

EFFECTIVENESS OF PULMONARY REHABILITATION PERFORMED THROUGH EXERCISE TRAINING FOR PATIENTS WITH STABLE COPD: A META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

UČINKOVITOST PLJUČNE REHABILITACIJE Z VKLJUČENO TELESNO VADBO PRI BOLNIKI S STABILNO KOPB: METAANALIZA RANDOMIZIRANIH KONTROLIRANIH ŠTUDIJ

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ABSTRACT

Keywords:

chronic obstructive pulmonary disease, rehabilitation, exercise training, systematic reviews/meta-analysis

Background: The application of pulmonary rehabilitation (PR) in chronic obstructive pulmonary disease (COPD) improves functional capacity and health-related quality of life (HRQoL) at all stages of disease severity. The aim of this study was to determine the effects of PR, performed through exercise training (PR-ET), on functional capacity and HRQoL in patients with stable COPD.

Methods: The meta-analysis was performed by including randomized controlled trials (RCTs) involving patients with stable COPD who participated in different types of PR-ET in which six-minute walk distance (6MWD) and/or St. George's Respiratory Questionnaire total scores (SGRQ) were measured. The data search was conducted in December 2020 and January 2021.

Results: The first meta-analysis showed a statistically significant positive effect (MD=31.73m; $p < 0.00001$) of PR-ET on 6MWD. Similarly, the second meta-analysis found a statistically significant favourable effect of pulmonary rehabilitation through exercise training on SGRQ total scores (MD=-8.09; $p = 0.002$).

Conclusions: PR, which includes several different types of exercise training, has a positive effect on the functional capacity and HRQoL of patients with stable COPD. Further studies should be conducted to determine the effects of home-based PR-ET and PR-ET >8 weeks on SGRQ total scores.

IZVLEČEK

Ključne besede:

kronična obstruktivna pljučna bolezen, rehabilitacija, telesna vadba, metaanalize

Uvod: Pljučna rehabilitacija (PR) bolnikov s kronično obstruktivno pljučno boleznijo (KOPB) omili simptome bolezni in izboljša kakovost življenja. Telesna vadba je kot element pljučne rehabilitacije pomembna za izboljšanje telesne zmogljivosti bolnika, poveča toleranco na napor ter izboljša strukturo in delovanje mišic. Zahtevnost telesne vadbe mora biti prilagojena omejitvam posameznika. Priporočila se izvajanje kombinirane oblike vadbe, ki jo sestavljajo vadba za vzdržljivost, moč in gibljivost. Namen raziskave je s pomočjo metaanalize ovrednotiti učinkovitost pljučne rehabilitacije, ki vključuje element telesne vadbe, na telesno zmogljivost in na z zdravjem povezano kakovost življenja bolnikov s stabilno KOPB.

Metode: Decembra 2020 in januarja 2021 je bilo izvedeno iskanje virov. V raziskavo smo vključili randomizirane kontrolirane študije, ki so: (i) preučevale bolnike s stabilno KOPB, (ii) vključevale pljučno rehabilitacijo s telesno vadbo, (iii) merile telesno zmogljivost s pomočjo 6-minutnega testa hojein/ali (iv) vrednotile z zdravjem povezano kakovost življenja s pomočjo vprašalnika »St. George's Respiratory Questionnaire«.

Rezultati: Prva metaanaliza (20 randomiziranih kontroliranih študij) je pokazala statistično značilen, pozitiven učinek (MD = 31,73m; $p < 0,00001$) pljučne rehabilitacije z vključeno telesno vadbo na prehojeno razdaljo. Podobno je druga metaanaliza (9 randomiziranih kontroliranih študij) pokazala statistično značilen, pozitiven učinek (MD = -8,09; $p = 0,002$) pljučne rehabilitacije z vključeno telesno vadbo na z zdravjem povezano kakovost življenja bolnikov s KOPB.

Razprava in zaključki: Pljučna rehabilitacija, ki vključuje različne oblike telesne vadbe izboljša telesno zmogljivost in z zdravjem povezano kakovost življenja pri bolnikih s stabilno KOPB. V nadaljevanju bi bila smiselna izvedba metaanalize, ki bi vrednotila učinek posameznih komponent telesne vadbe (vrsta, trajanje, pogostost izvajanja, intenzivnost) na telesno zmogljivost bolnikov s KOPB. Smiselna bi bila tudi izvedba metaanalize, ki bi vrednotila učinek pljučne rehabilitacije s telesno vadbo izvedeno v domačem okolju in PR daljše od 8 tednov, na z zdravjem povezano kakovost življenja pri bolnikih s KOPB.

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1 INTRODUCTION

Chronic obstructive pulmonary disease (COPD) “is a common, preventable, and treatable disease characterised by persistent respiratory symptoms and airflow limitation due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases” (4). Airflow limitation in COPD is caused by chronic inflammation and is characterized by obstructive bronchitis and emphysema. Systemic inflammation also plays an important role in the comorbidity of patients with COPD (1), including a markedly increased risk of cardiovascular diseases (2).

COPD is considered an important public health issue. It is the third leading cause of death worldwide (3), and is particularly prevalent in the aging population that has been exposed to tobacco smoke (4). The global prevalence of COPD in adults is estimated to be 11.7% (5). Due to the high prevalence of smoking and the increase in the elderly population in developing countries, the prevalence of COPD is expected to increase (6).

Pharmacological treatment of COPD is required to reduce the symptoms, severity, and frequency of exacerbation of the disease, improve exercise tolerance, and general health (4). Treatment of stable COPD also includes pulmonary rehabilitation (PR) as a key component in the management of COPD patients (4, 7). PR is a multicomponent intervention usually based on smoking cessation counselling, influenza and pneumococcal vaccination, education on the proper use of prescribed inhalation therapy, nutrition, and exercise training (4, 8). Exercise intolerance and limb muscle dysfunction are among the most troubling symptoms of COPD (7, 9). Considering an individual’s characteristics and comorbidities (7), institution- and home-based PR improves functional capacity and health related quality of life (HQoL) at all stages of disease severity (4).

HQoL is an important indicator of the impact of chronic disease, and can be severely impaired in patients with COPD (10). The St. George’s Respiratory Questionnaire (SGRQ) is a disease-specific instrument designed to measure the impact on general health, daily life, and perceived well-being in patients with obstructive airway disease (11). When monitoring these patients, a favourable change in the SGRQ score may indicate the effectiveness of a given treatment (12).

Exercise training is an important component of PR to stabilize COPD. It is the best available means to improve exercise tolerance and muscle function (13), and also contributes to cardiovascular health in COPD patients (14, 15). For example, COPD as an endothelial disorder (16) increases the risk of cardiovascular diseases (2). Apparently, impaired blood flow worsens endothelial dysfunction in moderate to severe COPD (17). Patients with severe airway

obstruction who are physically active are less susceptible to significant dysfunction of flow-mediated vasodilatation (17). It appears that higher levels of physical activity and/or long-term PR including exercise may improve quality of life and reduce cardiovascular risk in COPD patients (14). Before starting an exercise programme, an assessment of physical fitness is necessary to individualize the training protocol (18). Endurance training (EDT) programmes generally increase endurance performance by inducing adaptations in the cardiorespiratory and neuromuscular systems (18). Improved endurance performance results in reduced ventilatory demand, which is why EDT is strongly recommended in COPD (19). The American College of Sports Medicine recommends daily aerobic exercise (30-60 minutes) at moderate level. Exercise should be rhythmic, using large muscle groups, such as walking, cycling, and swimming (20). When endurance training is supplemented with resistance training (RT), muscle mass and strength improve (21). RT for the major muscle groups should be performed at least 2 days per week with moderate intensity (20). Flexibility exercises for the upper and lower limbs performed 2-3 days per week are commonly included in PR (22). A minimum of 8 weeks of training is required for clinically meaningful changes in exercise capacity and quality of life (22). Therefore, a maintenance program or at least sufficient support should be offered to patients with COPD (4).

