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# Use of Singing for Lung Health as an alternative training modality within pulmonary rehabilitation for COPD: an RCT

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**Take-home-message:**

Singing for Lung Health was non-inferior to physical exercise training in short-term improvement of 6-Minute Walk Test in COPD patients attending pulmonary rehabilitation. In both groups, effect was related to high adherence.

## ABSTRACT

**Background:** Pulmonary rehabilitation (PR) is a cornerstone in Chronic Obstructive Pulmonary Disease (COPD) management. However, PR adherence is generally low, and barriers include availability, economic issues, motivation, and inability to attend or perform physical training. Therefore, alternative, evidence-based PR activities are required. Singing may have benefits within quality of life (QoL), respiratory control, and wellbeing in COPD, but impact on PR key outcome, physical exercise capacity, is uncertain.

**Methods:** In this RCT (NCT03280355), we investigated effectiveness of 10-weeks of PR, including either "Singing for Lung Health" (SLH)-training or standard physical exercise training (PExT). Primary outcome: Change in exercise capacity (6-Minute Walk Test, distance (6MWD)) from baseline to post-PR. Secondary outcomes: Changes in QoL (St George's Respiratory Questionnaire (SGRQ)), Hospital anxiety and depression score (HADS), lung function, dyspnoea, and adherence.

**Results:** We included 270 COPD patients, and 195 completed the study. Demographics across groups were comparable, and both groups improved significantly in 6MWD and SGRQ. SLH was non-inferior to PExT in 6MWD (13.1 metres ±36.3/14.1 metres ±32.3; $p$=0.81 [95%CI=-7.28;9.30]) with 21.8% respectively 25.0% ($p$=0.57) reaching 6MWD Minimal Important Difference of 30 metres. We found no significant between-group differences concerning SGRQ, HADS, lung function, dyspnoea, or adherence.

**Conclusions:** Our study suggests that SLH is non-inferior to PExT in improving 6MWD during a 10-weeks PR programme. Future studies addressing reproducibility, long-term effects and health-economics are needed.



## KEYWORDS

Chronic obstructive pulmonary disease, Pulmonary rehabilitation, Randomised controlled trial, Singing, Quality of life, Six-Minute Walk Test

## INTRODUCTION

The prevalence of respiratory diseases is increasing rapidly, and chronic obstructive pulmonary disease (COPD) is now the third leading global cause of death [1]. COPD is associated with hospitalisation, mortality, multimorbidity, reduced quality of life (QoL), increased sick leave, reduced physical activity, and significantly increased economic costs for patients and society [2].

The central role of PR with physical exercise training (PExT) in COPD management is stated in the joint guidelines published by American Thoracic Society (ATS) and European Respiratory Society (ERS) [3]. PR supports lifestyle changes, improves exercise capacity, QoL and dyspnoea [1, 3]. Although well-documented to impact walking distance, QoL, and dyspnoea control positively, PR adherence is challenged by lack of access, costs, and participants' comorbidities and lack of motivation [3-6]. Only around 10% of those who would benefit from PR are currently referred. Approximately half of those referred do not show up and of those actually showing up, one third fails to complete [8]. It is a key priority to increase availability of PR and to develop alternative, motivating, and personalised solutions to supplement standard PR [1, 9].

Singing for people with respiratory disease is perceived to be beneficial in managing dyspnoea, increasing wellbeing and QoL, and reducing social isolation in COPD [10–20]. In regard to physical outcomes, singing may improve respiratory muscle strength, coordination, and performance [14, 15, 21–23], reduce hyperinflation [10, 24], improve lung function [25], and may enhance functional exercise capacity in COPD [14, 26]. The specific methodological concept "Singing for Lung Health" (SLH) was developed in the UK [10, 24, 27, 28], and has become increasingly popular, although heterogenous singing approaches are applied in other countries [24, 29, 30]. The growing body of research on SLH and singing in COPD is mostly based on small-scale and descriptive studies without primary focus on key objective variables, relevant in PR research [1, 10, 14, 24, 29].

In the present study, the objective was to investigate Singing for Lung Health as an alternative to conventional Physical Exercise Training as part of pulmonary rehabilitation in COPD, hypothesising that SLH is non-inferior compared to Physical Exercise Training with regard to change from pre to post 10-week PR programme, and measured by key objective variables in PR: Exercise capacity, QoL, anxiety and depression, lung function, dyspnoea, and adherence.

# METHODS

### Study design and oversight

Between August 2017 and May 2019, we conducted a multicentre, randomised, controlled, clinical trial in Denmark, comparing SLH with PExT (registered at ClinicalTrials.gov: NCT03280355). The study was performed in accordance with the Helsinki 2 declaration, and approved by the Regional Committee on Health Research Ethics, Region Zealand, Denmark (no. SJ-597) and by the Danish Data Protection Agency (no. REG-049-2017).

### Participants

In Denmark, PR in COPD is almost exclusively offered by community-based services [31]. Therefore, we enrolled 11 community PR services distributed across Denmark and screened for eligibility among patients with COPD referred for PR. Inclusion criteria were: a doctor's diagnosis of COPD (according to GOLD criteria [15], and see Table S1)), referral for and ability to attend PR, and acceptance of randomisation. Exclusion criteria were: 1) unstable coronary heart disease, 2) severe cognitive disabilities, 3) inability to speak or understand spoken/written Danish, and 4) participation in lung choir singing or PR (or other structured, disease-related physical training) within the previous six months. Uncertainty in the interpretation of the General Data Protection Regulation (GDPR) in European Union law (which was implemented in EU during our trial) resulted in loss of data on reasons for declining: some centres refused to record data on non-participating citizens, and other centres deleted already obtained data due to fear of breaking the then new GDPR law.

### Randomisation and blinding

Given that PR is performed as a group-based activity, randomisation to either SLH or PExT was performed across the planned number of PR classes as clusters, each representing approximately 10 participants. The randomisation procedure was performed by the study investigator (MK) using sequentially numbered, closed envelopes, and supervised by the principal investigator (UB). Randomisation was concealed at baseline to local health professionals and participants, and the study nurse was blinded to randomisation both at baseline and follow-up.

### Data collection procedure

At baseline, participants were assessed using objective tests and completed patient-reported questionnaires and data sheets on socio-demographic information, medication usage, and expectations

towards benefits of singing. All assessments were repeated at follow-up. One designated study nurse did all objective assessments and collected all data from all sites within two weeks before the onset of PR and again within two weeks after programme termination. Data were registered in web-based software (SurveyXact®, Rambøll Management Consulting, Aarhus, Denmark).

**Outcomes and measures**

The primary study outcome was change in exercise capacity from baseline to follow-up measured as change in 6-Minute Walking Test Distance (6MWD, minimal important difference, MID: 30 metres) [32]. Secondary outcomes were changes in Quality of Life, measured by St. George's Respiratory Questionnaire (SGRQ); Anxiety and Depression, measured by Hospital Anxiety and Depression Scale (HADS); Lung function and dyspnoea, measured by Forced Expiratory Volume in one second (FEV1 in mL, and as percentage expected: FEV1%), modified Medical Research Council Dyspnoea Scale (mMRC), and modified BORG-CR10-dyspnoea scale; and, finally, adherence to PR. See Table S1 for details and interpretation.

**Pulmonary rehabilitation**

Both study groups received a 10-week PR course that included either SLH or PExT twice weekly*, i.e.* a total of 20 sessions, delivered at the local community PR service. Sessions lasted 90 minutes and included individual supervision and guidance. In addition, both study groups received identical educational sessions as part of PR, attending once a week: Lifestyle changes, disease management, guidance on managing daily life, smoking cessation, inhaler technique, and dyspnoea control manoeuvres [1]. The PR content delivered to each study group is reported in Table 1 and in the Consensus on Exercise Reporting Template (CERT) [33] (Appendices S2 and S3).

**Table 1: Overview of content in the two study groups**

| | Singing for Lung Health | Physical exercise training |
|---|---|---|
| Per session (minutes) * | 90 | 90 |
| Warm-up exercise (body) | x | x |
| Warm-up exercise (voice) | x | - |
| Breathing techniques | x | x |
| Handling dyspnoea | x | x |
| Posture | x | x |
| Resting positions | x | x |
| Endurance exercises (circuit/interval) ** | x | x |
| Respiratory muscle training | x | - |
| Strength exercises and limb endurance training | - | x |
| Home exercise instructions/continuation of physical activity | x | x |
| Muscle stretching | x | x |
| Relaxation and body awareness | x | x |
| Singing | x | - |
| Education and self-management as part of PR *** | x | x |

**Table 1 text:**

* Dose of intervention for both groups was 90 minutes twice weekly during 10-weeks. ** Both groups trained coordination of breathing and use of pursed lip breathe (resistance on exhalation). SLH group did respiratory muscle training (resistance on inhalation). PExT group did strength exercises and limb endurance training. Endurance training was walking, stepping, stair climbing, exercise bikes, and if possible: jogging, cross trainer, and/or row machine. *** Dose of education and self-management for both groups varied between 60-120 minutes once weekly for 10-weeks. Content of course: Knowledge about COPD, behaviour change, smoking cessation, correct use of inhaler devices, nutrition, sexuality, handling of stress and anxiety, early recognition of exacerbation, decision-making and taking action on symptoms, goals of motivating, and maintenance post-PR.

*Singing for Lung Health*

SLH in the intervention arm was delivered by professional singing teachers who had all been specially trained before study initiation by the developers of the UK SLH-programme [10, 24, 27, 28]. SLH included physical, vocal, and breathing exercises – with a focus on improving strength, endurance, and flexibility of the respiratory muscles. SLH was carefully adapted to the respiratory challenges in COPD and included movement and/or dancing. Each session consisted of 20 minutes of physical warm-ups, 20 minutes of vocal warm-up with rhythm and pitch games, 40 minutes of singing, and 10 minutes of cooling down, *e.g.*, mindfulness or relaxation.

*Physical exercise training*

PExT in the control arm was delivered by local, experienced physiotherapists and conducted in accordance with Danish national clinical PR guideline [34], in the form of supervised strength and endurance training to enhance exercise tolerance and capacity [35–37], with modifications based on preferences, local decisions, and individual tailoring. Each session consisted of 20 minutes of physical warm-up, 60 minutes PExT including handling of dyspnoea, and 10 minutes of cooling down.

