

# Efficacy of respiratory tele-rehabilitation in COPD patients: Systematic review and meta-analysis

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## Abstract

Pulmonary rehabilitation (PR) is a proven and effective intervention for chronic obstructive pulmonary disease (COPD). The recent pandemic has raised interest on new services, such as telerehabilitation (Tele-R). The aim of this study was to systematically

review the effects of Tele-R in COPD on: i) exercise capacity evaluated by the 6-minute walk test (6MWT); ii) dyspnea (modified Medical Research Council - mMRC); 3) COPD control (the COPD assessment test - CAT). The analysis compared Tele-R *versus* no rehabilitation and Tele-R *versus* center-based rehabilitation. This meta-analysis was undertaken according to PRISMA recommendations. This pair-wise meta-analysis included data obtained from studies that enrolled 758 COPD patients. The tele-R compared to no rehabilitation improved the 6MWT distance of 48 m (CI: 24, 72;  $p < 0.001$ ) and the mMRC of -1.02U (CI: -1.49, -0.59;  $p < 0.001$ ), and the CAT of -5.74U (CI: -7.42, -0.407;  $p < 0.001$ ). The tele-R compared to center-based rehabilitation showed no difference on 6MWT distance ( $p = 0.563$ ), mMRC ( $p = 0.911$ ), and CAT ( $p = 0.85$ ). In COPD patients, Tele-R is effective in improving exercise tolerance and patient-reported outcomes and it seems to be a valid alternative to center-based rehabilitation, but more studies are needed to better understand how to select the right patients and which kind of Tele-R is more appropriate.

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## Introduction

Pulmonary rehabilitation (PR) is a proven and effective intervention for people with chronic respiratory diseases including chronic obstructive pulmonary disease (COPD) [1]. In COPD patients, PR improves symptoms, disease control, and emotional state [2], although an improvement in activity levels in daily life is not always demonstrable [3].

PR is traditionally delivered by a physiotherapist in a residential hospital or outpatient clinic. However, due to factors related both to the scarcity of territorial rehabilitation facilities and rehabilitation programs and to the logistical or health difficulties of patients, it is very often reserved for the most serious patients only therefore not everyone can access it [4]. In addition, the recent SARS-CoV-2 epidemic has further reduced the number of available rehabilitation facilities, dedicating some of them to COVID-19 patients or reducing the number of beds for the risk of contagion or closing centers. On the other hand, the same epidemic experience has shown how some alternative models of service delivery such as tele-medicine and tele-rehabilitation (Tele-R) can assist and replace medicine in general and rehabilitation in particular [5].

Tele-R is the provision of remote rehabilitation services, using information and communication technologies. There are several models of Tele-R and they can be supplemented with face-to-face rehabilitation [6]. The purpose of all Tele-R is to bring the service

to the patient and not the patient to the service, clinic or hospital.

This meta-analysis aims to evaluate the clinical efficacy of Tele-R in COPD patients and specifically its effectiveness in improving exercise tolerance and patient reported outcomes (PRO). Since Tele-R can be compared both with a group not undergoing rehabilitation (control group - CTRL) and with a group undergoing traditional rehabilitation (center-based rehabilitation), the objective of this meta-analysis is to demonstrate the superiority of Tele-R over the CTRL group and the non-inferiority compared to traditional rehabilitation.

## Methods

### Research strategy and eligibility of studies

This pairwise analysis was performed in accordance with Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P)[7], as shown in the diagram flow shown in Figure 1. This study met all the recommended items reported by the PRISMA-P checklist [8] and submitted to PROSPERO (ID: 276848).

The PICO (Patient problem, Intervention, Comparison, and Outcome) scheme was applied to develop the research strategy and demand of the literature, as previously reported. That is, the “*Patient problem*” included only patients with COPD; “*Intervention*” considered rehabilitation in telemedicine (respiratory Tele-R); “*Comparison*” included patients receiving Tele-R compared to those receiving center-based rehabilitation or no rehabilitation; the “*Outcomes*” included both exercise tolerance and PRO, specifically dyspnea measured as mMRC and CAT. A comprehensive literature search of randomized controlled trials (RCTs) was performed to consider respiratory Tele-R in patients with respiratory diseases. Prospective or retrospective non-randomized studies were discarded.