The six minute walk test (6MWT) can be used to predict cardiorespiratory fitness in the healthy population (23), and the usual result of the related tests is the six-minute walking distance (6MWD). Current data confirm that the 6MWT is valid and reliable for assessing functional exercise capacity and response to treatment in diverse patients’ groups (23, 24). The feasibility of the 6MWT has been studied in pulmonary diseases. It was found to be feasible in patients after mechanical ventilation (25) or lung transplantation (26), and in patients with chronic obstructive pulmonary disease (27, 28). Consequently, the 6MWT is a widely accepted method for evaluating the effects of PR performed through physical activity or exercise on functional exercise capacity in COPD (18).

The aim of this study was to perform a review and meta-analysis to investigate the effects of PR, as performed by exercise training (as at PR-ET), on functional capacity (measured by 6MWT) and health-related quality of life (measured by SGRQ) of patients with stable COPD.

In addition, the above effects will be assessed by comparing home- and institution-based PR-ET and PR-ET with a duration of ≤ 8 weeks and > 8 weeks. Supervised institutional-based PR-ET is expected to have a greater impact on 6MWD and SGRQ total score than home-based PR-ET. Based on summation of effects, PR-ET with longer duration would likely be more effective than the shorter ones.

COPD is considered an important public health issue. In this context, we present the following hypotheses (H), both of which refer to patients with stable COPD:

H1: PR-ET has a positive effect on 6MWD.

H2: PR-ET has a positive effect on SGRQ total score.

2 METHODS

2.1 Eligibility criteria

The search was performed using the PICO index: 1) population: COPD patients in a stable phase of the disease or defined free of exacerbations at least 4 weeks prior PR-ET; 2) intervention: any PR which includes any type of home- or institution-based exercise training with or without isolated respiratory muscle training; 3) comparison: patients in PR-ET (intervention group) with patients without PR-ET (control group); 4) outcomes: walking distance in the 6MWT and/or the SGRQ total score. Furthermore, one study where a combination of home-based and institution-based PR-ET was performed were not included in the meta-analyses.

2.2 Search strategy

The search of the following information sources - PubMed, EBSCO and PEDro - was performed in December 2020 and January 2021. There were no restrictions on the year of publication. The search strategy was based on the search terms within four core elements, each with the corresponding synonyms: i) COPD, ii) pulmonary rehabilitation, iii) physical exercise, iii) randomized controlled trial, iv) outcome parameters. Search terms referring to these elements in the title or abstract in all mentioned databases, were merged with Boolean operators.

2.3 Assessment of the methodological quality of the studies included

To determine the eligibility of the studies, the PEDro scale (29) was applied as it is considered a valid measure of methodological quality of clinical trials (30). All studies were rated as fair quality and above (4+/10), except one study which was rated as 3/10. The studies were performed in various settings, by using a variety of PR-ET on different groups of patients with COPD. In these circumstances it is not always possible to satisfy all PEDro criteria items (31). Hence, we decided to include the study rated as 3/10 in the meta-analyses as it reported all the required information. Furthermore, RCTs included in meta-analyses are assessed by using TIDieR checklist (32) (Appendix 1). To assess the certainty of the evidence, which reflects the extent to which our confidence in an estimate of effect (in our case determined from the meta-analyses) is sufficient to support a particular recommendation, Grading of Recommendations Assessment, Development

and Evaluation - GRADE (33) was adopted by using the web app GRADEproGDT (34).

2.4 Data extraction

The following data was extracted by the second and third authors: the article reference, intervention, the location of the RCT (home-based/institution based), type/duration of PR-ET, number of participants within the experimental/control group, 6MWT and SGRQ results as means and standard deviations. No discrepancies between the two authors were identified. If the results were provided using other measures of dispersion (e.g., SE, 95% CI), the required information was estimated using the available guidelines (35).

2.5 Statistical analysis

The results were analysed using Review Manager 5.3, and the random effects model with the inverse variance method was performed using the mean differences (MD) between the results of the experimental and control groups, where the MD of the measurements before and after PR-ET were considered. The threshold for statistical significance was 0.05. We evaluated the effect size (ES) and the corresponding confidence interval - CI (95%). The results were graphically presented with forest plots. The heterogeneity between the studies was determined by I^2 : <30% represents a negligible heterogeneity; 30%-75% moderate; and >75% considerable (36).

3 RESULTS

3.1 Literature search

The initial search resulted in 1,640 articles. After excluding those which did not meet the inclusion criteria, 20 remaining articles were considered in the further analysis. As already noted, one article (37) was excluded as it included a PR-ET where a combination of home-based and institution-based PR-ET was performed (Figure 1). However, its findings are presented in the Discussion and compared with the results of our study. For two articles, the corresponding authors were asked to provide additional data (i.e. MD and SD for the 6MWT and SGRQ). Only in one case was the request satisfied. Finally, 18 articles (38-55) were considered. As two articles reported the results of two independent RCTs, in total there were 20 RCTs included. For all of them 6MWD were provided, only nine RCTs also had SGRQ results. The details of RCTs are presented in Appendix 2.

3.2 The effects of PR-ET on 6MWD

The first meta-analysis included 20 RCTs performed on a total of 977 participants: 510 were in the experimental group and 467 in the control group. The 6MWT results are