**Statistics**

An *a priori* sample size calculation (power 95%, 2-sided alpha 5%, and non-inferiority margin: 8%) estimated a requirement of 87 participants in each study group (drop-out rate: +20% *i.e.* total sample size *n*=220) to detect a between-group 6MWD difference of MID (30 metres) in a non-inferiority design [38]. Continuous data were described as mean ± standard deviation (SD) and tested using *Student's* t-test, and categorical data as number and percentage and tested using $Chi^2$-test. The primary outcome was analysed according to the intention-to-treat principle. Within-group changes from baseline to follow-up were assessed using paired tests. Missing data were handled with last observation carried forward or next observation carried backward [39].

Logistic regression was used to test the relationship between training modality and achieving MID of the primary outcome. A multilevel mixed-effects logistic regression model was constructed to adjust for potential confounders, including age, sex, GOLD class, mMRC at baseline, 6MWD at baseline categorised into quartiles, body mass index (BMI), expectations towards benefits of singing, adherence to training (fixed effect variables), and training centre (random effects variables). Unless otherwise stated, no significant interactions were found. Differences in adherence to training were evaluated, including baseline characteristics of patients with high adherence (≥75%), and factors associated with high adherence were analysed using multivariable logistic regression. Sub-group analyses of the primary outcome included: 1) a per-protocol analysis excluding patients who dropped out before follow-up visit; 2) analyses of patients with high adherence; 3) analyses of patients with high expectations towards benefits of singing, and 4) analyses excluding patients who never attended training (zero adherence).

Statistical analyses were performed using SPSS 26.0, IBM, Chicago, USA; and STATA/IC 16.1, StataCorp LLC, Texas, USA. Statistical significance was reached at $p<0.05$.

Blinded results (presented as Treatment 0 compared to Treatment 1) of the study were presented to the research group, who interpreted the blinded results [40].

# RESULTS

**Participants**

*Insert Figure 1:* *Consort Flow Diagram*

More than half of the participants were females (62.2%), mean values for age was 69.5 ± 8.4 years, BMI 27.8 ± 6.0, pack years 40.5 ± 21.3, FEV1% predicted 51.4% ± 16.8%, 6MWD 382.3 ± 102.4 metres and 66.3% reported having positive expectations towards benefits of singing. The two study groups were comparable at baseline, except for lower lung function in the SLH group (Table 2 and Appendix S4). As drop-out rates were higher than expected, we continued inclusion to 270 participants in total (intention-to-treat population) to ensure sufficient power for the primary endpoint. Total dropout rate was 28% (*n*=75) and 195 completed the study (Table 2). Across the 11 participating community PR services, 29 PR classes were enrolled (median size: 9 patients; range 5-16). Four participants did not perform baseline 6MWD; however, their data were otherwise complete and they were included in secondary outcomes analyses (Figure 1). No adverse events were reported.

**Table 2: Baseline characteristics in intention-to-treat-population – Singing for Lung Health (SLH) vs. Physical Exercise Training (PExT)**

| | Singing for Lung Health (SLH) (n=145) | | Physical Exercise Training (PExT) (n=125) | | Between-group difference (*p*-value) |
|---|---|---|---|---|---|
| **Age, years** | 70.2 | ±8.8 | 68.8 | ±8.0 | 0.19 |
| **Female sex, n (%)** | 84 | (57.9%) | 84 | (67.2%) | 0.13 |
| **BMI** | 28.0 | ±6.2 | 27.7 | ±5.8 | 0.63 |
| **Smoking Status, n (%)** | | | | | |
| Current | 38 | (26.2%) | 29 | (23.2%) | 0.63 |
| Former | 99 | (68.3%) | 86 | (68.8%) | |
| Never | 8 | (5.5%) | 10 | (8.0%) | |
| **Pack years** | 41.0 | ±20.8 | 39.9 | ±22.0 | 0.68 |
| **FEV1 (% of predicted)** | 49.5 | ±16.9 | 53.6 | ±16.6 | 0.05 |
| **GOLD classification, n (%)** | | | | | |
| Class 1 | 2 | (1.4%) | 7 | (5.6%) | 0.03 |
| Class 2 | 68 | (46.9%) | 66 | (52.8%) | |
| Class 3 | 50 | (34.5%) | 44 | (35.2%) | |
| Class 4 | 23 | (16.0%) | 8 | (6.4%) | |
| **mMRC, n (%)** | | | | | |
| 0 | 6 | (4.1%) | 7 | (5.6%) | 0.52 |
| 1 | 42 | (29.0%) | 43 | (34.4%) | |
| 2 | 47 | (32.4%) | 41 | (32.8%) | |
| 3 | 19 | (13.1%) | 9 | (7.2%) | |
| 4 | 31 | (21.4%) | 25 | (20.0%) | |
| **Medication, n (%)** | | | | | |
| LAMA | 102 | (70.3%) | 89 | (71.2%) | 0.89 |
| LABA | 110 | (75.9%) | 99 | (79.2%) | 0.56 |
| ICS | 71 | (49.0%) | 59 | (47.2%) | 0.81 |
| OCS | 9 | (6.2%) | 4 | (3.2%) | 0.27 |
| Roflumilast | 0 | (0.0%) | 1 | (0.7%) | 1.00 |
| Theophylline | 2 | (1.6%) | 0 | (0.0%) | 0.21 |
| **Home-oxygen therapy, n (%)** | 6 | (4.1%) | 3 | (2.4%) | 0.51 |
| **Positive expectations towards benefits of singing, n (%)** | 94 | (64.8%) | 85 | (68.0%) | 0.61 |

## Table 2 text:

Data are presented as mean ±SD unless otherwise stated. BMI: body mass index; FEV1: forced expiratory volume in 1 second; mMRC: modified Medical Research Council dyspnoea score; GOLD: Global Initiative for Chronic Obstructive Lung Disease; LAMA: inhaled long-acting muscarinic antagonists; LABA: inhaled long-acting beta-2-agonists; ICS: inhaled corticosteroids; OCS: oral corticosteroids.

## Outcomes

*Primary outcome*

In the intention-to-treat analysis, SLH was non-inferior to PExT in improvement of 6MWD and in rate of participants reaching 6MWD MID of 30 metres (Table 3; Figure 2). Both study groups improved statistically significantly in 6MWD.

## Table 3. Physical performance and quality of life

| | Singing for Lung Health (SLH) | Physical Exercise Training (PExT) | Between-group difference (*p*-value) | 95% CI |
|---|---|---|---|---|
| ***PRIMARY OUTCOME*** | | | | |
| **6MWD, metres** | | | | |
| Baseline | 374.1 ±105.0 | 391.6 ±99.0 | 0.17 | |
| Follow-up | 387.2 ±100.5 | 405.7 ±104.5 | 0.14 | |
| *Change from baseline* | *13.1 ±36.3**** | *14.1 ±32.3**** | *0.81* | [-7.28;9.30] |
| MID achieved | 31 (21.8%) | 31 (25.0%) | 0.57 | |
| ***SECONDARY OUTCOMES*** | | | | |
| **St. George's Respiratory Questionnaire (SGRQ)** | | | | |
| **Total score** | | | | |
| Baseline | 46.1 ±17.1 | 44.0 ±17.0 | 0.32 | |
| Follow-up | 43.0 ±16.6 | 42.5 ±18.9 | 0.81 | |
| *Change from baseline* | *-3.0 ±8.8**** | *-1.5 ±9.2* | *0.16* | [-0.62;3.73] |
| MID achieved | 51 (35.2%) | 35 (28.0%) | **0.21** | |
| **Symptoms score** | | | | |
| Baseline | 48.9 ±22.4 | 47.8 ±22.7 | 0.71 | |
| Follow-up | 45.0 ±21.9 | 43.5 ±24.4 | 0.61 | |
| *Change from baseline* | *-3.9 ±15.0*** | *-4.3 ±17.2*** | *0.83* | [-4.32;3.48] |
| MID achieved | 53 (36.6%) | 46 (36.8%) | **0.97** | |
| **Activity score** | | | | |
| Baseline | 65.4 ±20.6 | 64.0 ±21.4 | 0.59 | |
| Follow-up | 63.9 ±20.0 | 61.6 ±23.2 | 0.39 | |
| *Change from baseline* | *-1.5 ±10.4* | *-2.4 ±11.5** | *0.49* | [-3.56;1.71] |
| MID achieved | 44 (30.3%) | 44 (35.2%) | **0.40** | |
| **Impact score** | | | | |
| Baseline | 34.2 ±18.1 | 31.3 ±18.1 | 0.20 | |
| Follow-up | 30.5 ±18.1 | 31.3 ±19.1 | 0.74 | |
| *Change from baseline* | *-3.7 ±12.1**** | *-0.1 ±10.5* | ***0.01*** | [0.88;6.35] |
| MID achieved | 52 (35.9%) | 28 (22.4%) | **0.02** | |
| **Hospital Anxiety and Depression Scale (HADS)** | | | | |
| **Anxiety score** | | | | |
| Baseline | 4.8 ±3.8 | 5.1 ±3.7 | 0.52 | |
| Follow-up | 4.9 ±3.7 | 4.9 ±3.7 | 0.97 | |
| *Change from baseline* | *0.1 ±2.4* | *-0.2 ±2.3* | ***0.33*** | [-0.85;0.29] |
| **Depression score** | | | | |
| Baseline | 3.4 ±3.2 | 3.0 ±2.9 | 0.28 | |
| Follow-up | 3.2 ±2.9 | 3.1 ±3.0 | 0.78 | |
| *Change from baseline* | *-0.2 ±2.1* | *0.1 ±1.5* | ***0.19*** | [-0.14;0.74] |
| **FEV1%predicted** | | | | |
| Baseline | 49.7 ±16.9 | 53.6 ±16.6 | 0.06 | |
| Follow-up | 50.8 ±17.8 | 53.9 ±17.4 | 0.14 | |
| *Change from baseline* | *1.1 ±6.6** | *0.4 ±4.6* | ***0.01*** | [-2.12;-0.65] |
| **BORG CR 10 – after 6MWD** | | | | |
| Baseline | 7.1 ±2.8 | 6.6 ±2.8 | 0.10 | |
| Follow-up | 6.9 ±2.7 | 6.4 ±2.5 | 0.15 | |
| *Change from baseline* | *-0.3 ±1.8* | *-0.2 ±2.2* | ***0.66*** | [-0.38;0.60] |
| **mMRC** | | | | |
| Baseline | 2.2 ±1.2 | 2.0 ±1.2 | 0.25 | |
| Follow-up | 2.0 ±1.2 | 2.0 ±1.3 | 0.97 | |
| *Change from baseline* | *-0.2 ±0.7**** | *-0.1 ±0.8* | ***0.07*** | [-0.02;0.35] |
| **Adherence to intervention** | | | | |
| **Participation, number of sessions** | 16.6 ±3.0 | 16.3 ±3.1 | 0.41 | [-2.06;0.98] |
| Adherence rate 0-24% | 22 (15.2%) | 21 (16.8%) | 0.90 | |
| Adherence rate 25-49% | 11 (7.6%) | 12 (4.4%) | | |
| Adherence rate 50-74% | 24 (16.6%) | 21 (16.8%) | | |
| Adherence rate 75-100% | 88 (60.7%) | 71 (56.8%) | | |
| **Drop-out rate, n (%)** | 37 (25.5%) | 38 (30.4%) | **0.42** | |

## Table 3 text:

Data are presented as mean ±SD unless otherwise stated. 6MWD: 6-minutes walking test; MID: minimal important difference; FEV1%predicted: forced expiratory volume in 1 second expressed as % of predicted; mMRC: modified Medical Research Council dyspnoea score. Within-group significance is shown as: No star: p≥0.05, *: p<0.05, **: p<0.01; ***: p<0.001.