The search was performed in MEDLINE and Google Scholar, in order to predict the relevant studies published until August 30<sup>th</sup> 2021.

The searched words were [telerehabilitation OR tele-rehabilitation] AND pulmonary rehabilitation” and the search string was as follows: (“telerehabilitation”[MeSH Terms] OR “telerehabilitation”[All Fields] OR (“telerehabilitation”[MeSH Terms] OR “telerehabilitation”[All Fields] OR (“tele”[All Fields] AND “rehabilitation”[All Fields]) OR “tele rehabilitation”[All Fields])) AND (“lung”[MeSH Terms] OR “lung”[All Fields] OR “pulmonary”[All Fields]) AND (“rehabilitant”[All Fields] OR “rehabilitants”[All Fields] OR “rehabilitate”[All Fields] OR “rehabilitated”[All Fields] OR “rehabilitates”[All Fields] OR “rehabilitating”[All Fields] OR “rehabilitation”[MeSH Terms] OR “rehabilitation”[All Fields] OR “rehabilitations”[All Fields] OR “rehabilitative”[All Fields] OR “rehabilitation”[MeSH Subheading] OR “rehabilitation s”[All Fields] OR “rehabilitational”[All Fields] OR “rehabilitator”[All Fields] OR “rehabilitators”[All Fields])).

Subsequently, the research was limited only to COPD by eliminating the articles that referred to other pathologies.

In addition, previously published meta-analysis citations and literature reviews on the subject were verified to select additional relevant studies [9,10].

### Selection of studies

All RCTs concerning Tele-R in patients with COPD were selected in accordance with previously mentioned criteria and

included in the quantitative analysis. Two reviewers independently audited the studies reviewed and any differences of opinion on the selection of studies were resolved by consensus.

### Data extraction

Data from the included studies were extracted and controlled for study characteristics, number and characteristics of patients analyzed, age, sex, forced expiratory volume in 1 second (FEV<sub>1</sub>), 6MWT and PRO. Data were extracted in accordance with recommendations of Data Extraction for Complex Meta-anALysis (DECiMAL) [11].

### Endpoint

The main endpoints of this pairs meta-analysis were the impact of Tele-R in patients with COPD on exercise tolerance, measured as the distance covered in meters during 6MWT and on PRO evaluated through questionnaires (CAT, mMRC).

### Risk of bias

The heterogeneity test ( $I^2$ ) was performed to quantify the dissimilarity between studies, as previously reported [12].

### Data summary and analysis

A pairs meta-analysis was performed to determine the impact of Tele-R in patients with COPD. The results were expressed as mean difference (MD) and 95% confidence interval (95%CI).

Since the data were selected from a number of studies performed by researchers operating independently and it is not possible to assume a common effect size, a binary model of random effects was used to balance the weights of the studies and adequately estimate 95%CI of the average distribution of the effect of PR on the variables studied [13].

OpenMetaAnalyst software [12] was used to perform meta-analysis in pairs and to make data graphs. Statistical significance was assessed for  $p < 0.05$  and moderate to high levels of heterogeneity were taken into account for  $I^2 > 50\%$ .

## Results

### Studies’ characteristics

Of the 26 studies identified as potentially eligible in the initial research, only 8 studies were considered eligible for quantitative synthesis, the main characteristics of the studies are summarized in Table 1 and Figure 1. Overall, this meta-analysis included data obtained from eight RCT studies that enrolled 758 patients.

Specifically, 4 RCT [14-17] compared Tele-R to patients who did not perform any rehabilitation and 3 RCT [9,18,19] compared Tele-R to an active group who perform center based rehabilitation. The Vasalipoulou *et al.*’ study [20] included both groups and data were analyzed according the group to which they belonged.

### Effect of tele-rehabilitation vs control group on exercise tolerance

Four studies [14,16,17,20] were included in the evaluation of the distance traveled at 6MWT after Tele-R compared to CTRL with an improvement of 33 meters (CI: -9, +75;  $p = 0.123$ ), but a high level of heterogeneity ( $I^2 = 82\%$ ,  $p < 0.01$ ) (Figure 2a). Removing the Cameron-Tucker *et al.*’s study [16] the improvement turns out to be 48 meters (CI: 24, 72;  $p < 0.001$ ) and the heterogeneity decreased to a not significant level ( $I^2 = 49\%$ ,  $p < 0.35$ ) (Figure 2b).