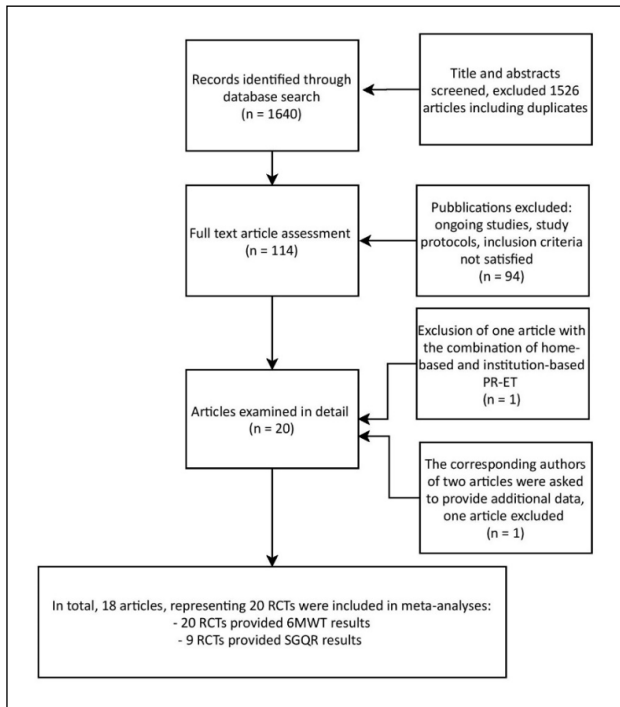


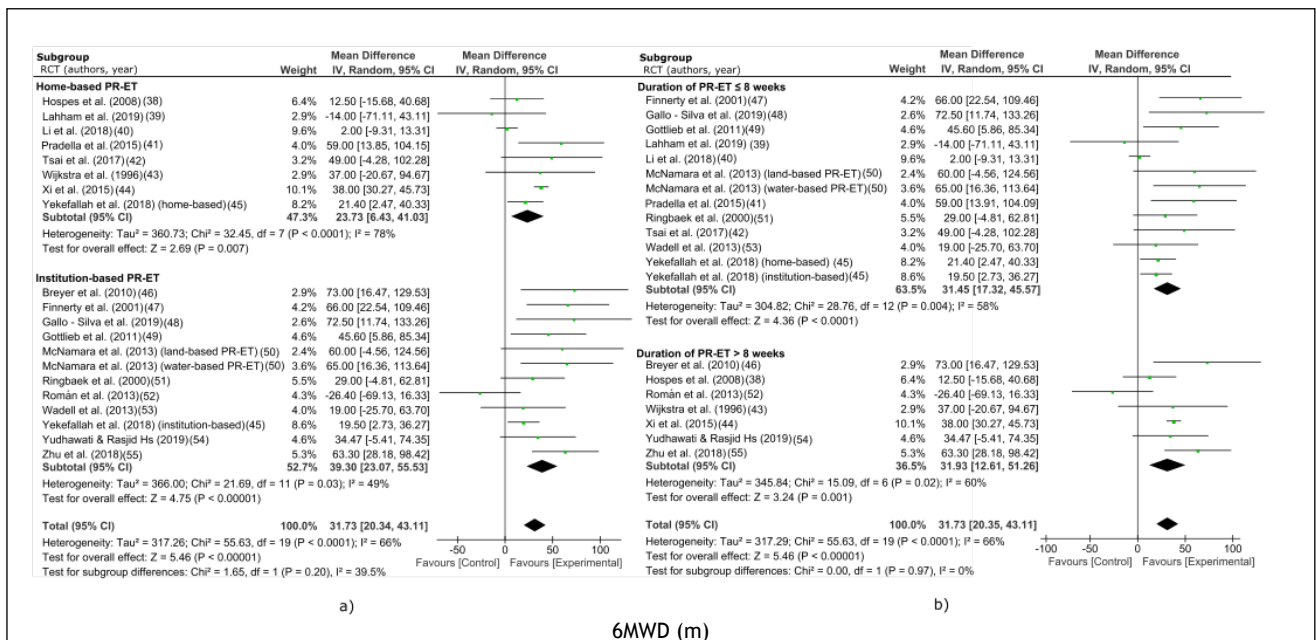
Figure 1. Database search flowchart.

reported as six-minute walking distance in metres (m). The pooled ES indicated a statistically significant positive, i.e. favourable effect of PR-ET on 6MWD (MD=31.73m, [20.34m, 43.11m], Z=5.46, p<0.00001). The forest plot (Figure 2a) also presents the pooled ES separately for

home- and institution-based PR-ET. In both cases the effect of PR-ET on 6MWD was positive and statistically significant (home-based PR-ET: MD=23.73m, [6.43m, 41.03m], Z=2.69, p=0.007; institution-based PR-ET: MD=39.30m, [23.07m, 55.53m], Z=4.75, p<0.00001). Furthermore, the forest plot in Figure 2b also presents the pooled ES separately for the duration of PR-ET ≤8 weeks/>8 weeks. In both cases the effect of PR-ET on 6MWD was positive and statistically significant (duration of PR-ET ≤8 weeks: MD=31.45m, [17.32m, 45.57m], Z=4.36, p<0.0001); duration of PR-ET >8 weeks: MD=31.93m, [12.61m, 51.26m], Z=3.24, p=0.001). Statistical heterogeneity was moderate for: all included RCTs (I²=66 %, p<0.0001), institution-based RCTs (I²=49%, p=0.03), PR-ET of the duration ≤8 weeks (I²=58 %, p=0.004), PR-ET of the duration >8 weeks (I²=60 %, p=0.02), while for home-based RCTs was high (I²=78 %, p<0.0001).

3.3 The effects of PR-ET on SGRQ score

The second meta-analysis included nine RCTs performed on a total of 364 participants: 190 were in the experimental, 174 in the control group. The pooled ES showed a statistically significant negative, i.e. favourable, effect of PR-ET on the SGRQ total score, which was expressed in units (MD=-8.09, [-13.25, -2.94], Z=3.08, p=0.002). The forest plot (Figure 3a) also presents the pooled ES separately for institution-based and home-based PR-ET. The sub-meta-analysis for institution-based PR-ET indicates the statistically significant effect of PR-ET on SGRQ total score (MD=-9.23, [-14.96, -3.50], Z=3.16, p=0.002), while for home-based PR-



Legend: Green squares represent the average mean differences between intervention and control group outcomes, their horizontal lines represent a 95% confidence interval (CI). The black diamond shape represents the pooled mean difference within each analysis.

Figure 2. Effects of PR-ET on 6MWD: a) home-/institution-based and b) duration of PR-ET ≤8 weeks/>8 weeks.

ET the mentioned effect was not statistically significant (MD=-5.53, [-14.02, 2.96], Z=1.28, p=0.20). Furthermore, the forest plot in Figure 3b also presents the pooled ES separately for the PR-ET of the duration ≤8 weeks and >8 weeks. In the case of RCTs with the PR-ET of the duration ≤8 weeks, the pooled ES on SGRQ total results was favourable and statistically significant (MD=-7.19, [-10.95, -3.43], Z=3.75, p=0.0002) as opposed to the experiments of the PR-ET duration >8 weeks, where it was not statistically significant (MD=-10.78, [-25.88, -4.31], Z=1.40, p=0.16). Statistical heterogeneity was high for all included RCTs (I²=80 %, p<0.0001) and for PR-ET of the duration >8 weeks (I²=91%, p<0.0001), and moderate for home-based RCTs (I²=70%, p=0.04) and institution-based RCTs (I²=66%, p=0.01), while it was not statistically significant for the PR-ET of the duration ≤8 weeks (I²=23 %, p=0.26).

4 DISCUSSION

Pulmonary rehabilitation (PR), including exercise training (ET), is recognized as an important component of treatment for patients with chronic respiratory disease. PR is designed to reduce symptoms and improve functional capacity and health-related quality of life in COPD (13). In this study, the effect of PR, performed by exercise training (PR-ET), on the six-minute walk distance (6MWD) and St. George’s Respiratory Questionnaire (SGRQ) total scores in patients with stable COPD was investigated.

The 6MWT is the gold standard for assessing functional capacity in COPD patients (18) and a valid predictor of potential hospitalisation (56) - the longer the 6MWD, the lower the risk of hospitalization. Our meta-analysis shows that PR-ET including various forms of exercise training significantly improves 6MWD (31.73m) (Figure 2), indicating

the relevant beneficial effect of PR-ET on functional capacity in COPD. A number of studies have reported a threshold for the minimal clinically significant difference in changes in 6MWD of 25-35m (57). Therefore, according to the study hypothesis H1, i.e. that PR-ET has a positive effect on 6MWD in COPD, can be confirmed. Moreover, the increase in 6MWD after PR-ET was of clinical significance. Our meta-analysis included studies that considered different forms of exercise training relevant to increasing functional capacity. This variability of PR-ET is probably one of the main reasons for the moderate heterogeneity of the results (I²=66%, p<0.0001).