*Insert Figure 2: Change in 6MWD*

Across the two study groups, we found no difference in 6MWD MID after adjustment for age, sex, BMI, GOLD class, and expectations towards benefits of singing, using multivariable logistic regression (Odds Ratio 0.96, *p*=0.89 [95%CI 0.53 to 1.73]). We found significant correlation in both groups between adherence to PR and reaching the 6MWD MID of 30 metres (Appendix S6).

*Secondary outcomes*

We observed no between-group differences in BORG-CR10, mMRC, lung function, HADS, attendance rate, or drop-out rate. Concerning SGRQ Total Score, we found no significant between-group difference (Table 3), whereas data suggest a beneficial effect of SLH on SGRQ Impact Score (≥ 4 points improvement: SLH 35.9% and PExT 22.4%, p=0.02) (Table 3).

*Insert Figure 3: Change in SGRQ*

**Subgroup analyses**

The per-protocol analysis showed non-inferiority in primary and secondary outcomes, with only minor differences observed in SGRQ impact score and lung function (Appendix Table S3). Stratified analyses for sex, age, and lung function (GOLD class) showed no significant differences between groups. Further, we found no significant differences between the 29 PR classes regarding primary outcome.

There was no correlation between baseline characteristics or other factors and high adherence (75% or more) (Tables S7-S8). Non-adherence to PR was associated with living alone, current smoking, and high symptom burden (Appendices S6-S8).

The 75 participants who dropped out differed at baseline from study completers by displaying poorer lung function, shorter 6MWD, more symptoms, and a higher prevalence of current smokers (Appendix S9).

## DISCUSSION

In this multicentre, randomised, controlled trial of community-based PR in patients with COPD, we compared Singing for Lung Health (SLH) with conventional Physical Exercise Training (PExT) in regard to primary study outcome: Changes in 6MWD after 10 weeks, and we found that SLH was non-inferior to PExT (6MWD difference; *p*=0.81 [95% CI=-7.28;9.30]). Previous studies on singing in COPD are small and heterogeneous with low quality of evidence [10, 14]. No previous study on SLH included key objective criteria as primary endpoint, but *e.g.* Lord *et al*. included incremental shuttle walk test as a secondary outcome with insufficient power to detect change [41].

We observed a modest and lower improvement in 6MWD compared to those reported in the latest Cochrane review on PR in stable COPD (mean improvement: 43.9 [95%CI 36.2;55.2] metres) and in real-life reports of national PR services from UK (improvement ≥MID (30 m) in 70% of participants) and Denmark (mean improvement: 45 [95%CI 38;46] metres) [31, 42, 43]. Our findings may suggest that we compared SLH to an ineffective PR programme, yet we reported an effect size comparable to that found in the largest study included in the Cochrane review [43]**:** a community-based trial (*n*=165) with a mean 6MWD improvement of 13.9 [CI 3.1;24.7] metres. In Denmark, PR is conducted almost exclusively as community-based PR with easy, free, and close access for all Danish citizens. A systematic review on home- or community-based PR found lower 6MWD improvement (33.8 [CI 6.0-61.5] metres; ≤50 patient in 8 of 10 trials) than the above mentioned Cochrane review [43], suggesting a lower effect size in PR conducted outside larger centres [45]. Interestingly, the evidence level of PR's impact on 6MWD was assessed as "very low" in the Cochrane review due to substantial study heterogeneity and significant reporting bias (27/38 studies with ≤50 patients; *Egger* bias = 1.24 [95%CI 0.18-2.30]; *p*=0.023) [43]. In many of the well-conducted RCTs that demonstrate positive effect on 6MWD [43, 46], the effect is measured as change in mean difference and compared to usual care (without training). Lastly, concerns were raised in the UK report on real-life PR [42] that only 6% of PR programs used the recommended walking course length, and that almost half the programmes used no walking tests. In the Danish observational KOALA study [31] only data from PR completers were included, thus excluding 28% of the intention-to-treat population, which impairs the generalisability of this study. We therefore consider our findings to be honest, real-life observations in a large-scale community-based RCT, however we strongly encourage replication of our study in other PR settings.

Currently, there is no international consensus guideline on singing as a training intervention for lung disease. Generally, singing for people with respiratory disease has evolved as a leisure activity rather than a structured health-related activity, and most lung choirs still have heterogeneous leadership and lack of standard training or guideline [10, 24, 29, 30]. The British Lung Foundation initiative SLH includes systematic training of singing teachers in lung physiology/pathophysiology and a methodological approach to singing as a physical activity providing respiratory control [10, 27, 28]. This aligns well with recommendations on both physical and psychosocial elements in PR [1, 3]. So far, SLH is the best documented singing training programme in respiratory disease, though the evidence is primarily based on qualitative research [10, 24, 29, 30]. Several studies suggest that SLH improves QoL [11, 19, 20], yet we did not find that SLH improved QoL significantly (secondary outcome) (Table 3). Future interventions may be combined, as a recent network meta-analysis suggests that techniques based on diaphragmatic breathing training and yoga breathing are more effective than singing in improving QoL in COPD [47]. Likewise, our study failed to confirm that SLH improves anxiety, depression, dyspnoea, or lung function [10, 11, 17, 19, 20, 29]. In this paper, we only reported FEV1, but as singing is proposed to improve diaphragmatic control [11, 25], a mechanistic paper on inspiratory and expiratory lung function measurements from our RCT is in preparation.

We found identical adherence rates, and adherence was equally related to 6MWD improvement in both groups. Further, we found that adherence was not related to specific patient characteristics or factors such as sex or age (Tables 3, S7-S8). This suggests that SLH is more than a leisure time activity for adherent patients not preferring to engage in PExT [48]. In our study, participants were referred for conventional PR with PExT and not for PR with SLH. Future studies should clarify if an active choice of SLH affects attendance rate and 6MWD improvement [9].

*Strengths and limitations*

Our study has both strengths and limitations. Most importantly, our study is a short-term proof-of-concept study of SLH's impact on 6MWD improvement. Currently, there are no data on long-term outcomes of SLH as part of PR, and SLH is not validated with respect to any key outcomes of PR. Additionally, due to the decentralised structure of Danish PR, only a multicentre design would allow for sufficient recruitment and sample size. The multicentre design increased internal heterogeneity in delivery of both SLH and PExT. However, study groups were comparable at baseline and follow-up including expectations towards benefits of singing, and with no significant differences in primary endpoint between-sites (Tables 2 and 3). Furthermore, it is unlikely that selection bias explains our findings as participants were recruited from community-based PR-centres after referral for standard care (PR with PExT) from their general practitioner,

who was not informed about the trial. We included only well-established outcome variables used in PR trials (6MWD, SGRQ, FEV1, HADS, BORG-CR10, mMRC), and did not include any singing-specific outcomes. Furthermore, we used only basic and fully transparent statistical models, which further enhances transferability and external validity of our results.

Our findings need validation in other settings including highly-specialised/centralised COPD PR centres, and our results are not directly transferable to other lung diseases. Evidence suggests that PR and SLH are effective in both obstructive and interstitial lung diseases [10], but future studies should clarify the generic properties of PR with SLH.

Due to the proof-of-concept nature of our study, we did not include health economics, which is a needed aspect when investigating long-term effects of PR on health-care usage, hospital admission rates, and mortality [43].

*Conclusion*

This randomised, controlled trial in patients with COPD attending pulmonary rehabilitation (PR) demonstrated that Singing for Lung Health (SLH) provides positive and clinically relevant physiological and psychological changes in COPD, and that SLH was non-inferior to Physical Exercise Training in improving 6-Minute-Walk Test Distance (6MWD) post-10-weeks in community-based PR. 6MWD improvement in both study arms showed a dose-response relationship with adherence. Future studies in SLH should validate our findings in other PR settings, and further, investigate key long-term outcomes such as hospital admission rates, mortality, and health economics.

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# APPENDIX

## Contributors

Abbreviations: Mette Kaasgaard (MK); Daniel Bech Rasmussen (DB); Karen Hjerrild Andreasson (KA); Ole Hilberg (OH); Anders Løkke (AL); Peter Vuust (PV); Uffe Bodtger (UB).

MK, UB, OH, AL, and PV contributed substantially to the concept and design of this trial. The trial investigator (MK) developed manuals for recruitment, assessment, and treatment, written information, applications for grants, and approval assignments, made a registry at ClinicalTrial.gov, introduced the recruitment, introduced and supervised the treatment procedures to all involved singing teachers, and led the data collection. Principal investigator (UB) supervised registration, recruitment, assessment, and data collection procedure. Analyses were performed by MK, re-performed by DB, and checked by UB. OH, AL, KA, and PV gave feedback. MK and KA made the descriptions of intervention and control study group content, and UB, OH, AL, DB, and PV gave feedback. MK drafted the manuscript, and UB, OH, AL, DB, KA, and PV provided important intellectual input and feedback on the manuscript and approved the final version.

**Conflicts of interest**

MK holds a Diploma Graduate Degree from the Royal Danish Academy of Music in Voice and Voice Pedagogy. PV is leader of the research centre, Center for Music in the Brain. The other authors had no prior experience of or knowledge within any singing field. None of the authors had prior relationships with any training facilitator or study participant. No author or close relative has economic interests within the field of singing, including lung choirs, or pulmonary rehabilitation, including physical exercise training.

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**Ethics and registration**

Ethical approval was obtained by the Regional Committee on Health Research Ethics, Region Zealand, Denmark (no. SJ-597) and the Danish Data Protection Agency (no. REG-049-2017). The trial was conducted in accordance with the Helsinki 2 Declaration and according to the Act on Processing of Personal Data. Trial protocol is available at ClinicalTrials.gov (number NCT03280355).

**Data sharing**

Consent forms will not be available according to Danish legislation. De-identified data collected for the study will be available from Jan 1, 2023, upon reasonable request. Contact study investigator (MK), mk@clin.au.dk.