**Table 1. Demography and characteristics of patients, basic features of studies.**

NCT number identifier; first author, year	Study characteristics (type of randomization)	Duration of study, weeks	Patients analyzed	Patients' characteristics	Age, years $\pm$ SD	FEV <sub>1</sub> , % $\pm$ SD	Male, %	Tele-rehabilitation	Comparison group	Investigated outcome
NCT02289618, Bernocchi, 2018	RCT (1:1)	16	112	Post-rehabilitation maintenance program in COPD patients with heart failure	70.5 $\pm$ 9.2	66.4 $\pm$ 17.5	82	A weekly phone call made by a nurse offering advice on diet, lifestyle and therapy, and a weekly phone call made by a physiotherapist checking the level of training once a week and planning the targets for the following week.	No rehabilitation	6MWTmMRCCAT
NTR2440, Tabak, 2013	RCT (1:1)	4	34	Stable COPD	66.5 $\pm$ 7.3	52.6 $\pm$ 13.7	63	Center based rehabilitation plus Tele-R, which consisted of monitoring patients through an electronic "activity coach" system equipped with an accelerometer, a smartphone with connection to a portal to monitor daily activities and an electronic diary.	Just center-based rehabilitation	mMRC
NCT02706613, Bourne, 2017	RCT (2:1)	6	90	COPD	70.2 $\pm$ 8.2	59.6 $\pm$ 21.9	62	Rehabilitation through an online portal with the same physiotherapist who provided services to the group in presence and educational sessions on the anatomy and physiology of the lungs, instructions on pathology, on the management of exacerbations, anxiety and depression and on specific techniques.	Center based rehabilitation	6MWTmMRC CAT
ACTRN12611001034921, Cameron-Tucker, 2018	RCT (1:1)	8	65	Stable COPD	69.0 $\pm$ 8.6	N/A	45	A phone call twice a week performed by a community nurse acting as a mentor nurse.	No rehabilitation	6MWT CAT
NCT02667171, Hansen, 2016	RCT (1:1)	10	134	Stable COPD	68.3 $\pm$ 9.0	33.1 $\pm$ 9.4	45	A group-based, supervised and standardized program performed by patients in their homes three times weekly for 10 weeks via a videoconference software system installed on a single touch screen.	Center based rehabilitation	6MWT CAT
NCT02618746, Vasilopoulou, 2017	RCT (1:1:1)	48	150	Post-rehabilitation maintenance program in COPD	65.8 $\pm$ 8.3	51.0 $\pm$ 20.0	79	144 sessions performed over 12 months, including: 1) individualised action plan; 2) physical exercise sessions to remote monitoring; 3) access to the call centre 5 days per week, 10 h per day; 4) psychological support; and 5) dietary and self-management advice.	- No rehabilitation - Center-based rehabilitation	6MWTmMRCCAT

To be continued on next page

Table 1. Continued from previous page.

NCT number identifier; first author, year	Study characteristics of study, analyzed (type of randomization)	Duration of study, weeks	Patients characteristics	Age, years ± SD	FEV <sub>1</sub> , % ± SD	Male, %	Tele-rehabilitation	Comparison group	Investigated outcome
ACTRN12612001263886, Tsai, 2016	RCT (1:1)	8	Stable COPD	74.0±8.5	64.0±21.0	49	Group sessions supervised three times a week through a videoconferencing system with saturation monitoring. Participants could both communicate with the physiotherapist and with other participants.	No rehabilitation	6MWTmMRCCAT
NCT01423227, Holland, 2016	RCT (1:1)	166	Stable COPD	69.0±11.5	50.5±19.0	60	Home visit by a physical therapist to set exercise goals, evaluate the inhaler's technique, and supervise the first exercise session, followed by seven structured phone calls once a week by a physical therapist, using a motivational interview approach and a pedometer to record the distance traveled	Center-based rehabilitation	6MWTmMRC

6MWT, 6-minute walk test; mMRC, modified British Medical Research Council Questionnaire; CAT, COPD assessment test; COPD, chronic obstructive pulmonary disease; Tele-R, Tele-Rehabilitation; RCT, randomized controlled trial; SD, standard deviation; N/A, not available.