Considering that PR-ET is very effective in improving functional capacity in COPD (13), our meta-analysis examined the effects of institutional- and home-based PR-ET on 6MWD. The results suggest that significant improvement in 6MWD is also achieved with home-based PR-ET. However, 23.73 m (Figure 2) for the mean change in 6MWD in the case of home-based PR-ET does not reach the minimum clinically relevant required change of 25 m (57). This suggests that home-based PR-ET significantly improves the functional capacity of COPD patients, but institutional-based PR-ET produces a clinically relevant mean change in 6MWD (39.30 m). Home-based PR-RT could be an alternative to outpatient or hospital-based programs for those patients who, for various reasons, cannot attend PR-ET in specialized institutions. One way to improve the efficiency of home-based PR-ET could be to enable patients to self-manage their own training, not to mention to receive adequate expert support (22). For example, PR-ET, which is performed partly under professional supervision and partly without, increases tolerance to exercise (37). The use of multimedia in the home-based PR also improves exercise performance in COPD patients (58). Certain forms of home-based PR-ET

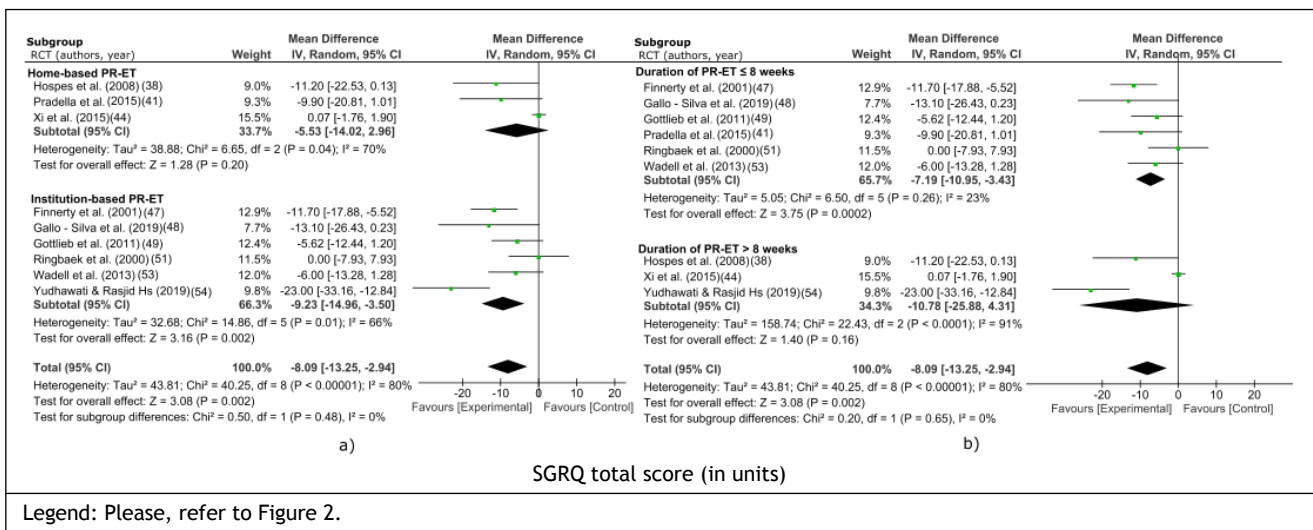


Figure 3. Effects of PR-ET on SGRQ total score: a) home-/institution-based and b) duration of PR-ET ≤8 weeks/>8 weeks.

may facilitate the maintenance of benefits acquired in outpatients PR (59).

Compared with baseline, a significant improvement in walking distance was observed for PR-ET of duration ≤ 8 weeks (31.45 m) and PR-ET of duration > 8 weeks (31.92 m) in patients with stable COPD (Figure 2). Therefore, to achieve clinically meaningful gains in functional capacity, PR-ET ≤ 8 weeks may be acceptable. This is encouraging in terms of patient motivation. We must consider that in our meta-analysis, most RCTs that included a short PR-ET were exactly 8 weeks long, and no studies were shorter than 4 weeks. Indeed, the GOLD report (4) summarizes that the optimal benefit of PR is achieved in programmes lasting 4-8 weeks. The available evidence suggests that extending PR to 12 weeks does not add any benefit. However, if the results of PR are not supported, its benefits diminish over time. Therefore, it is important to participate in maintenance programmes after PR (4, 60). In our meta-analysis, RCTs that included PR-ET lasting > 8 weeks showed a significant, moderate heterogeneity of the results (Figure 2b: $I^2=60\%$, $p=0.020$). The reason for this is likely to be found in the study by Xi et al. (44), in which a significant improvement in walking distance was observed after PR-ET consisted of high-frequency training (≥ 5 times per week). While, in the study by Román et al. (52), no improvement in walking distance was found in patients with COPD and low impairment when PR-ET includes low-intensity peripheral muscle training.

The SGRQ is suitable to assess health-related quality of life (HRQoL) in patients with COPD (12, 49). In our meta-analysis, the overall effect of PR-ET on the SGRQ score and thus on the quality of life of COPD patients was favourable and statistically significant (Figure 3: -8.09). Based on this result H2, i.e., PR-ET has a positive effect on SGRQ total score, can be confirmed. Similarly, other meta-analyses found a statistically significant effect of PR-ET on HRQoL as assessed by SGRQ (62-64). The submeta-analyses of the institution-based PR-ET (Figure 3a) and also PR-ET with a duration of ≤ 8 weeks (Figure 3b) were found to be favourable and statistically significant, in contrast to the submeta-analyses of the home-based PR-ET and PR-ET with a duration of > 8 weeks, where the results were not statistically significant. Before making further conclusions, it should be noted that the latter two submeta-analyses were performed on only three RCTs, which is below the recommended minimum (65). Therefore, further studies should be conducted to evaluate the effects of PR-ET on SGRQ score in home-based PR, and those that have a duration of > 8 weeks.

Before drawing any further conclusions about the results of the meta-analyses, the following limitations should be considered. In this study there were RCTs with different types of ET and different groups of patients with stable COPD. This probably contributed to the substantial heterogeneity of the results. Our results suggest that different types of ET, included in PR, are beneficial for COPD patients. However, further meta-analyses with different types of ET and different groups of COPD patients should be performed to determine the efficacy of each type of PR-ET. Currently, because of the relatively small number of RCTs that satisfy the inclusion criteria, it is not possible to meet the criterion of the recommended minimum number of RCTs in the meta-analysis by grouping the RCTs according to different types of ET and different groups of COPD (please, refer also to Appendix 2). Another important limitation of this study is the problem of adherence - that is, the degree to which an intervention was delivered in the manner planned by the investigators - in the RCTs included in the meta-analysis. As shown in Appendix 1, of the 18 RCTs included in our study, only nine reported how adherence to the intervention should be assessed (item 11 of the TIDieR), and of these, only two RCTs reported the actual extent to which the intervention was delivered as planned (item 12). Furthermore, the results of certainty of evidence (GRADE) were low for both meta-analyses. This fact certainly detracts from the relevance of our meta-analyses, and particular caution should be exercised in generalizing our results. Moreover, this fact is also an urgent call to researchers in the field to improve the design and reporting of RCTs in this area.