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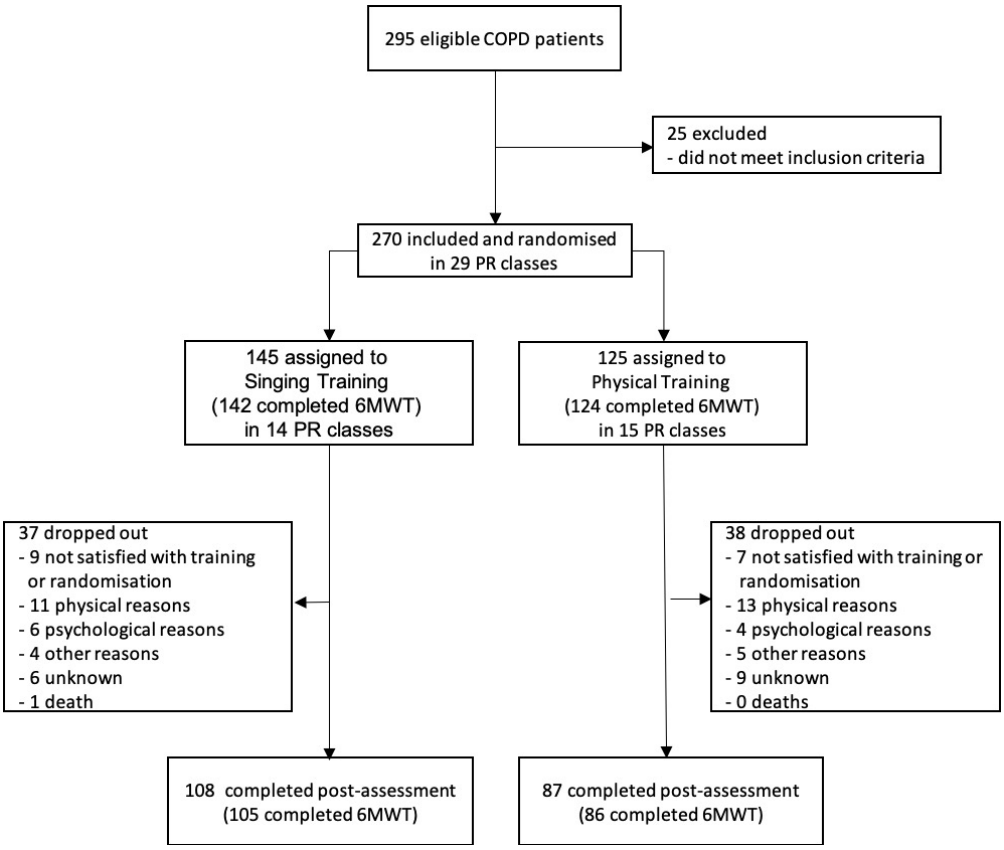
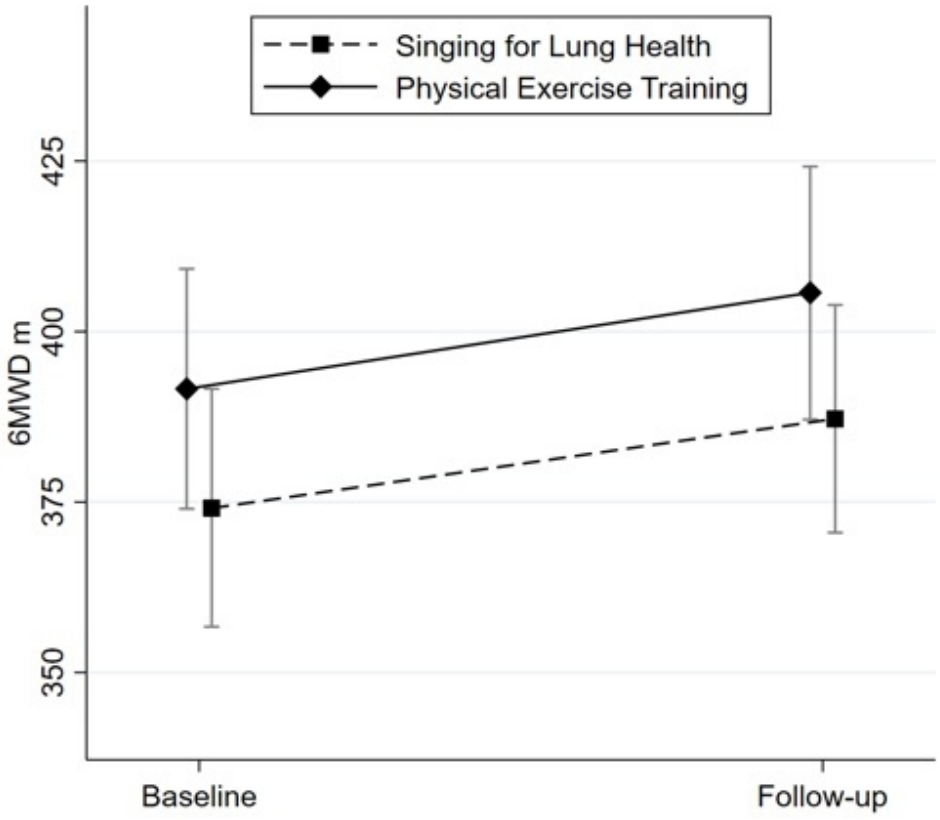
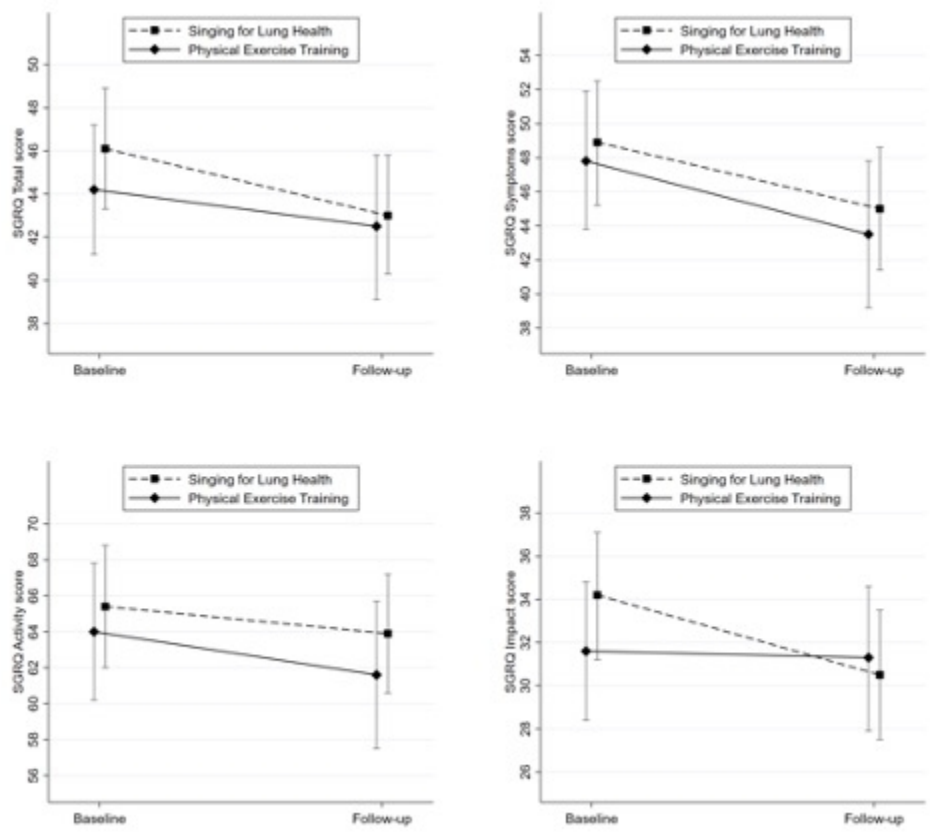



Consort Flow Diagram




Change in 6MWD




Change in SGRQ

# Supplementary materials to manuscript:

## "Use of Singing for Lung Health as an alternative training modality within pulmonary rehabilitation for COPD: an RCT"

Kaasgaard, M, Rasmussen, DB, Andreasson, K, H, Hilberg, O, Løkke, A, Vuust, P, Bodtger, U.

## Content

Appendix S1: Overview of secondary study outcomes ..... 2
Appendix S2: Consensus on Exercise Reporting Template (CERT) for both study groups ..... 3
Appendix S3: CERT – Elaborated version for intervention group (SLH) ..... 8
Appendix S4: Baseline characteristics in intention-to-treat-population ..... 18
Appendix S5: Per protocol analyses i.e. excluding patients who dropped out before study completion ..... 19
Appendix S6: Relationship between training modality and accomplishing minimal important difference of 6MWD (30 metres) ..... 20
Appendix S7: Baseline characteristics and physical performance of patients with high adherence (75% or more) to the interventions ..... 21
Appendix S8: Factors associated with high adherence (75% or more) to the interventions ..... 22
Appendix S9: Baseline characteristics of Per protocol population ("Completers" vs. "Non-completers") ..... 23
References for Appendix ..... 25

## Appendix S1: Overview of secondary study outcomes

| Outcome | Measure | Test/Scoring | Minimal important difference (MID) |
|---|---|---|---|
| **Quality of Life (QoL)** | St. George's Respiratory Questionnaire (SGRQ): Disease-specific QoL and health impairment | **Self-reported.**<br>SGRQ has 50 items with 76 weighted responses and four scores: Total, Symptom, Activity, Impact. Each score ranges from 0 to 100, with 100 representing worst possible health status and 0 best possible. | 4 points [1] |
| **Lung function** | Forced Expiratory Volume in one second (FEV1) expressed in ml and percent of expected (FEV1%) | **Assessor-collected.**<br>Reversibility test using a mobile spirometer (Medikro Pro, Product Code M915, SW version 3.1-03, OY Finland ) and was categorised according to Global Initiative for Chronic Obstructive Lung Disease (GOLD): FEV1% > 80 = GOLD 1 (mild); 50 ≤ FEV1% < 80 = GOLD 2 (moderate); 30 ≤ FEV1% < 50 = GOLD 3 (severe); FEV1% < 30 = GOLD 4 (very severe) [2]. Reference values: height, age, sex and ethnicity. | MID for FEV1 is considered to be 120ml [3] |
| **Dyspnoea** | BORG CR10-dyspnoea scale: Self-perceived dyspnoea. | **Self-reported.**<br>The scale ranges from 0 to 10 points, where 0 represents no dyspnoea and 10 represents maximal dyspnoea. | 1 point [4, 5] |
| **Dyspnoea** | Modified Medical Research Council Dyspnoea Scale (mMRC): self-reported data on general, experienced dyspnoea and functional capacity. | **Self-reported.**<br>The scale with scores from 0-4, grade 0 corresponding to "Dyspnoea only when strenuous exercise" and grade 4 corresponding to "too dyspneic to leave house or breathless when dressing"[23, 24] | 1 point [4, 5] |
| **Anxiety and depression** | Hospital Anxiety and Depression Scale (HADS). | **Self-reported.**<br>Comprising 14 items, seven related to anxiety and seven related to depression | 1.32 (anxiety component) and 1.40 (depression component) [8, 9] |
| **Expectations of singing benefits** | Patient-reported (developed for the study) | **Self-reported.**<br>Reported as value positive, neutral, or negative. | N/A |
| **Adherence** | PR adherence and drop-out rate (%): participation status and eventual drop-out | **Facilitator-collected.**<br>Continuously registered at all training sessions by each centre.<br>Subsequently, adherence rate was divided into four categories (quartiles), and drop-out rate was calculated.<br>High adherence was defined as ≥75% of all sessions. | N/A |