**Effect of tele-rehabilitation vs control group on PRO**

Four studies [14,15,17,20] were included in the assessment of mMRC after Tele-R compared to CTRL with an improvement of -0.75 U (CI: -1.43, -0.08; p=0.029), but with a high level of heterogeneity (I<sup>2</sup>=91%, p<0.001) (Figure 3a). Removing the Bernocchi's study [14] the improvement turns out to be -1.02U (CI: -1.49, -0.59; p<0.001), but the heterogeneity decreased to a moderate grade (I<sup>2</sup>=69%, p=0.04).

Four studies [14,16,17,20] were included in the evaluation of CAT after telerehabilitation compared to CTRL with an improvement of -4.04 U (CI: -7.15, -0.93; p=0.011), but with a high level of heterogeneity (I<sup>2</sup>=77%, p<0.005) (Figure 3b). Removing the Cameron-Tucker *et al.*'s study [16] the improvement turns out to be -5.74U (CI: -7.42, -0.407; p<0.001), and the heterogeneity decreased to a not significant level (I<sup>2</sup>=0%, p=0.407) (Figure 3c).

**Effect of tele-rehabilitation vs center-based rehabilitation on exercise tolerance**

Four studies [9,18-20] were included in the assessment of distance traveled at 6MWT (6MWTd) after Tele-R compared to center based rehabilitation with an improvement of 0.061 meters (CI: -0.15, 0.27; p=0.563) (Figure 4a).

**Effect of tele-rehabilitation vs center-based rehabilitation on PRO**

Three studies [9,18,20] were included in the assessment of mMRC after Tele-R compared to INT with an improvement of -0.29 U (CI: -0.53, +0.47; p=0.911) (Figure 4b); the same were included in the evaluation of CAT after telerehabilitation compared to CTRL with an improvement of -1.83 U (CI: -3.28, -0.38; p=0.85) (Figure 4c).

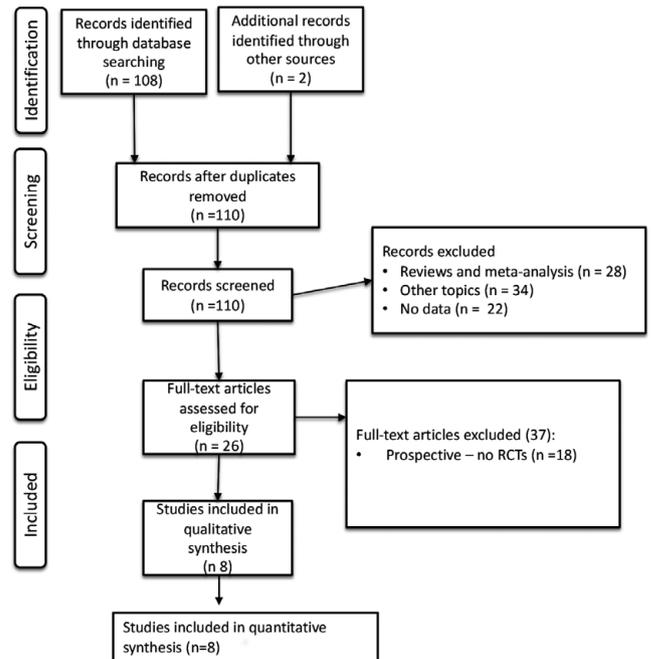


Figure 1. PRISMA-P flow diagram.