5 CONCLUSION

Our meta-analyses show that PR-ET including different types of ET has a significant, beneficial effect on functional capacity and HRQoL in COPD patients because: (i) overall it improves 6MWD and SGRQ total scores; (ii) produces a clinically significant improvement in 6MWD when performed as institutional-based PR-ET, and in the case of PR-ET ≤ 8 weeks and PR-ET > 8 weeks; (iii) the institutional-based PR-ET and PR-ET ≤ 8 weeks subcategories also show significant, favourable effects on SGRQ total scores.

The results are positive in that they suggest that patients can include the exercise training that is most appropriate for them in their PR. They also suggest that the benefits to functional capacity in COPD can be achieved even when PR-ET is performed at home. To achieve clinically important improvements in functional capacity, PR-ET proved more effective when performed in specialized institutions. Special attention should be paid to determining the impact of home-based PR-ET and PR-ET > 8 weeks on the SGRQ score.

Therefore, it is recommended that healthcare institutions include PR-ET in the management of patients with stable COPD, as it is an effective, complementary intervention to conventional pharmacological treatments. However, for better planning of PR-ET in COPD patients, further studies should be conducted to clarify the effects of different training variables on their functional capacity.

CONFLICTS OF INTEREST

The authors declare that no conflicts of interest exist.

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ETHICAL APPROVAL

Not required.

REFERENCES

- Barnes PJ. Inflammatory mechanisms in patients with chronic obstructive pulmonary disease. *J Allergy Clin Immunol.* 2016;138(1):16-27. doi: 10.1016/j.jaci.2016.05.011.
- Müllerova H, Agustí A, Erqou S, Mapel DW. Cardiovascular comorbidity in COPD. *Chest.* 2013;144(4):1163-78.
- World Health Organisation. Chronic obstructive pulmonary disease (COPD). Accessed September 1st, 2022 at: [https://www.who.int/news-room/fact-sheets/detail/chronic-obstructive-pulmonary-disease-\(copd\)](https://www.who.int/news-room/fact-sheets/detail/chronic-obstructive-pulmonary-disease-(copd)).
- Global initiative for chronic obstructive lung disease: global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease 2019 report. Accessed February 23th, 2021 at: <https://goldcopd.org/wp-content/uploads/2018/11/GOLD-2019-v1.7-FINAL-14Nov2018-WMS.pdf>.
- Adeloye D, Chua S, Lee C, Basquill C, Papana A, Theodoratou E, et al. Global and regional estimates of COPD prevalence: systematic review and meta-analysis. *J Glob Health.* 2015;5(2):020415. doi: 10.7189/jogh.05-020415.
- World Health Organisation. COPD predicted to be third leading cause of death in 2030. Accessed February 23, 2021 at: https://www.who.int/respiratory/copd/World_Health_Statistics_2008/en/.
- Wouters EF, Posthuma R, Koopman M, Liu W-Y, Sillen MJ, Hajian B, et al. An update on pulmonary rehabilitation techniques for patients with chronic obstructive pulmonary disease. *Expert Rev Respir Med.* 2020;14(2):149-61. doi: 10.1080/17476348.2020.1700796.
- Škrat S, Triller N, Košnik M, Poplas Susič T, Petek D, Vodopivec Jamšek V, et al. Priporočila za obravnavo bolnika s kronično obstruktivno pljučno boleznijo na primarni in specialistični pulmoški ravni v Sloveniji. *Zdrav Vest.* 2017;86(1-2):65-75. doi: 10.6016/ZdravVestn.2471.
- Maltais F, Decramer M, Casaburi R, Barreiro E, Burelle Y, Debigaré R, et al. An official American Thoracic Society/European Respiratory Society statement: update on limb muscle dysfunction in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med.* 2014;189(9):e15-62. doi: 10.1164/rccm.201402-0373ST.
- Zamzam MA, Azab NY, El Wahsh RA, Ragab AZ, Allam EM. Quality of life in COPD patients. *Egypt J Chest Dis Tuberculosis.* 2012;61(4):281-9. doi: 10.1016/j.ejcdt.2012.08.012.
- Jones PW, Quirk FH, Baveystock CM, Littlejohns P. A self-complete measure of health status for chronic airflow limitation: the St. George's Respiratory Questionnaire. *Am Rev Respir Dis.* 1992;145(6):1321-7. doi: 10.1164/ajrccm/145.6.1321.
- Jones PW. Quality of life, symptoms and pulmonary function in asthma: long-term treatment with nedocromil sodium examined in a controlled multicentre trial: Nedocromil Sodium Quality of Life Study Group. *Eur Respir J.* 1994;7(1):55-2. doi: 10.1183/09031936.94.07010055.
- Spruit MA, Singh SJ, Garvey C, ZuWallack R, Nici L, Rochester C, et al. An official American Thoracic Society/European Respiratory Society statement: key concepts and advances in pulmonary rehabilitation. *Am J Respir Crit Care Med.* 2013;188(8):e13-64. doi: 10.1164/rccm.201309-1634ST.
- Sievi N, Franzen D, Kohler M, Clarenbach C. Physical inactivity and arterial stiffness in COPD. *Int J Chron Obstruct Pulmon Dis.* 2015;10:1891-7. doi: 10.2147/COPD.S90943.
- Reis LFF, Guimarães FS, Fernandes SJ, Cantanhede LA, Dias CM, Lopes AJ, et al. A long-term pulmonary rehabilitation program progressively improves exercise tolerance, quality of life and cardiovascular risk factors in patients with COPD. *Eur J Phys Rehabil Med.* 2013;49(4):491-7.
- Polverino F, Celli BR, Owen CA. COPD as an endothelial disorder: endothelial injury linking lesions in the lungs and other organs? (2017 Grover Conference Series). *Pulm Circ.* 2018;8(1):1-18. doi: 10.1177/2045894018758528.
- Clarenbach CF, Senn O, Sievi NA, Camen G, van Gestel AJR, Rossi VA, et al. Determinants of endothelial function in patients with COPD. *Eur Respir J.* 2013;42(5):1194-204. doi: 10.1183/09031936.00144612.
- ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. ATS statement: guidelines for the six-minute walk test. *Am J Respir Crit Care Med.* 2002;166(1):111-7. doi: 10.1164/ajrccm.166.1.at1102.
- Porszasz J, Emtner M, Goto S, Somfay A, Whipp BJ, Casaburi R. Exercise training decreases ventilatory requirements and exercise-induced hyperinflation at submaximal intensities in patients with COPD. *Chest.* 2005;128(4):2025-34. doi: 10.1378/chest.128.4.2025.
- American College of Sports Medicine. General Principles of Exercise Prescription. In: Pescatello LS, Arena R, Riebe D, Thompson PD, editors. *ACSM's Guidelines for Exercise Testing and Prescription.* 9th ed. Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins, 2013: 162-193.
- Spruit MA, Gosselink R, Troosters T, De Paepe K, Decramer M. Resistance versus endurance training in patients with COPD and peripheral muscle weakness. *Eur Respir J.* 2002;19(6):1072-8. doi: 10.1183/09031936.02.00287102.
- Garvey C, Bayles MP, Hamm LF, Hill K, Holland A, Limberg TM, et al. Pulmonary rehabilitation exercise prescription in chronic obstructive pulmonary disease: review of selected guidelines: an official statement from the American Association of Cardiovascular and Pulmonary Rehabilitation. *J Cardiopulm Rehabil Prev.* 2016;36(2):75-83. doi: 10.1097/HCR.0000000000000171.
- Mänttari A, Suni J, Sievänen H, Husu P, Vähä-Ypyä H, Valkeinen H, et al. Six-minute walk test: a tool for predicting maximal aerobic power (VO₂ max) in healthy adults. *Clin Physiol Funct Imaging.* 2018;38(6):1038-45. doi: 10.1111/cpf.12525.
- Holland AE, Spruit MA, Troosters T, Puhan MA, Pepin V, Saey D, et al. An official European Respiratory Society/American Thoracic Society technical standard: field walking tests in chronic respiratory disease. *Eur Respir J.* 2014;44(6):1428-46. doi: 10.1183/09031936.00150314.
- Malamud AL, Ricard PEH. Feasibility of the six-minute walk test for patients who have cystic fibrosis, are ambulatory, and require mechanical ventilation before lung transplantation. *Phys Ther.* 2016;96(9):1468-76. doi: 10.2522/ptj.20150235.