# Appendix S2: Consensus on Exercise Reporting Template (CERT) for both study groups

**Abbreviations used in CERT (Appendices S2 and S3)**

| | |
|---|---|
| COPD: | Chronic Obstructive Pulmonary Disease |
| SLH: | Singing for Lung Health |
| PT: | Physio therapist |
| ST: | Singing teacher |
| AE: | Adverse events |

## Consensus on Exercise Reporting Template (CERT) for both study groups

| Item category | Item description | Singing for Lung Health | Physical Exercise Training |
|---|---|---|---|
| What: materials | 1. Type of exercise equipment (e.g., weights, machines, exercise bicycle, treadmill) | • Music player and music (CD/smartphone) during warm-up and relaxation.<br>• Chairs for sitting, breathing exercises, resting positions, and moving/dancing around.<br>• Paper sheets (music and/or text), Danish and/or international exercises and songs (and appertaining games/dances). Majority of songs taught "by ear".<br>• Balloons, drum sticks, scarfs, umbrellas, ropes, balls, fly swappers to support movement/activity during singing.<br>• Straw and glass with water (to make vocal sounds through a straw put into the water)<br>• Piano (or similar) for accompaniment for some songs during the last 10 sessions. | • Music player and music (CD/smartphone) during warm-up, exercises and relaxation.<br>• Chairs, training mats/plints<br><br>For warm up and endurance training:<br>• Exercise bicycles, treadmill, cross trainer, staircases, balls, balloons, rackets etc. and individual body weight<br><br>For strengthening training:<br>• Kettle balls/filled water bottles/weights, weight training machines, elastic bands, individual body weight |
| Who: provider | 2. Qualifications, and teaching/supervising expertise of the exercise instructor | • Danish singing teachers (ST) with professional academic training in voice/music studies.<br>• Participated in a mandatory workshop of 16 hours (2 days), supplemented a handout with theoretical background on pathophysiology and best-practice lung choir methodology from the British team of experts (info in the elaborated CERT below this table).<br>• The *patient education* (see item 10) was delivered by professionals of the given topic or the PT (equal in the two groups) | • Physiotherapist (or occupational therapist or nurse) (PT) employed at the local healthcare center with basic educational background.<br>• Experienced in pulmonary rehabilitation in COPD.<br>• The *patient education* (see item 10) was delivered by professionals of the given topic or the PT (equal in the two groups) |

| | | | |
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| **How: delivery** | 3. Exercises performed individually or in a group?<br>4. Exercises are supervised or unsupervised? | • Sessions were delivered in classes of approximately 10 participants.<br>• Supplementary individual supervision and guidance throughout.<br>• Exercises were supervised on class-level and individually throughout by the ST. | • Sessions were delivered in classes of approximately 10 participants.<br>• Supplementary individual supervision and guidance throughout.<br>• Exercises were supervised on class-level and individually throughout by the PT. |
| | 5. How adherence to exercise is to be measured and reported | • Number of attended sessions by each participant was registered by the ST.<br>• Adherence and progression were registered and reported in a mandatory logbook. Reporting style and form varied, since there was no template for systematic reporting.<br>Adherence is reported in the results section of the manuscript | • Number of attended sessions by each participant was registered by the PT.<br>• Adherence and progression were reported in local registration system.<br>• Adherence is reported in the results section of the manuscript. |
| | 6. Details of motivation strategies | • An encouraging and acknowledging attitude of the ST (as described in previous literature [10, 11].<br>• Building a safe atmosphere and group dynamic.<br>• Endeavor to match levels of ability in muscle strength and endurance of each participant.<br>• Combination of endurance and strengthening training.<br>• Inclusion of participants' preferences (in musical taste). | • An encouraging and acknowledging attitude of the PT, especially for participants with more severe COPD (best practice). Participation based on the individual motivation to participate.<br>• Participants were screened systematically to find the individual ability level (level of dyspnea, level of loss of muscle strength).<br>• Endeavor to match the chosen exercises to the levels of ability in muscle strength and endurance individually for each participant.<br>• Combination of endurance and strengthening training to increase adherence[12, 13]. |
| | 7. Specify/describe the way in which it is decided to progress through an exercise programme | • Progression from a basic programme to build awareness and control (voice, breath, and body) and to include additional elements and complexity.<br>• Progression of strength/endurance requirements in the SLH along the way, e.g. increasingly prolonged outbreaths, extended vocal range and flexibility, and duration of standing.<br>• Ensure a positive experience to build confidence and self-esteem. | Individually progression of workload intensity, supervised by the PT every 2-3 week:<br>• <u>Strengthening training</u> in continuum from '3 sets of 8-10 repetitions, weight increased if >10 reps'[14] to '65-80% of 1 Repetition max (RM)'.<br>• The duration of/speed during endurance training aiming at sets of 10 minutes increasing to 25 minutes [12], achieving load of continuum over 'no definition', '11-13 or 13-14 on BORG Rate of Perceived exertion scale (Borg RPE)', to '60% of VO2 max, measured on Borg CR10'. |
| | 8. Specify/describe each exercise so that it can be | Examples (the following elements are available in the elaborated CERT for SLH below this table): | The physical training combined endurance and/or strengthening training as these training methods appear to be equally |

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| replicated (eg, photographs, illustrations, online appendixes) | • Physical warm-ups (stretching, movement, flexibility, accelerating heartbeat, body awareness).<br>• Posture exercises<br>• Breathing exercises<br>• Rhythm and pitch games, call-response.<br>• Vocal exercises (vocal range and flexibility, phonation, resonation, articulation)<br>• Physical and vocal stamina<br>• Songs with and without additional movement/dancing/activity<br>• Relaxation and body awareness exercises<br>• Planned choreography to support moving/dancing during singing/game songs.<br>Exercise equipment varied and was tailored to the singing class by each ST. | effective in rehabilitation programme for COPD patients [12, 14].<br>• Warm up exercises for joints, muscles, circulation and breathing.<br>• Preferably combination of endurance and strengthening training, and secondary strengthening training alone.<br>• Large muscle groups of the extremities were prioritized.<br>• Daily life-related activities (sit-to-stand, gait, lifting “bags”, stair climb, bicycling)<br>• Floor games, Circuit training<br>• Cool down: Stretching of muscles; relaxation.<br>• Management of dyspnea: Posture exercises, resting positioning, relaxation, breathing techniques (i.e. Pursed Lip Breathe)<br>• Instruction in positive expiratory pressure (pep) and clearance techniques as needed. |
| 9. Content of any home programme component | • Instruction and encouragement to practice methods of breathing techniques, vocal exercises/songs, relaxation, and body awareness at home, however without specific/ generic requests. | • Instruction and encouragement to do appropriate exercises at home (see item 14). |
| 10. Describe the nonexercise components of the intervention (eg, cognitive behavioral therapy) | Supplementary *patient education* (part of standard PR):<br>Knowledge about COPD (communicated in a considerate manner that did not create unnecessary concern (best practice), behavior change, smoking cessation, correct use of inhaler devices, nutrition, sexuality, handling of stress and anxiety, early recognition of exacerbation, decision-making and taking action of symptoms, goals of motivation and maintenance post PR. | Supplementary *patient education* (part of standard PR):<br>• Knowledge about COPD (communicated in a considerate manner that did not create unnecessary concern (best practice), behavior change, smoking cessation, correct use of inhaler devices, nutrition, sexuality, handling of stress and anxiety, early recognition of exacerbation, decision-making and taking action of symptoms, goals of motivation and maintenance post PR. |
| 11. Report adverse events (AE) that occur during an exercise intervention | • STs/health professionals reported any AE to the research group however, AE were not systematically collected for this trial. | • PT/health professionals reported any AE to the research group however, AE were not systematically collected for this trial.<br>• Muscle soreness was anticipated and not reported as an AE. |

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| **Where: location** | 12. Setting in which exercise is to be performed | • Sessions were delivered in a standard, spacious training studio (normally used for PR) in each local health-care center.<br>• The training studio was in a separate and undisturbed room. | • Sessions were delivered in a standard, spacious training studio (normally used for PR) in each local health-care center.<br>• The training studio was in a separate and undisturbed room. |
| **When, how much: dosage** | 13. Specify and explicitly describe the exercise intervention (i.e., number of exercise repetitions, number of exercise sets, number of sessions, duration of each session, duration of intervention or programme) | 20 sessions, i.e. twice weekly during 10 weeks.<br><br>Each session was 90 minutes, including a 10-15 minutes break for water/tea/coffee and toilet visit.<br>• 20 minutes of physical warm-ups: posture and breathing exercises, warming up body<br>• 20 minutes of vocal warm-ups and rhythm and pitch games.<br>• 40 minutes of singing songs, often with additional games/moving/dancing (including 10-15 minutes break).<br>• 10 minutes of cool down (e.g. mindfulness or relaxation). | 20 sessions, i.e. twice weekly during 10 weeks.<br><br>• Each session was 90 minutes, including a 10-15 minutes break for water/tea/coffee and toilet visit.<br>• 20 minutes of physical warm-up<br>• 45-50 minutes physical training (see item 8) including handling of dyspnea<br>• 10 minutes cool down |
| **Tailoring: what, how** | 14. Specify whether exercises are generic or whether, and how, they are tailored to the individual | Exercises and songs were generic (examples and elaboration in elaborated CERT below this table), as basic exercises/songs can easily be graduated to meet/challenge all levels of competence.<br>All activities delivered at class level were combined with individual supervision and guidance throughout.<br><br>Exercises and songs were tailored in relation to following:<br>If impaired, participants were allowed to:<br>• Sit more often instead of standing/moving.<br>• Perform shorter outbreath than other participants.<br>Competence:<br>• Each participant was instructed individually in relation to breathing technique, posture, and muscle work/tension/relaxation.<br>• Participants with prior musical competence were asked to add advanced elements to songs.<br>Preferences:<br>• ST's/participants' personal taste in musical repertoire [10, 15]. | Exercise were tailored by the PT depending on:<br>• The severity of COPD of the individual participant.<br>• Personal preferences of combination (or uni-method use) of strengthening and endurance training.<br>• Physical limitations (e.g. injured joint, paresis): modifications of exercises as needed to prevent damage and improve function.<br>Furthermore:<br>• Participants who were unable to do endurance (anaerobic) training due to high level of dyspnea, were encouraged to do strengthening training alone.<br>• The PTs followed the Danish national clinical guideline[16] if this was decided by the local health-care centre, therefore the physical training was not standardized but represent the real world clinical practice in Danish municipalities. |