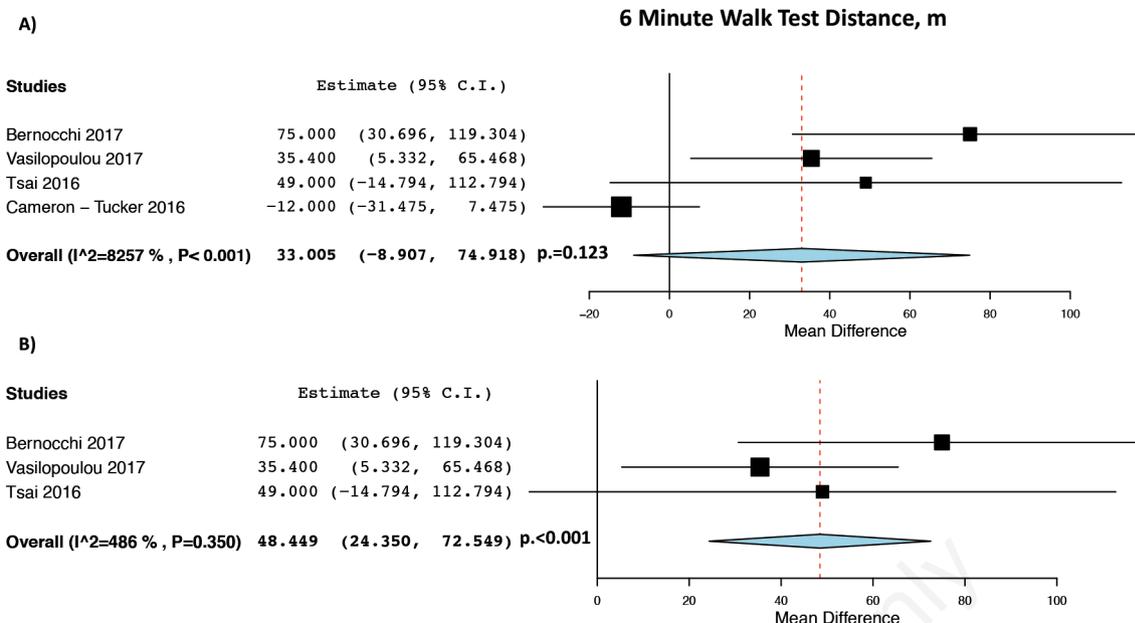


Figure 2. Effect of tele-rehabilitation *vs* control group on exercise tolerance; a) all studies; b) without the Cameron-Tucker *et al.*'s study.