26. Seoane L, Alex S, Pirtle C, Gupta M, Taylor DE, Valentine VG, et al. Utility of the 6-minute walk test following lung transplantation. *Ochsner J.* 2010;10(4):227-30.
27. Brooks D, Solway S, Weinacht K, Wang D, Thomas S. Comparison between an indoor and an outdoor 6-minute walk test among individuals with chronic obstructive pulmonary. *Arch Phys Med Rehabil.* 2003;84(6):873-6. doi: 10.1016/S0003-9993(03)00011-X.
28. Valeiro B, Hernández C, Barberán-García A, Rodríguez DA, Aibar J, Llop L, et al. Viabilidad de la evaluación domiciliar del estado funcional de pacientes con enfermedad pulmonar obstructiva crónica en fase de recuperación de una exacerbación. *Arch Bronconeumol.* 2016;52(5):256-61. doi: 10.1016/j.arbres.2015.10.010.
29. Physiotherapy Evidence Database. PEDro scale. Accessed February 15, 2021 at: <https://staging-pedro.neura.edu.au/english/resources/pedro-scale/>.
30. de Morton NA. The PEDro scale is a valid measure of the methodological quality of clinical trials: a demographic study. *Aust J Physiother.* 2009;55(2):129-33. doi: 10.1016/S0004-9514(09)70043-1.
31. Cashin AG, McAuley JH. Clinimetrics: Physiotherapy Evidence Database (PEDro) Scale. *J Physiother.* 2020;66(1):59. doi: 10.1016/j.jphys.2019.08.005.
32. Hoffmann TC, Glasziou PP, Boutron I, Milne R, Perera R, Moher D, et al. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. *BMJ.* 2014;348:g1687-8. doi: 10.1136/bmj.g1687.
33. Austin TM, Richter RR, Sebelski CA. Introduction to the GRADE approach for guideline development: considerations for physical therapist practice. *Phys Ther.* 2014;94(11):1652-9. doi: 10.2522/ptj.20130627.
34. GRADEpro GDT: GRADEpro guideline development tool. McMaster University and Evidence Prime, 2022. Accessed August 30th, 2021 at: <https://gdt.grade.org/app/>.
35. Higgins JPT, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ.* 2003;327(7414):557-60. doi: 10.1136/bmj.327.7414.557.
36. Higgins JPT, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Statist Med.* 2002;21(11):1539-58. doi: 10.1002/sim.1186.
37. Farias CC, Resqueti V, Dias FAL, Borghi-Silva A, Arena R, Fregonezi GAF. Costs and benefits of pulmonary rehabilitation in chronic obstructive pulmonary disease: a randomized controlled trial. *Braz J Phys Ther.* 2014;18(2):165-73. doi: 10.1590/s1413-3552012005000151.
38. Hospes G, Bossenbroek L, Ten Hacken NHT, van Hengel P, de Greef MHG. Enhancement of daily physical activity increases physical fitness of outclinic COPD patients: results of an exercise counseling program. *Patient Educ Couns.* 2009;75(2):274-8. doi: 10.1016/j.pec.2008.10.005
39. Lahham A, McDonald CF, Moore R, Cox NS, Rawlings S, Nichols A, et al. The impact of home-based pulmonary rehabilitation on people with mild chronic obstructive pulmonary disease: a randomised controlled trial. *Clin Respir J.* 2020;14(4):335-44. doi: 10.1111/crj.13138.
40. Li Y, Feng J, Li Y, Jia W, Qian H. A new pulmonary rehabilitation maintenance strategy through home-visiting and phone contact in COPD. *Patient Prefer Adherence.* 2018;12:97-104. doi: 10.2147/PPA.S150679.
41. Pradella CO, Belmonte GM, Maia MN, Delgado CS, Luise APT, Nascimento OA, et al. Home-based pulmonary rehabilitation for subjects with COPD: a randomized study. *Respir Care.* 2015;60(4):526-32. doi: 10.4187/respcare.02994.
42. Tsai LLY, McNamara RJ, Moddel C, Alison JA, McKenzie DK, McKeough ZJ. Home-based telerehabilitation via real-time videoconferencing improves endurance exercise capacity in patients with COPD: the randomized controlled TeleR study. *Respirology.* 2017;22(4):699-707. doi: 10.1111/resp.12966.
43. Wijkstra PJ, van der Mark TW, Kraan J, van Altena R, Koeter GH, Postma DS. Effects of home rehabilitation on physical performance in patients with chronic obstructive pulmonary disease (COPD). *Eur Respir J.* 1996;9(1):104-10. doi: 10.1183/09031936.96.09010104.
44. Xi F, Wang Z, Qi Y, Brightwell R, Roberts P, Stewart A, et al. Long-term effect of respiratory training for chronic obstructive pulmonary disease patients at an outpatient clinic: a randomised controlled trial. *Clin Transl Med.* 2015;4(1):31. doi: 10.1186/s40169-015-0073-2.
45. Yekefallah L, Zohal MA, Keshavarz-sarkar O, Barikani A, Gheraati M. Comparing the effects of upper limb and breathing exercises on six-minute walking distance among patients with chronic obstructive pulmonary disease: a three-group randomized controlled clinical trial. *Adv Respir Med.* 2019;87(2):77-82. doi: 10.5603/ARM.2019.0013.
46. Breyer M-K, Breyer-Kohansal R, Funk G-C, Dornhofer N, Spruit MA, Wouters EFM, et al. Nordic walking improves daily physical activities in COPD: a randomised controlled trial. *Respir Res.* 2010;11:112. doi: 10.1186/1465-9921-11-112.
47. Finnerty JP, Keeping I, Bullough I, Jones J. The effectiveness of outpatient pulmonary rehabilitation in chronic lung disease: a randomized controlled trial. *Chest.* 2001;119(6):1705-10. doi: 10.1378/chest.119.6.1705.
48. Gallo-Silva B, Cerezer-Silva V, Ferreira DG, Sakabe DI, Kel-Souza LD, Bertholo VC, et al. Effects of water-based aerobic interval training in patients with COPD: a randomized controlled trial. *J Cardiopulm Rehabil Prev.* 2019;39(2):105-11. doi: 10.1097/HCR.0000000000000352.
49. Gottlieb V, Lyngsø AM, Nybo B, Frølich A, Backer V. Pulmonary rehabilitation for moderate COPD (GOLD 2) - does it have an effect? *COPD.* 2011;8(5):380-6. doi: 10.3109/15412555.2011.610393.
50. McNamara RJ, McKeough ZJ, McKenzie DK, Alison JA. Water-based exercise in COPD with physical comorbidities: a randomised controlled trial. *Eur Respir J.* 2013;41(6):1284-91. doi: 10.1183/09031936.00034312.
51. Ringbaek TJ, Broendum E, Hemmingsen L, Lybeck K, Nielsen D, Andersen C, et al. Rehabilitation of patients with chronic obstructive pulmonary disease: exercise twice a week is not sufficient! *Respir Med.* 2000;94(2):150-4. doi: 10.1053/rmed.1999.0704.
52. Román M, Larraz C, Gómez A, Ripoll J, Mir I, Miranda EZ, et al. Efficacy of pulmonary rehabilitation in patients with moderate chronic obstructive pulmonary disease: a randomized controlled trial. *BMC Fam Pract.* 2013;14:21. doi: 10.1186/1471-2296-14-21.
53. Wadell K, Webb KA, Preston ME, Amornputtisathaporn N, Samis L, Patelli J, et al. Impact of pulmonary rehabilitation on the major dimensions of dyspnea in COPD. *COPD.* 2013;10(4):425-35. doi: 10.3109/15412555.2012.758696.
54. Yudhawati R, Rasjid Hs M. Effect of yoga on FEV1, 6-minute walk distance (6-MWD) and quality of life in patients with COPD group B. *Adv Respir Med.* 2019;87(5):261-8. doi: 10.5603/ARM.2019.0047.
55. Zhu S, Shi K, Yan J, He Z, Wang Y, Yi Q, et al. A modified 6-form Tai Chi for patients with COPD. *Complement Ther Med.* 2018;39:36-42. doi: 10.1016/j.ctim.2018.05.007.
56. Kessler R, Faller M, Fourgaut G, Mennecier B, Weitzenblum E. Predictive factors of hospitalization for acute exacerbation in a series of 64 patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med.* 1999;159(1):158-64. doi: 10.1164/ajrccm.159.1.980317.
57. Holland AE, Nici L. The return of the minimum clinically important difference for 6-minute-walk distance in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med.* 2013;187(4):335-6. doi: 10.1164/rccm.201212-2191ED.
58. Santiworakul A, Piya-amornphan N, Jianramas N. A home-based multimedia pulmonary rehabilitation program improves clinical symptoms and physical performance of patients with chronic obstructive pulmonary disease. *Int J Environ Res Public Health.* 2021;18(21):11479. doi: 10.3390/ijerph182111479.
59. de Souza Y, da Silva KM, Condesso D, Figueira B, Noronha Filho AJ, Rufino R, et al. Use of a home-based manual as part of a pulmonary rehabilitation program. *Respir Care.* 2018;63(12):1485-91. doi: 10.4187/respcare.05656.
60. Imamura S, Inagaki T, Terada J, Nagashima K, Katsura H, Tatsumi K. Long-term efficacy of pulmonary rehabilitation with home-based or low frequent maintenance programs in patients with chronic obstructive pulmonary disease: a meta-analysis. 2020;9(5):2606-15. doi: 10.21037/apm-19-581.