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| | 15. Decision rule that determines the starting level at which participants commence exercise (i.e., beginner, intermediate, or advanced) | • No prior exercise or vocal/musical competences were required.<br>• Individuals with COPD with mMRC<2, and potentially weak/untrained, but able to participate in the rehabilitation programme.<br>• Since the intervention and background methodology is new in Denmark, all participants were regarded as beginners.<br>• However, participants with experience/competence within singing were regarded intermediate and were challenged, e.g. with adding polyphony. | • No prior exercise competences were required.<br>• Individuals with COPD with mMRC<2, and potentially weak/untrained, but able to participate in the rehabilitation programme, thus starting level was typically regarded 'beginner'.<br>• However, participants with better fitness were regarded intermediate. |
| **How well: planned, actual** | 16. How adherence or fidelity to the exercise intervention will be assessed or measured | • Each ST received supervision throughout by study investigator (MK) at visits twice and telephonic contact.<br>• ST were encouraged to build peer-network with knowledge-sharing.<br>• In case of absence of ST, sessions were conducted by local health professional (singing together) or cancelled.<br>• Each ST kept a logbook of all sessions, including reporting of reflective practice.<br>• Subsequent video interview of experiences of the ST. | • In case of absence of PT, sessions were conducted by other local health professional. |

# Appendix S3: CERT – Elaborated version for intervention group (SLH)

**WHAT: materials**

**Item no. 1: Type of exercise equipment (e.g., weights, machines, exercise bicycle, treadmill)**

**Materials for preparation:**
Initially, singing teachers (ST) participated in a mandatory workshop to gain knowledge and ideas for exercises, songs, and physical movements, and to prepare the singing sessions. Further, they were equipped with a handout and a CD for inspiration: "Singing for breathing", link: https://www.rbhcharity.org/shop/singing-for-breathing-audio-cd

The intervention in Sing-a-Lung was conducted with inspiration from the best-practice approach within singing for lung patients ("Singing for Lung Health"/"Singing for Breathing"), based on a decade's thorough, empirical fieldwork and offered to British lung choir singing teachers through the British Lung Foundation.[17] Content of workshop, handout, and CD represented the "Singing for Lung Health"/"Singing for Breathing" concept as it was delivered in the UK in 2017.

The British team of experts (concept founders, music therapist and singing teacher, BMus Hons, PGDip MT, MA, Phoene Cave, The Musical Breath (http://www.themusicalbreath.com), and Respiratory Physiotherapist, Dr. Adam Lewis (Physiotherapy and Physician Associate, Department of Health Sciences, College of Health, Medicine and Life Sciences, Brunel University, London, UK) developed the basic materials (handout and CD), and conducted the mandatory workshop.

Handout was translated into Danish by study investigator, Mette Kaasgaard and research secretary, Hella Kastbjerg (Center for Music in the Brain, Dept. of Clinical Medicine, Aarhus University, Denmark) with supplementary materials suited for Danish context (background literature, and repertoire for exercises, songs, and games/dances).

Session structure, focus, and approach were predefined. Exercises, songs, and recorded music (for movements and relaxation) were selected by the ST in concurrence with recommendations in workshop and handout. Focus of sessions and in the selection of exercises, music, and approach: Meeting the disease-specific, pathophysiological challenges and the psychosocial needs of patients with COPD, e.g., through:

1) Extending outbreaths through sung phrases.
2) Improving respiratory muscle strength and co-ordination.
3) Returning to an optimum breathing pattern and reduce 'top up' breaths, improve using diaphragm and abdominal muscles (such as the internal and external obliques and the transverse abdominus) rather than accessory respiratory muscles (these include primarily upper trapezius, scalene, sternocleidomastoid, levator scapulae, and pectoralis minor).
4) Building physical and vocal stamina and ensure safe, balanced, and efficient phonation and articulation.
5) Building positive group dynamics through interaction and having fun.

Overview of content elements:

- Physical warm-ups
- Posture exercises
- Breathing exercises
- Rhythm and pitch games, call-response
- Vocal exercises (flexibility, ambitus, phonation, resonation, articulation)
- Exercises for physical and vocal stamina
- Songs with and without additional movements/dancing/activity/use of artefacts
- Relaxation and body awareness exercises

**Materials for sessions:**
Musical materials:

- Paper sheets (music and/or text), Danish and/or international songs and game songs/dances. Songs mostly learned by ear/heart, eventual text/music sheets on paper. Singing teachers mainly used music from standard Danish song books (e.g. "Sangbogen 1-5"[18](collections of classic, traditional, and popular songs), supplemented by international (mainly English/American) songs and by ST's own materials/songs and/or participants' suggestions for material/songs. Further, they applied e.g. African work songs, native songs from all over the world, children songs, non-verbal songs, and rounds and circle songs. Improvisation and imitation (call-response) was also included, especially during warm-up (as instructed in workshop and handout). Alongside, the ST focused on musical content and interpretation, and introduced different moods, genres, and expressions via exercises, games, and songs.
- Music player for recorded music during warm-up and relaxation.
- After 10 sessions (halfway through the intervention), singing teachers were allowed to introduce piano (or similar) accompaniment for some songs, however, with singing still mainly performed "a cappella" (without accompaniment) in the circle.
- Some singing teachers occasionally included other instrumental accompaniment, e.g. African drum (djembe), guitar, bells, and singing bowls.

Non-musical materials:

- Chairs for sitting down (when needed), for breathing exercises, for resting positions, and for moving/dancing around.
- Additional artefacts to supplement exercises and songs: E.g. balloons, drum sticks, scarfs, umbrellas, ropes, balls, and fly swappers to support movements/activity during singing.
- Straws and glasses with water (to make vocal sounds through a straw put into the water).
- Planned choreography to support movements/dancing during singing/game songs, and either predefined or participant-invented. Exercises and songs were combined with movements or dancing whenever possible, both to add an endurance aspect, and to underline the social aspect and joy of singing together.
- Exercise equipment varied and was tailored to the singing class by each singing teacher.

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**WHO: provider**

**Item no. 2: Qualifications, teaching/supervising expertise and/or training of the exercise instructor**

- Inclusion criteria for the Danish singing teachers were prior academic professional training in voice/music studies. In the job advertisement and subsequent screening process, we asked for personal and social competences such as openness, empathy, and humour, as previously recommended for lung choir teachers [3][8][9]. No prior healthcare education or experience within lung diseases or lung choirs was required.
- 20 singing teachers were selected and prior to the intervention, all 20 singing teachers participated in the mandatory, specialised training workshop (see item 1) of 16 hours during 2 days with the British team of experts.
- During trial conduct, singing teachers were further supervised twice at visits and were allowed support by telephone with the study investigator, Mette Kaasgaard, who is trained in classical singing and voice pedagogy. Also, they were encouraged to build peer-network with knowledge-sharing and mutual support. Besides the workshop handout and the singing-for-Breathing-CD for inspiration, singing teachers had access to a closed Facebook-group with video examples of songs and exercises (recorded during the workshop) and posting of ideas, and a Dropbox-folder for mutual sharing of materials.
- Eight singing teachers participated in the training workshop but did not participate fully in the trial due to other employment or their geographical area related to the subsequent randomisation. However, they were facilitators in the trial. Some of them (n=5) led only one singing class whereas others led two (n=1) or three (n=2) classes.
- The *patient education* (see item 10) was delivered by professionals of the given topic or the local physiotherapist (equal in the two study groups).

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**HOW: delivery**

**Item no. 3: Whether exercises are performed individually or in a group**

- Sessions were delivered in classes of approximately 10 participants (range 7-16) across 14 classes totally.
- Whenever appropriate, the singing teacher explained relevant aspects of respiratory anatomy and physiology to the class (tailored to the participants in the class and individually when needed) and transferred these explanations to practical breathing/vocal exercises and songs.
- Exercises, song, and games/dances were performed in classes.

**Item no. 4: Whether exercises are supervised or unsupervised**

- Sessions were supervised throughout by each singing teacher, both on class-level and individually. The participants and the singing teacher formed a circle, mostly standing up, but also sitting down for an exercise, or when needed, e.g., because of tiredness or dizziness.
- The ST provided immediate individual observation, supervision, and correction of each participant, e.g., in relation to breathing pattern, vocal functioning, posture, jaw tension, muscle work, flexibility, unintended tension, vocal function, articulation, sound, expression/interpretation, relaxation, and body awareness.
- The circle allowed for the singing teacher to be able to be close to every participant, and for an experience of participants being mutually equal. Furthermore, the circle position allowed easy implementation of different activities and improved dynamics in the session, e.g. combining singing with movements, dancing, and using/playing with various artefacts (see Item 1 and Item 8).

**Item no. 5: Measurement and reporting of adherence to exercise**

- Adherence to exercise was registered on group level and reported in the logbook, which each singing teacher was asked to use (the log book further included a section with self-evaluation the for ST). Reporting style and form varied, as no standardized template for reporting was provided.
- Number of attended sessions by each participant was registered (in a predesigned matrix) by each singing teacher. Adherence is reported in the result paragraph.

**Item no. 6: Details of motivation strategies**

- We focused on building a safe atmosphere and group dynamic, e.g. through an encouraging and acknowledging attitude of the singing teacher[10, 11, 17] and creating a space in which participants would be among peers in an accepting atmosphere and having fun giving a positive experience of singing together, while building new competences, strategies, and self-esteem.[10, 11, 17]
- The singing teacher made endeavor to match levels of ability in muscle strength and endurance of each participant, and the session content consisted of both endurance and embedded strengthening training for posture and respiratory muscles.
- Inclusion of participants' preferences (in musical taste).
- During the 10-15 minutes break, some of the classes received tea/coffee/cocoa milk and biscuit/fruit (varied from centre to centre aligned to the local habits in the community.

