentary and active bout frequency with mortality risk in older men using accelerometry. *J Am Geriatr Soc* 2023; 71: 1547–1557.
33 Glass NL, Bellettiere J, Jain P, *et al.* Evaluation of light physical activity measured by accelerometry and mobility disability during a 6-year follow-up in older women. *JAMA Netw Open* 2021; 4: e210005.
34 Piercy KL, Troiano RP, Ballard RM, *et al.* The physical activity guidelines for Americans. *JAMA* 2018; 320: 2020–2028.
35 Butterworth P, Crosier T. The validity of the SF-36 in an Australian National Household Survey: demonstrating the applicability of the Household Income and Labour Dynamics in Australia (HILDA) Survey to examination of health inequalities. *BMC Public Health* 2004; 4: 44.
36 Cruz LN, Fleck MP, Oliveira MR, *et al.* Health-related quality of life in Brazil: normative data for the SF-36 in a general population sample in the south of the country. *Cien Saude Colet* 2013; 18: 1911–1921.
37 Garratt AM, Stavem K. Measurement properties and normative data for the Norwegian SF-36: results from a general population survey. *Health Qual Life Outcomes* 2017; 15: 51.
38 Majumdar SR, Eurich DT, Gamble JM, *et al.* Oxygen saturations less than 92% are associated with major adverse events in outpatients with pneumonia: a population-based cohort study. *Clin Infect Dis* 2011; 52: 325–331.
39 Brown CJ, Redden DT, Flood KL, *et al.* The underrecognized epidemic of low mobility during hospitalization of older adults. *J Am Geriatr Soc* 2009; 57: 1660–1665.
40 Yoshida M, Hiramoto T, Moriwaki A, *et al.* Impact of extrapulmonary comorbidities on physical activity in chronic obstructive pulmonary disease in Japan: a cross-sectional study. *PLoS One* 2022; 17: e0270836.
41 Alzahrani H. Dose-response association between physical activity and health-related quality of life in general population: a population-based pooled study. *Healthcare (Basel)* 2022; 10: 1460.
42 Alsubaie SF, Alkathiry AA, Abdelbasset WK, *et al.* The physical activity type most related to cognitive function and quality of life. *Biomed Res Int* 2020; 2020: 8856284.
43 Kirk AG, Behm KJ, Kimmel LA, *et al.* Levels of physical activity and sedentary behavior during and after hospitalization: a systematic review. *Arch Phys Med Rehabil* 2021; 102: 1368–1378.

44 Wanigatunga AA, Gill TM, Marsh AP, *et al.* Effect of hospitalizations on physical activity patterns in mobility-limited older adults. *J Am Geriatr Soc* 2019; 67: 261–268.

45 Gilchrist SC, Bennett A, Judd SE, *et al.* Sedentary behavior and physical functioning in middle-age and older adults living in the United States: the reasons for geographic and racial differences in stroke study. *Med Sci Sports Exerc* 2022; 54: 1897–1903.

46 O'Brien WJ, Rauff EL, Shultz SP, *et al.* Replacing sedentary time with physically active behaviour predicts improved body composition and metabolic health outcomes. *Int J Environ Res Public Health* 2022; 19: 8760.

47 Ingle L, Ruilova S, Cui Y, *et al.* Substituting bouts of sedentary behavior with physical activity: adopting positive lifestyle choices in people with a history of cancer. *Cancer Causes Control* 2022; 33: 1083–1094.

48 Valenzuela PL, Saco-Ledo G, Morales JS, *et al.* Effects of physical exercise on physical function in older adults in residential care: a systematic review and network meta-analysis of randomised controlled trials. *Lancet Healthy Longev* 2023; 4: e247–ee56.

49 Zhao Y, Li Y, Wang L, *et al.* Physical activity and cognition in sedentary older adults: a systematic review and meta-analysis. *J Alzheimers Dis* 2022; 87: 957–968.

50 Kunutsor SK, Seidu S, Laukkanen JA. Physical activity reduces the risk of pneumonia: systematic review and meta-analysis of 10 prospective studies involving 1,044,492 participants. *Geroscience* 2022; 44: 519–532.

51 Little JP, Langley J, Lee M, *et al.* Sprint exercise snacks: a novel approach to increase aerobic fitness. *Eur J Appl Physiol* 2019; 119: 1203–1212.

52 Rafiei H, Omidian K, Myette-Côté É, *et al.* Metabolic effect of breaking up prolonged sitting with stair climbing exercise snacks. *Med Sci Sports Exerc* 2021; 53: 150–158.

53 Stamatakis E, Huang BH, Maher C, *et al.* Untapping the health enhancing potential of vigorous intermittent lifestyle physical activity (VILPA): rationale, scoping review, and a 4–pillar research framework. *Sports Med* 2021; 51: 1–10.

54 Mangen MJ, Huijts SM, Bonten MJ, *et al.* The impact of community-acquired pneumonia on the health-related quality-of-life in elderly. *BMC Infect Dis* 2017; 17: 208.

55 van der Sar-van der Brugge S, Talman S, Boonman-de Winter L, *et al.* Pulmonary function and health-related quality of life after COVID-19 pneumonia. *Respir Med* 2021; 176: 106272.