61. Gallefoss F, Bakke PS, Rsgaard PK. Quality of life assessment after patient education in a randomized controlled study on asthma and chronic obstructive pulmonary disease. *Am J Respir Crit Care Med.* 1999;159(3):812-7. doi: 10.1164/ajrccm.159.3.9804047.
62. Dong J, Li Z, Luo L, Xie H. Efficacy of pulmonary rehabilitation in improving the quality of life for patients with chronic obstructive pulmonary disease: evidence based on nineteen randomized controlled trials. *Int J Surg.* 2020;73:78-86. doi: 10.1016/j.ijssu.2019.11.033.
63. Rugbjerg M, Iepsen UW, Jørgensen KJ, Lange P. Effectiveness of pulmonary rehabilitation in COPD with mild symptoms: a systematic review with meta-analyses. *Int J Chron Obstruct Pulmon Dis.* 2015;10:791-801. doi: 10.2147/COPD.S78607.
64. Wu W, Liu X, Wang L, Wang Z, hu jun, Yan J. Effects of Tai Chi on exercise capacity and health-related quality of life in patients with chronic obstructive pulmonary disease: a systematic review and meta-analysis. *COPD.* 2014;1253. doi: 10.2147/COPD.S70862.
65. Jackson D, Turner R. Power analysis for random-effects meta-analysis: power analysis for meta-analysis. *Res Syn Meth.* 2017;8(3):290-302. doi: 10.1002/jrsm.1240.

Appendix 1. Assessment of the 12 TIDieR items for the RCTs included in the meta-analyses.

RCT	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Item 11	Item 12
Breyer et al. (2010)	yes	yes	yes	yes	yes	yes	yes	yes	yes	no	no	no
Finnerty et al. (2001)	yes	yes	yes	yes	yes	yes	unclear	yes	no	no	no	no
Gallo-Silva et al. (2019)	yes	yes	yes	yes	unclear	yes	yes	yes	yes	no	yes	no
Gottlieb et al. (2011)	yes	yes	yes	yes	unclear	yes	unclear	yes	no	no	yes	no
Hospes et al. (2009)	yes	yes	yes	yes	yes	yes	yes	yes	yes	no	no	no
Lahham et al. (2020)	yes	yes	yes	yes	yes	yes	yes	yes	yes	no	yes	no
Li et al. (2018)	yes	yes	yes	yes	unclear	yes	yes	yes	yes	no	yes	yes
McNamara et al. (2013) (land-based PR-ET)	yes	yes	yes	yes	yes	yes	yes	yes	yes	no	no	no
McNamara et al. (2013) (water-based PR-ET)	yes	yes	yes	yes	yes	yes	yes	yes	yes	no	no	no
Pradella et al. (2015)	yes	yes	yes	yes	unclear	yes	unclear	yes	no	no	yes	no
Ringbaek et al. (2000)	yes	yes	yes	yes	yes	yes	yes	yes	yes	no	no	no
Román et al. (2013)	yes	yes	yes	yes	yes	yes	yes	yes	no	no	no	no
Tsai et al. (2017)	yes	yes	yes	yes	yes	yes	yes	yes	yes	no	yes	no
Wadell et al. (2013)	yes	yes	yes	yes	yes	yes	unclear	yes	yes	no	yes	unclear
Wijkstra et al. (1996)	yes	yes	yes	yes	yes	yes	yes	yes	yes	no	yes	no
Xi et al. (2015)	yes	yes	yes	yes	unclear	unclear	yes	yes	no	no	no	no
Yekefallah et al. (2019) (home-based PR-ET)	yes	yes	yes	yes	yes*	yes	yes	yes	unclear	no	unclear	no
Yekefallah et al. (2019) (institution-based PR-ET)	yes	yes	yes	yes	yes*	yes	yes	yes	unclear	no	no	no
Yudhawati and Rasjid Hs (2019)	yes	yes	yes	yes	yes	yes	unclear	yes	no	no	no	no
Zhu et al. (2018)	yes	yes	yes	yes	yes	yes	unclear	yes	no	no	yes	yes

Note: Please refer to TIDieR checklist (32) for further details.