**Item no. 7: Decision rules for progressing the exercise programme**

- Along the way, the singing teachers supervised growth and progress, both in the class and in individuals, and gradually increased/challenged the level of strenght and endurance for posture and respiratory muscles.

    1) Starting with a basic programme to build knowledge, and initial awareness, stamina and control (vocal, breathing (in- and exhalation, posture, articulation, avoid accessory muscle tension).
    2) Continuing with the basic elements and adding elements, strength, endurance, and complexity along the way.
    3) Progression of strength/endurance requirement in the singing, for example gradually prolonging outbreaths, extending vocal tone range (ambitus), or duration of standing up.

- Progression was registered and reported in the log book (definition of log book, see Item 5).
- Beside from the Danish handout and supplementary materials, there was no specific and detailed protocol for the intervention or for progression. SLH, therefore, to some extend was delivered diversely across the centers, due to variety in singing teachers' background and personal styles, and to specific composition and dynamics in each class (pragmatical design).

**Item no. 8: Each exercise is described so that it can be replicated (e.g. illustrations, photographs)**

- Inclusion of aspects of respiratory anatomy and physiology, refer to item 3.
- See Item no. 7 for description of diversity and progression.

Overview of key activities/content elements:

- Physical warm-ups (stretching, movement, flexibility, accelerating heartbeat, body awareness).
- Posture exercises
- Breathing exercises
- Rhythm and pitch games, call-response.
- Vocal exercises (vocal range and flexibility, phonation, resonation, articulation)
- Physical and vocal stamina
- Songs with and without additional movement/dancing/activity
- Relaxation and body awareness exercises
- Planned choreography to support moving/dancing during singing/game songs.

Exercise equipment varied and was tailored to the singing class and the individual participants by each singing teacher.

**Elaboration of content elements (see Item no. 1):**

| Content | Description of content | Music/exercise examples, links, illustrations/photographs |
|---|---|---|
| Physical warm-ups | • Recorded music to support each activity – starting slowly and increasing energy and tempo (Energizing up-tempo music for warm-up)<br><br>**Seated and/or standing:**<br>• Body and breathing awareness<br>• Stretching and "opening"/awaken the the whole body (all directions: up, "picking apples", to the sides, down)<br>• Moving/stretching lips/mouth/jaw/face/tongue<br>• Massage of jaws/chin/neck (own and others')<br>• Yawning, sighing, sirening: wakening breath and voice)<br>• Lower body: Hip circles, knee bends/lifts, ankle rolls, feet movement<br>• Upper body: Side bend, head, neck and shoulder rolls, arm swings, rotating spine/centre | **Examples of recorded music for warm-ups:**<br>The Temptations: "My Girl"<br>Leo Mathiesen: "Take it easy, boy, boy"<br>Tommy Steele: "A Handful Of Songs"<br>Michael Bublé: "Everything"<br>Van Morrison: "Brown Eyed Girl"<br><br>  <br>  |
| Posture exercises | **Seated and/or standing:**<br><br>Body "walk-through"/body awareness (from feet to the top of the head). Focus on:<br>• Lengthening the spine and neck<br>• Balance between back and front<br>• A feeling of space inside the body: space for the breath, space for the voice<br>• Soft joints (ankles, hips, knees, shoulders, neck)<br>• Avoiding collapse of posture and thorax |  |
| Breathing exercises | **Seated:**<br>Examples:<br>• Leaning forward, resting elbows and back of the forearms on thighs.<br>Focus on:<br>• Feeling the breath in the back of the body<br>• Freeing the neck/jaw/face<br>• Allowing the inbreath – relax and release tummy<br>• Controlled, long exhaling on unvoiced sounds (FFFFFFF/SSSSSSS) and voiced sounds (VVVVV/ZZZZZZZ), and allow a spontaneous, deep |  |

inbreath afterwards

**Standing (or seated):**
First step (examples):

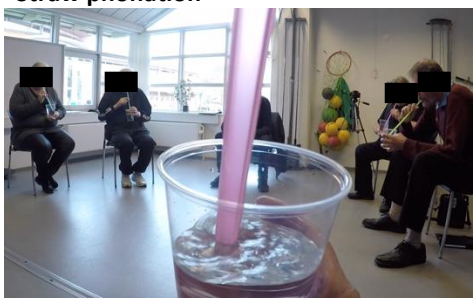
- Observing the breathing
- Connecting breath to movement. Participants asked to illustrate breathing, e.g.: Watch their hands while opening and closing hands like a flower (opening on inhale, closing on exhale). Further, breathing/vocal sound may be illustrated with movement with the arms or by moving the whole body forwards and backwards in rhythm with inhalation and expiration.
- Using the imagination: Smelling a beautiful rose (fosters a deep diaphragmatic inhalation)

Second step (examples):

- Controlling outbreath to sounds: Playing with exhaling on unvoiced (FFFFFFF/SSSSSSS) and voiced (VVVVV/ZZZZZZZ) sounds. Prolonging the exhalations gradually.
- Wakening and strengthening breath support muscles function and coordination through natural sounds and impulses: laughter, cough, sneeze, surprise etc.
- Using voiced fricatives (unpitched and pitched) in a rhythmic pattern (e.g. VVV VVV VVV or ZZZ ZZZ ZZZ with inhalation between sounds).
- Noticing movement in waistband: Placing hands in waistband and feel the muscles engaging under the hands, while the belly draws gently inwards towards spine during the exhalation. Singing teacher may assist participants and put a hand on abdomen/sides/back to enhance the body awareness.
- Breathing/humming/singing through a large straw (at least 10 mm) into a glass of water, keeping airflow consistent when beginning to phonate: "Straw phonation".[19]

**Singing teacher supports awareness of breathing (inhalation and exhalation)**

**"Straw phonation"**



**Rhythm and pitch games, call-response**

Examples of elements/activities:

- Making "body percussion": clapping on the body, stomping with feet etc. while making vocal sounds, words, sentences, rhymes, sung phrases.
- "Call and response"- making nonsense sounds or short spoken/sung sentences, eventual with additional movement/dancing: The singing teacher makes a sound and the class replies (repeats/imitates).
- Exploring rhythm, pitch, dynamics, duration and different vocal qualities: High and low sounds, loud and quiet, fast and slow, vowels and consonants, legato and staccato, parts of scales, arpeggios, expressing different moods (e.g. sad, happy, exited, angry, tired).

**Example of body percussion warm-ups** (clip from search on Youtube): https://www.youtube.com/watch?v=lNbZLgq5Oy0 (Source: Musical Futures)

**Example of call and response** (clip from search on Youtube): https://www.youtube.com/watch?v=hsI8pnsacx8 (Source: Musical Futures)

**Example of included artefacts:**
Balloons, drum sticks, scarfs, umbrellas, ropes, balls, fly swappers to support movement/activity during singing.

**Vocal exercises (flexibility, vocal tone range (ambitus), phonation, resonation, articulation)**

- Humming: Closed vowels (e.g., E) and open vowels (e.g., A), and voiced and unvoiced fricatives (unpitched and pitched), e.g., in a rhythmic pattern.
- Using artefacts for implementing play/movement while making sounds or spoken/sung phrases.

First step (examples):

- Sirening (freely playing with sounds e.g.: "SING", "ING", "NG" – focus on the "NG" sound and ensure tongue and soft palate forming a seal).
- "Crying": "Cry" vocal quality (e.g.:"Oh dear" – with descending sounding sad/whiney) to encourage optimal vocal fold closure.
- Speaking: "Modal/speech" vocal quality ("uh-oh", "hey", "yeah") to experiment with glottal onset and thicker vocal folds.

Second step (examples):

- Major/minor scales and arpeggios to different vowels – up and down, expanding the tone range.
- Melodic exercises to different sounds such as the vocal sirening, the lipbuzz/liprolled rrr.
- Articulation exercises, e.g. nonsense words/sentences, "tongue twisters", or call-response vocal games using lots of different consonants.
- Variation in tempo, dynamics, legato/staccato.
- Continuously extending of the phrase length (= prolonging of the outbreath).

**Physical and vocal stamina**

Examples of elements/activities:

- Prolonging time of standing up.
- Strengthening posture and endurance (through extending complexity, duration and intensity of exercises, songs, and movement/dancing).
- Varying and extending exercises and songs in speed/tempo, dynamics, legato/staccato, strengthening phonation, articulation, and vocal tone range, flexibility, and strength.
- Prolonging expiration through exercises and sung phrases, improving respiratory muscle strength and co-ordination (inspiration and expiration).

**Songs with and without additional movement /dancing**

Repertoire:

- Regular unison songs, and simple polyphonic songs, rounds, and circle songs.
- Music from standard Danish song books, supplemented by international (mainly English/American) songs.
- African and/or native songs, children songs, and non-verbal songs.

**Examples of songbooks:**
Sangbogen 1-5 (5 books with a selection of Danish and international songs from different time periods and genres), Edition Wilhelm Hansen, ISBN 9788759808801)[18]

**Examples of suitable songs (recognizable to English readers):**

- "My Bonnie is over the ocean"

Approach and focus:

- The singing teacher introduced both new and unfamiliar material and familiar material (for example popular songs from the time of participants' youth, e.g. from the 1950-70's).
- Participants were also able to suggest songs to ensure the maximum level of identification, pleasure, and comfort, as well as the experience of relevance, variety in emotional expressions, and acknowledgement of preferences.[11, 15]

- Songs were mostly learned by ear/heart, eventual with text/music sheets on paper for support.

- The singing teacher also focused on musical content and interpretation, and introduced different mood and genres to stimulate various emotions and to enhance social cohesion and a sense of belonging in the class.

- The singing teacher Included as much choreography and movement/dancing as possible, either predefined or participant-invented. Purpose: Both to add an endurance/training aspect, and to underline the social aspect and joy of singing together.

- Artefacts were often included to add elements of play and to support/supplement dancing/movements during singing.

- "Moon river"
- "On the road to Mandalay" (in Danish: "Åh, den vej til Mandalay")
- "The Lion Sleeps Tonight" (in Danish: "Vimmersvej")

**Examples of songs with additional movement/dancing**
(video clips from search on Youtube):

- https://www.youtube.com/watch?v=Utr-V7OeJOE (Source: Efcfie Va)
- https://www.youtube.com/watch?v=wWzQ-Pj4Xt0&list=PLEC531643A4FE480D&index=6 (Source: Vincent Bates)
- https://www.youtube.com/watch?v=GXqCyp7GUIw (Source: Vincent Bates)

**Example of included artefacts:**
Balloons, drum sticks, scarfs, umbrellas, ropes, balls, fly swappers to support/supplement dancing/movement during singing.