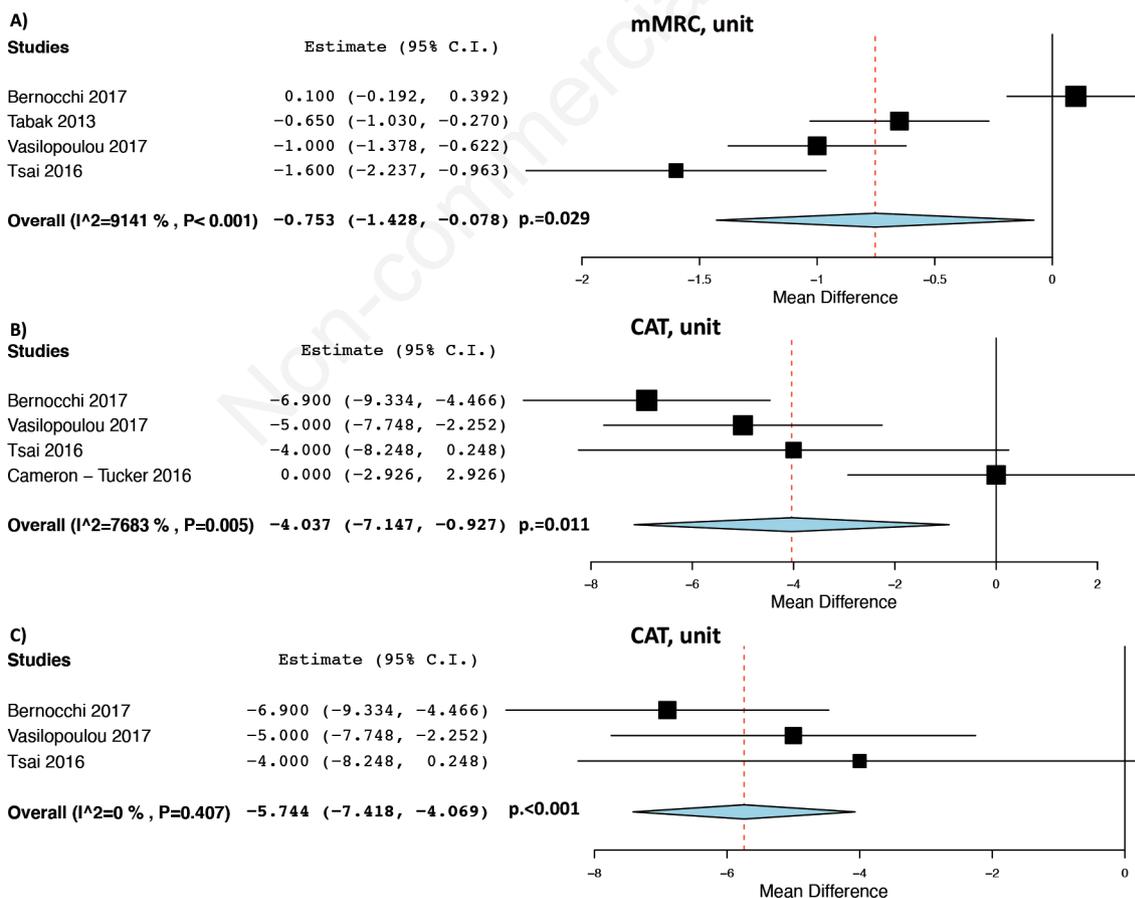


Figure 3. Effect of tele-rehabilitation *vs* no rehabilitation group on: a) modified Medical Research Council (mMRC); b) COPD assessment test (CAT); c) CAT without the Cameron-Tucker *et al.*'s study.

## Discussion

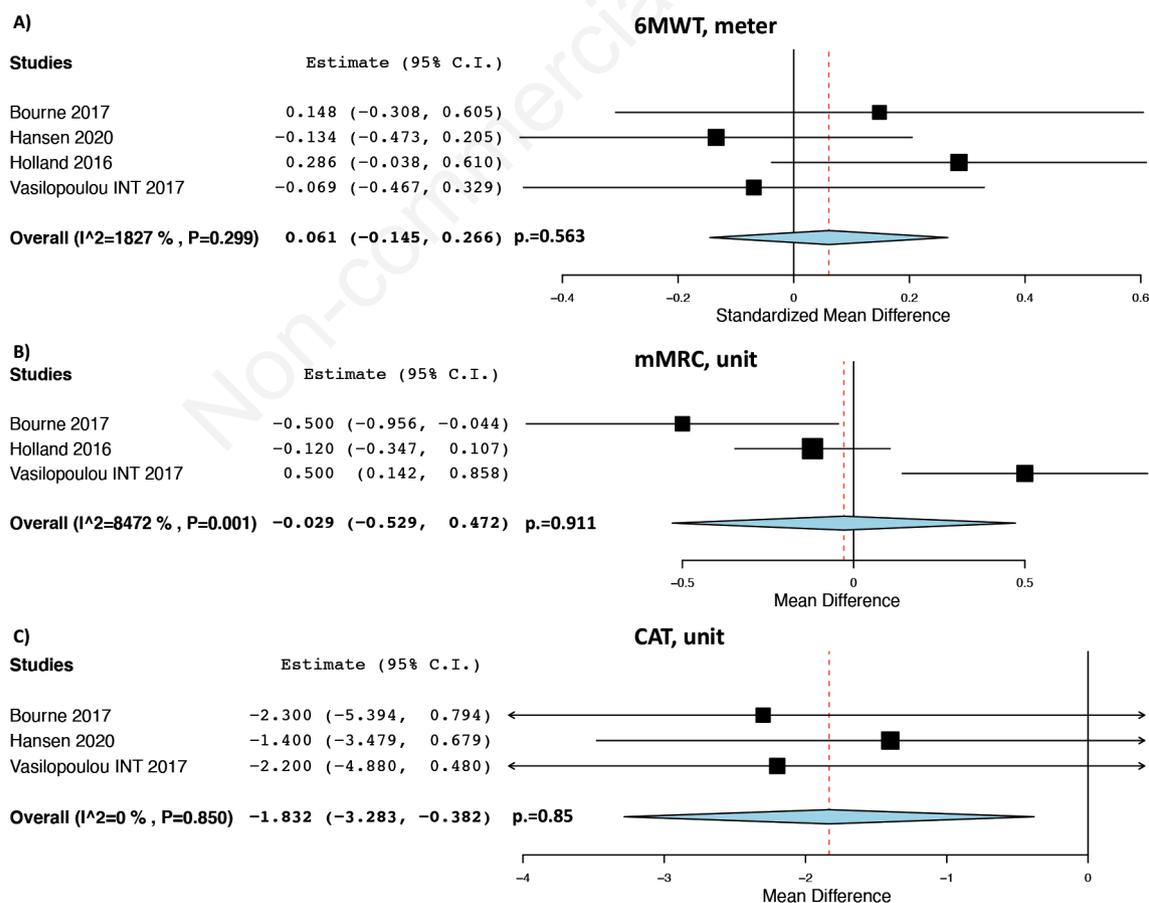
This study shows that Tele-R improves exercise tolerance and PRO in COPD patients compared to the no-rehabilitation group and that it has the same effectiveness as center-based rehabilitation performed face to face.