Legend: *Identified in the secondary sources.

Appendix 2. Characteristics of RCTs: type and duration of intervention, intervention at home or in an institution, frequency and duration of sessions including relevant details.

RCT	Intervention	Home-/Institution-based	Duration	Frequency of sessions	Session duration	Details
Breyer et al. (2010)	Nordic walking	Institution	3 mo.	3 / w.	1h	75% of the initial maximum heart rate. Total duration of intervention: 9 months, data assessment after 3 months was used in meta-analysis.
Finnerty et al. (2001)	Walking	Home	3 mo.	1 / w.	1h	Walking program with nine levels, the maximum level being 10 min of rest and then 10 min of walking. Total duration 6 months, assessment after 3 months was used in meta-analysis.
Gallo-Silva et al. (2019)	Water based physical training	Institution	8 w.	3 / w.	30 - 50 min	Intervention consisted of warm-up (10 min) and aerobic exercises - upper limbs, and lower limbs that involved the hips, feet, ankles, hands/wrists, and shoulders (initial duration was eight 20-min sessions, progressing to eight sessions of 30 min and finishing with eight 40-min sessions). The prescribed intensity was based on a Borg CR-10 scale rating of 4 to 6.
Gottlieb et al. (2011)	Physical training	Institution	7 w.	2 / w.	90 min	Endurance training, static circuit training, free brisk walking and breathing techniques. The aim was an intensity of 16-17 on a 20-point Borg scale.
Hospes et al. (2009)	Pedometer-based exercise	Home	12 w.	Individualized - see details	Individualized - see details	Individual pedometer-based exercise counselling program promoting daily physical activities and usual care. Predominantly based on the principles of individualized goal setting and implementation of goals to enhance patients' daily physical activities and to develop a more physically active lifestyle.
Lahham et al. (2020)	Resistance training	Home	8 w.	Goal: 5 / w.	Goal: 30 min.	Work towards achieving the goal of 30 min of whole-body resistance training (upper and lower limb exercises using home stairs for step-ups and sealed water bottles as weights) and record their exercise participation using the home-exercise diary. Training programme calculated at 80% of initial walking speed from the baseline 6MWT. The intensity was gauged using the Borg scale.
Li et al. (2018)	Aerobic training (A), upper limb resistance training (UR), and respiratory training (R)	Home	8 w.	A: 3 / w. UR: 3 / w. R: 1 / d.	A: 5 - 20 min UR: (see details) R: 30 min.	A: 70%-80% of maximum HR (duration: 5 min from the onset, and then accumulate to 20 min.). UR: 0.5 kg-weight load, hold on for 5 s at the end of inspiration and then expire slowly. R: Half-closed-lip abdominal respiratory training and sputum drainage. Health education was included.
McNamara et al. (2013) -land-based PR-ET	Land-based exercise training	Institution	8 w.	3 / w.	60 min.	Warm-up (8 min), lower limb endurance (20 min), rest period (3 min), lower limb endurance (15 min), rest period (2 min), upper limb endurance (10 min), cool down (2 min). Intensity of 80% of the average 6MWT speed either over ground or on a treadmill.
McNamara et al. (2013) -water-based PR-ET	Water-based exercise training	Institution	8 w.	3 / w.	60 min.	Similar to above. Exercise in water and on land was matched as closely as possible for intensity duration and muscle groups trained, considering the different exercise media.
Pradella et al. (2015)	Walking, climbing stairs and upper limb exercises	Home	8 w.	3 / w.	70 min.	Walking (40 min), climbing stairs (15 min), and exercising the arms with an oil can (1 kg) using diagonal movements (15 min).

RCT	Intervention	Home-/ Institution-based	Duration	Frequency of sessions	Session duration	Details
Ringbaek et al. (2000)	Exercise programme (see details)	Institution	8 w.	2 / w.	60 min.	Warming-up, mobility training, coordination tests, dynamic strength exercise of upper and lower extremities and abdominal musculature, stair climbing and jogging as endurance training, stretching and relaxation. The intensity and load of the exercise were individualized so the patients achieved a dyspnoea-score of 4-5 out of 10 on a Borg scale.
Román et al. (2013)	Respiratory physiotherapy + low intensity peripheral muscle training	Institution	3 m.	1 / w.	60 min.	Respiratory physiotherapy (self-conscious breathing control, diaphragmatic breathing control) and exercises for the chest wall and abdominal muscle walls (15 min) and low intensity peripheral muscle training (abdominal and upper and lower limb exercises, shoulder and full arm circling, weight-lifting and other exercises - each exercise was repeated 8-10 times over 45 min).
Tsai et al. (2017)	Supervised group exercise Telerehabilitation training	Home	8 w.	3 / w.	41-55 min + lower limb exercises	Participants received a laptop computer with an in-built camera, a stationary lower limb cycle ergometer, and a fingertip pulse oximeter. Warm-up (5 min) and cardiovascular exercises were performed on lower limb cycle ergometer (15-20 min), followed by the rest period (3-5 min), walking training (15-20 min), rest period (3-5 min) and lower limb strengthening exercises (3 x 10 sit to stand, 3 x 10 squats).
Wadell et al. (2013)	Graduated exercise training for upper and lower limbs and exercises to increase mobility	Institution	8 w.	3 / w.	2.5 h	Graduated exercise training for upper and lower limbs, i.e., walking on treadmill and in corridor, cycle ergometer, arm ergometer, strength/resistance exercises for upper and lower limbs, and mobility exercises. Subjects worked at their highest attainable work rate for the longest tolerable duration by targeting at least a "moderate" intensity of breathing discomfort on the modified 10-point Borg scale.
Wijkstra et al. (1996)	Exercise programme (see details)	Home	12 w.	2 / d.	30 min	Relaxation exercises, breathing retraining, upper limb training, target-flow inspiratory muscle training (IMT - 15 min), and exercise training on a home-trainer (4-12 min). During IMT, the patients had to generate 70% of their maximal inspiratory pressure during 3 s, whilst the unloaded expiration was 4 s.
Xi et al. (2015)	Exercise programme (see details)	Home	12 m.	See details.	See details.	Pursed-lip breathing (three times 5 min per day), abdominal breathing (two times 10 min per day) and upper and lower limb exercises (daily: 5 min each time, gradually increasing to 20 min).
Yekefallah et al. (2019) -home-based PR-ET	Breathing exercises	Home	1 m.	4 / d.	Not specified (see details)	Pursed-lip and diaphragmatic breathing exercises performed at home (morning, noon, evening, and night).
Yekefallah et al. (2019) -institution-based PR-ET	Exercise programme (see details)	Institution	1 m.	3 / w	30 min.	Warm-up (5 min), upper limb strengthening exercises using one- or two-kilogram dumbbells (20 min), cool-down exercises (5 min).
Yudhawati and Rasjid Hs (2019)	Yoga	Institution	12 w.	2 / w.	60 min.	Yoga classes with emphasis on breathing techniques.
Zhu et al. (2018)	Tai Chi	Institution	3 m.	1 / w.	40-50 min	Supervised modified Tai Chi training, adapted to patients with COPD.