Author's response to reviews

Title: Exercise training for asbestos-related and other dust-related respiratory diseases: a randomised controlled trial

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Author's response to reviews: see over
Dear BioMed Central Editorial Team,

Re: Manuscript 1297546485134183
Exercise training for asbestos-related and other dust-related respiratory diseases: a randomised controlled trial
Marita T Dale, Zoe J McKeough, Phillip A Munoz, Peter Corte, Peter TP Bye and Jennifer A Alison

Thank you for providing us with the reviewers’ comments on the above manuscript and the opportunity to respond to each comment.

We have addressed each of the reviewers’ comments below and made corresponding changes in the revised manuscript where necessary.

Reviewer 1 (Fatima Rodrigues):

1. All participants were male. Therefore this should be pointed in the text, including title, abstract, materials, discussion and conclusions.

Both males and females with dust-related respiratory diseases were invited to participate in the study and it was not our intention to only recruit male participants. However, no females volunteered to participate. We have clarified this in the Methods section (line 149 “Both males and females were eligible to participate”).

In the Results section of the Abstract we have added “Thirty-three of 35 male participants completed the study”.

Line 279 in the Results section states “Forty-four male participants were assessed with 35 included in the study.”

We have now addressed this as a limitation in the Discussion (line 428-430) “Only male participants volunteered to participate in the study, therefore these results cannot be extrapolated to females with dust-related respiratory diseases.”

2. There was heterogeneity in the diagnosis of study participants, and although the different diagnosis was well distributed between exercise and control groups, it still limits the generalization of the results. There’s a paucity of literature data on exercise training in dust-related ILD and this study added eleven patient’s data (7 versus 4). There’s no data on exercise training in people with dust-related pleural disease, and this study evidenced the benefits of exercise training in 24 patients (11 versus 13). Therefore other studies are welcome to add more data on these subjects.

This issue has now been more clearly addressed in the limitations paragraph in the Discussion (lines 433-437).

“Finally, there was some heterogeneity in the diagnoses of study participants which limit the generalisation of the findings. More studies of each specific disease group are needed to address the paucity of literature on the specific effects of exercise
training in people with dust-related pleural disease and dust-related interstitial lung disease”

3. As authors pointed, the majority of participants (69%) had pleural and not parenchymal lung disease. Also, patients on long-term oxygen therapy were excluded from the study. Therefore it is expectable that the results would be different from Holland’s study in apparently more severe patients with ILD, predominantly IPF. This should also be addressed in the Discussion (see line 341-346).

This issue has now been more clearly addressed in the Discussion (lines 347-353).

“One possible explanation is that our cohort included participants with mild to moderate dust-related pleural and interstitial dust diseases rather than more severe ILD. Our participants also had relatively stable disease over the study period, as evident by the stability of the FVC over 26 weeks, compared to the significant decline in FVC over a similar period in the study by Holland et al, indicating the progressive and severe nature of ILD in their cohort.”

In the line 379 of Discussion, authors state that the “…statistically significant improvement in CRQ total score and domains of dyspnoea and emotional function, did not reach the MID established for COPD”. This should be more detailed as the MID usually accepted for CRQ in COPD is 0.5 and in this study all these scores were greater than 0.5.

There are inconsistencies throughout the literature regarding the reporting of CRQ scores which commonly result in confusion to the reader. To address this, we contacted Professor Gordon Guyatt (the author of the CRQ) prior to writing the manuscript to seek advice and clarify the best way to report CRQ scores. Professor Guyatt advised it is best to present data as ‘total’ scores rather than dividing the scores by the number of items per domain. Reporting as ‘total’ scores per domain rather than ‘total’ score divided by the number of items per domain alters the MID. If the scores provided are divided by the number of items per domain, then the MID in COPD for each domain is 0.5. However, if total scores are presented then the MID is 0.5 multiplied by the number of items in each domain. For example in the dyspnoea domain there are 5 items giving a possible range of scores of 7 (maximum impairment) to 35 (no impairment) and the MID of change is 2.5.

To provide clarification for the reader on the MID for the CRQ in people with COPD we have made an amendment in the Methods section (lines 241-245).