Tele-R is a new model of rehabilitation that has the advantage of being performed at home, of creating less discomfort for patients, especially fragile ones, and offers new opportunities for pulmonary rehabilitation to break down those barriers related to the patient or to geographical restrictions or mobility itself [21]. This meta-analysis shows that Tele-R is a valid option for patients who would not undergo any rehabilitation as it improves exercise tolerance by about 48 meters (the minimal clinical important difference (MCID) - is 25-33 meters [22]) and CAT by 5.7 points (MCID estimated around 2 points [23]) compared to no rehabilitation.

Moreover, our meta-analysis shows that Tele-R is not inferior to center-based rehabilitation and in this perspective, it could be a valid alternative for patients who cannot do rehabilitation on site or for mixed programs that provide center-based rehabilitation and Tele-R as maintenance therapy. However, Tele-R is a very generic term that includes different programs and possible methods ranging from telephone monitoring, to the application of instruments that communicate electronically to real online physiotherapy sessions [21]. Although all the studies were analyzed as a whole, they

present different Tele-R programs that may justify some differences in results. For example, in the Cameron-Tucker *et al.*'s study [16] conducted on 65 clinically stable COPD patients, Tele-R showed no success compared to the CTRL, but Tele-R consisted of a phone call twice a week performed by a community nurse acting as a mentor and the same authors pointed out that it was not possible just with phone calls alone to monitor the effectiveness of the intervention and that probably a physiotherapist trained in this field would have been more effective. Completely opposite results were found by Tsai *et al.* [17], who compared Tele-R in 19 patients with stable COPD to a similar group of 17 COPD patients who did not receive physiotherapy. In this case the Tele-R consisted of group sessions three times a week supervised through a videoconferencing system with saturation monitoring. Participants could both communicate with the physiotherapist and with other participants. This study showed a significant improvement in exercise tolerance measured with Endurance Shuttle Walk Test, but not with 6MWT and an improvement in some PROs such as Hospital Anxiety Depression Score.

Another problem of PR is the ability to maintain long-term effects after its end, and on the other hand long-term access and utilization of PR is limited by insufficient funding, resources, or other patient-related barriers. Benefits of maintenance exercise training are evident [4], but the dropout rate is high and effects vanish after a year [24,25]. Tele-R could be very useful as a home extension of hospital rehabilitation. Vasilopoulou *et al.* [20] com-



**Figure 4.** Effect of tele-rehabilitation *vs* center-based rehabilitation group on: a) six minute walk test (6MWT) distance; b) modified Medical Research Council (mMRC); c) COPD assessment test (CAT).

pared a group of 47 stable COPD patients followed for 12 months with maintenance Tele-R after 2 months of PR, with a group of patients who continued PR in the hospital (50 patients) and with another group (50 patients) who do not perform any rehabilitation, not even the initial one. The conclusions of this study are very similar to those of our meta-analysis, confirming the superiority in terms of effectiveness of Tele-R compared to the CTRL that did not perform maintenance rehabilitation, and the non-inferiority compared to center-based maintenance respiratory rehabilitation. A similar study was conducted by Bernocchi *et al.* [14], who explored the effect of four months of Tele-R post-rehabilitation as a maintenance program in 56 COPD patients with heart failure compared to a similar group of 56 patients followed according to normal clinical practice. This study was very positive with regard to Tele-R both on exercise tolerance (difference between the two groups 75 m,  $p < 0.001$ ), and on different indices taken into account such as MRC ( $p = 0.0500$ ), PASE ( $p < 0.005$ ), Barthel ( $p < 0.001$ ), MLHFQ ( $p < 0.001$ ) and CAT ( $p < 0.001$ ) and demonstrated that the Tele-R program not only had positive effects, but also that these effects were maintained for at least another two months after the suspension of the program.

Both these studies are excellent models of integration between on site rehabilitation followed by Tele-R. The availability of multiple effective models may allow patients to be offered the program in which they are most likely to succeed, which may vary based on factors such as disease stage, comorbidities, psychosocial characteristics, digital literacy, and patient choice.

Vasilopoulou *et al.* [20], for example, implemented patient tele-consultation based on vital sign data transmitted to an ICT web-based platform via patients' tablets and feedback to maintain progress in respect to executing home exercise drills. Differently, the Bernocchi *et al.*'s Tele-R consisted of a weekly phone-call by the nurse, and an exercise program monitored weekly by the physiotherapist [14]. Tabak *et al.* [15] monitored patients through an electronic "activity coach" system equipped with an accelerometer, a smartphone with connection to a portal to monitor daily activities and an electronic diary. Bourne *et al.* [18] provided Tele-R through an online portal with the same physiotherapist who provided services to the group in presence (to ensure uniformity of the service). In addition, the portal provided educational sessions on the anatomy and physiology of the lungs, lessons on pathology, on the management of exacerbations, anxiety and depression and on specific techniques such as the *Active Cycle of Breathing Technique*. Hansen *et al.* [19] supervised patients in their homes three times a week for 10 weeks via a videoconferencing software system installed on a single touch screen. Holland *et al.*'s [9] Tele-R consisted of a home visit by a physical therapist to set exercise goals, evaluate the inhaler technique, and supervise the first exercise session, followed by seven structured phone calls once a week by a physical therapist, using a motivational interview approach and a pedometer to record the distance traveled. Several forms of Tele-R have been experimented, from the simplest ones that consisted of just a phone call to the more complex ones equipped with accelerometers, dedicated portals, or video classes. Although new models offer the opportunity to incorporate innovations in behavioral changes and education, it is also a limit for the meta-analysis which considers any intervention as a Tele-R, without any distinction. The paucity of studies does not make any sub-analysis possible.

Another point in favor of Tele-R is the reduction of costs. Although this meta-analysis did not make a cost-benefit analysis, there is still limited evidence about its economic evaluation. The existing recent economic analyses from RCTs showed contrasting results in cost-effectiveness [26,27]. Haesum *et al.* [28] evaluated

the economic impact of Tele-R in the Danish TELE- KAT project (a telehealth project on COPD patients) and demonstrated a higher cost-effectiveness of Tele-R compared to the conventional rehabilitation program, mainly reducing hospital admission, ambulatory and emergency physician contacts. However, Tele-R has a cost, which must be weighed against the economic benefits such as reduction in hospitalizations and mortality. Furthermore, if it were extended too widely, to the whole population, it could lose its economic advantages.

This meta-analysis has some limitations. Tele-R programs were very different in schedule and duration but, due to the scarcity of RCTs, they were considered together. As pointed out in the discussion, the term Tele-R includes very different interventions ranging from contacting the patient every day by phone to integrated programs including pre-program visits and education and home instrumentation. All these differences probably have an impact on the effectiveness of Tele-R but currently, due to the few studies, it is not possible to know which intervention is better, nor if there are ineffective interventions. Moreover, the duration of Tele-R programs ranges from 4 to 48 weeks. It was not possible to normalize this data because it is not possible to assume a linear growth of the parameters considered (tolerance to the exercise or dyspnea) during the rehabilitation program, therefore only the parameters at the beginning and at the end of the intervention were considered.

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## Conclusions

This study demonstrates the effectiveness of Tele-R in improving stress tolerance and symptom control in COPD patients compared to the CTRL and demonstrates the non-inferiority of Tele-R compared to respiratory rehabilitation performed in presence. The scarcity of available studies does not allow to date to distinguish the different effectiveness between the different Tele-R programs in terms of necessary equipment, exercises and duration of the program.

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