As we presented total scores (rather than scores divided by the number of items), the improvements in the CRQ scores in our patient population did not reach the MID established for COPD as stated in the Discussion.

In Key-words: I suggest authors to include also “Pulmonary rehabilitation” and replace “Quality of life” with “Health-related quality of life”.

These amendments have been made to the Keywords
6. In the line 118-119: in the sentence: “Higher levels of daily physical activity have health benefits for people with chronic obstructive pulmonary disease (COPD), including greater exercise capacity and a higher single breath diffusing capacity for carbon monoxide (DLCO)” authors should include a reference about physical activity improving single breath diffusing capacity for carbon monoxide. The reference to this statement (Garcia-Aymerich J, Serra I, Gomez FP, Farrero E, Balcells E, Rodriguez DA, de Batlle J, Gimeno E, Donaire-Gonzalez D, Orozco-Levi M et al: Physical activity and clinical and functional status in COPD. Chest 2009, 136(1):62-70.) was located in the following sentence. The reference has now been moved to immediately after the sentence “Higher levels of daily physical activity have health benefits for people with chronic obstructive pulmonary disease (COPD), including greater exercise capacity and a higher single breath diffusing capacity for carbon monoxide (DLCO).[14]” (line 118).

In the line 62 of Abstract, there should be a space between “2.1 to” and “10.7” This amendment has been made.

In the line 369 of Discussion, “…the MID ranging from of 100-200 seconds…” the word “of” should be deleted. This amendment has been made.

Reviewer 2 (Anne Holland):

The sample size states that 26 participants would be required but 35 were randomised. Why?

We had a very good response to our recruitment strategy through the Dust Diseases Board of NSW. As the study progressed we noticed two distinct participant groups, those with pleural disease and those with interstitial lung disease, and decided to recruit more than originally planned to account for this heterogeneity in the study participants.

Some elements of the methodology would benefit from further justification or clarification. Why were people on long term oxygen therapy excluded? Were all three exercise sessions supervised each week? Why was strength training not included, given it is considered a standard component of pulmonary rehabilitation? Why was the exercise group not provided with advice regarding ongoing exercise?

People on long term oxygen therapy were excluded from the study as two of our outcome measures, the incremental cycle test and the endurance cycle test, could not be conducted on people requiring supplemental oxygen as breath by breath metabolic outcomes were collected simultaneously.
All three exercise sessions were supervised. This has been clarified in the Methods of the manuscript (line 169) “All participants completed supervised aerobic exercise training”.

To ensure consistency of training, strength training was not included in the exercise program due to difficulty in standardising strength training at seven different training sites. We have now addressed this as a limitation in the Discussion (lines 426-428) “In addition, participants did not complete resistance training as part of the exercise training therefore the effects of resistance training in this population remain unclear.”.

The exercise group were not provided with advice regarding ongoing exercise, as we were interested in the long term effects specific to the eight week training program.

The statistical analysis section states that data were analysed by intention to treat, however this does not tell the reader anything about how missing data were dealt with.

We had very little missing data, therefore, based on advice from the statistician, no specific statistical methods, such as imputation of data from the last observation, were used.

It would be useful if the limitations section of the discussion gave a clearer picture of to whom these results can be applied. For instance, the exclusion of people on LTOT and the relatively well preserved functional capacity in this group at baseline indicate that these findings apply to those with relatively mild disease.

The limitations paragraph in the Discussion has been amended to address this issue (lines 430-433).

“This since our study population did not include people with dust-related pleural and interstitial respiratory diseases who were on long term oxygen therapy and as our participants did not have severe disease, the findings of our study cannot be extrapolated to such sub-groups.”

Results for 6MWT at week 8 are shown in figure 1, Table 2 and Table 3. At least one of these should be deleted

Although 6MWT results appear in two tables and one figure, each of these provides different findings. Table 2 provides data on effects of the 8 week exercise training or control period on 6MWT and Table 3 provides the data at 26 weeks. We believe Figure 1 provides a helpful visual representation of the change in functional exercise capacity (6MWT) over the study period.

Thank you again for allowing us to address the reviewers’ comments.

Kind regards,
Marita Dale