**Relaxation and body awareness exercises**

Examples of elements/activities:

- Relaxation/body and breathing awareness in the beginning and ending of each session.
- Guided mindful meditation and body "walk-through"' (see above).

- Accompanied by calm, slow music (recorded music, played through music equipment) for mindful relaxation and body awareness.

Examples of recorded music:
Chopin - Nocturne op.9 No.2
Pachelbel - Canon In D Major
Yiruma: Kiss The Rain

**Item no. 9: Content of any home programme component**

- Participants were encouraged to practice exercises and methods from the sessions at home, e.g. breathing techniques, vocal exercises/songs, and body awareness. However, there were no specific requests or programme for this.

**Item no. 10: Nonexercise programme**

Supplementary *patient education* (part of standard PR):

- Knowledge about COPD (communicated in a considerate manner that did not create unnecessary concern (best practice), behavior change, smoking cessation, correct use of inhaler devices, nutrition, sexuality, handling of stress and anxiety, early recognition of exacerbation, decision-making and taking action of symptoms, goals of motivation and maintenance post PR.

**Item no. 11. How adverse events that occur during exercise are documented and managed**

- Singing teachers were instructed to seek assistance and contact local health professionals immediately in case of any adverse event (AE). Further, singing teachers and health professionals of the local health-care center were asked to contact the research group in doubt or in case of any AE.
- However, data on AE were not systematically collected for this trial.

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**WHERE: location**

**Item no. 12: Setting in which exercises are performed**

- Sessions were delivered in a standard, spacious training studio (normally used for PR) in each local health-care center.
- The training studio was in a separate and undisturbed room.

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**WHEN, HOW MUCH: dosage**

**Item no. 13: Detailed description of the exercises (e.g. sets, repetitions, duration, intensity)**
**Overview of intervention:**

- In total, 20 sessions, i.e. twice weekly during 10 weeks.
- Each session had a duration of 90 minutes, including a 10-15 minutes break for water/tea/coffee and toilet visit.

**Session structure:**

- 20 minutes of physical warm ups: posture and breathing exercises
- 20 minutes of vocal warm up's and rhythm and pitch games
- 40 minutes of singing songs
- 10 minutes of cool down (mindfulness or relaxation)

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**TAILORING: what, how**

**Item no. 14: Whether exercises are generic ("one size fits all") or tailored to the individual**

- Exercises and songs were generic and suitable for all, however tailored to each class.
- Basic exercises/songs could easily be graduated to meet/challenge all levels of vocal/musical/physical competence.

**Exercises and songs were however tailored in relation to following:**
**If impaired, participants were allowed to:**

- Sit more often instead of standing/moving.
- Perform shorter outbreath than other participants.

**Competence:**

- Each participant was instructed individually in relation to breathing technique, posture, and muscle work/tension/relaxation.
- Participants with any prior musical competence were asked to add advanced elements to songs, e.g. second/extra voice and/or rhythms.

**Preferences:**

- Singing teachers' personal taste in repertoire/genres.
- Participants' personal taste in repertoire.[11, 15]

**Item no. 15: Decision rule that determines the starting level for exercise**

- No prior exercise or vocal/musical competences were required.
- Individuals with COPD with mMRC<2, and potentially weak/untrained, but able to participate in the rehabilitation programme.
- Since the intervention and background methodology is new in Denmark, all participants were regarded as beginners in relation to singing.

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**HOW WELL: planned, actual**

**Item no. 16: Whether the exercise intervention is delivered and performed as planned**

- Singing teachers kept a registration of attending frequency by participants.
- Each singing teacher used a logbook of all sessions, reporting of reflective practice as a singing teacher.
- Each singing teacher received supervision throughout by study investigator (MK) at visits twice and telephonic contact to ensure deliverance according to workshop and handout guidelines.
- Singing teachers were encouraged to build peer-network with knowledge-sharing.
- There was no specific and detailed protocol for the intervention. SLH, therefore, was to some extend delivered diversely across the centers, due to variety in singing teachers' background and personal styles, and to specific composition and dynamics in each class.
- Video recordings and interviews were made at two sites.
- At the end of the intervention period, video interviews were made about the experiences of the singing teacher.
- In case of cancelled sessions due to absence of singing teacher, sessions were conducted by another singing teacher in the project, by a local health professional (singing together with the participants), or cancelled.

## Appendix S4: Baseline characteristics in intention-to-treat-population

| | Singing for Lung Health (n=145) | | Physical Exercise Training (n=125) | | Between-group difference (*p*-value) |
|---|---|---|---|---|---|
| **Educational level, n (%)** | | | | | |
| Low education | 55 | (37.9%) | 48 | (38.4%) | 0.98 |
| Medium education | 56 | (38.6%) | 49 | (39.2%) | |
| High education | 34 | (23.4%) | 28 | (22.4%) | |
| **Occupational status, n (%)** | | | | | |
| Full- or part time job | 15 | (10.3%) | 15 | (12.0%) | 0.70 |
| Unemployed/retired | 130 | (89.7%) | 110 | (88.0%) | |
| **Income, n (%)** | | | | | |
| Low income | 114 | (78.6%) | 94 | (75.2%) | 0.39 |
| Medium income | 23 | (15.9%) | 27 | (21.6%) | |
| High income | 8 | (5.5%) | 4 | (3.2%) | |
| **Living place, n (%)** | | | | | |
| Urban | 9 | (6.2%) | 7 | (5.6%) | 0.44 |
| Mixed urban-rural | 37 | (25.5%) | 41 | (32.8%) | |
| Rural | 99 | (61.3%) | 77 | (61.6%) | |
| **Marital status, n (%)** | | | | | |
| Married/co-habiting | 84 | (57.9%) | 82 | (65.6%) | 0.21 |
| Single/widowed | 61 | (42.1%) | 43 | (34.4%) | |
| **Medication, number of all COPD controller drugs, n (%)** | | | | | |
| None | 20 | (13.8%) | 15 | (12.0%) | 0.67 |
| Usage of 1 type of medication | 16 | (11.0%) | 17 | (13.6%) | |
| Usage of 2 types of medication | 56 | (38.6%) | 45 | (36.0%) | |
| Usage of 3 types of medication | 47 | (32.4%) | 46 | (36.8%) | |
| Usage of 4 types of medication | 6 | (4.1%) | 2 | (1.6%) | |

Table S4 text: Data are presented as mean ±SD unless otherwise stated. BMI: body mass index; FEV1: forced expiratory volume in 1 second; mMRC: modified Medical Research Council dyspnoea score; GOLD: Global Initiative for Chronic Obstructive Lung Disease; LAMA inhaled long-acting muscarinic antagonists; LABA: inhaled long-acting beta-2-agonists; ICS: inhaled corticosteroids; OCS: oral corticosteroids; COPD: chronic obstructive lung disease.

# Appendix S5: Per protocol analyses *i.e.* excluding patients who dropped out before study completion

| | | Singing for Lung Health (n=108) | | Physical Exercise Training (n=87) | | Between-group difference (*p*-value) |
|---|---|---|---|---|---|---|
| Age | | 70.5 | ±8.4 | 69.0 | ±7.4 | 0.18 |
| Female sex, n (%) | | 61 | (56.5%) | 61 | (70.1%) | 0.05 |
| BMI | | 28.3 | ±5.8 | 29.9 | ±6.0 | 0.05 |
| FEV1 (baseline) | | 1.2 | ±0.5 | 1.2 | ±0.5 | 0.92 |
| FEV1 % predicted (baseline) | | 50.9 | ±16.0 | 51.9 | ±15.6 | 0.65 |
| Expectations towards benefits of singing | Positive | 74 | (68.5%) | 61 | (70.1%) | 0.12 |
| Adherence to the intervention | 0-24% | 0 | (0.0%) | 2 | (2.3%) | 0.18 |
| | 25-49% | 5 | (4.6%) | 1 | (1.1%) | |
| | 50-74% | 18 | (16.7%) | 18 | (20.7%) | |
| | 75-100% | 85 | (78.7%) | 66 | (75.9%) | |
| 6MWD (at baseline), metres | | 387.3 | ±104.7 | 400.4 | ±96.3 | 0.37 |
| 6MWD (follow-up), metres | | 407.3 | ±97.2 | 420.6 | ±101.8 | 0.37 |
| Change from baseline, metres | | 17.2 | ±40.8 | 20.1 | ±37.1 | 0.61 |
| 6MWD MID (30m) reached | | 31 | (38.7%) | 31 | (35.6%) | 0.30 |
| FEV1 MID (120ml) reached | | 27 | (25.2%) | 17 | (19.5%) | 0.35 |
| SGRQ total score MID | | 51 | (47.2%) | 35 | (40.2%) | 0.33 |
| FEV1 and SGRQ MID reached | | 17 | (15.7%) | 4 | (4.6%) | 0.01 |

## Appendix S6: Relationship between training modality and accomplishing minimal important difference of 6MWD (30 metres)

| Variable | OR | 95% CI | P-value |
|---|---|---|---|
| Training modality | | | |
| Physical Exercise Training | 1.00 | | |
| Singing for Lung Health | 0.89 | 0.47 - 1.68 | 0.711 |
| Age | | | |
| -60 | 1.00 | | |
| 61-70 | 0.67 | 0.24 - 1.93 | 0.462 |
| 71-80 | 0.45 | 0.15 - 1.35 | 0.156 |
| >80 | 0.25 | 0.05 - 1.18 | 0.079 |
| Sex | | | |
| Woman | 1.00 | | |
| Male | 0.67 | 0.33 - 1.34 | 0.258 |
| Gold class | | | |
| 1 | 0.93 | 0.15 - 5.76 | 0.940 |
| 2 | 1.00 | | |
| 3 | 0.77 | 0.39 - 1.53 | 0.450 |
| 4 | 0.28 | 0.07 - 1.13 | 0.073 |
| mMRC | | | |
| mMRC 0-2 | 1.16 | 0.52 - 2.56 | 0.717 |
| mMRC 2 | 1.00 | | |
| mMRC 3 | 0.42 | 0.11 - 1.57 | 0.196 |
| mMRC 4 | 1.00 | 0.38 - 2.64 | 0.998 |
| BMI | | | |
| <18.5 | 2.71 | 0.33 - 22.26 | 0.354 |
| 18.5-24.9 | 1.00 | | |
| 25-29.9 | 1.33 | 0.58 - 3.06 | 0.497 |
| 30 - | 1.22 | 0.53 - 2.82 | 0.646 |
| Expectations towards benefits of singing | | | |
| Neutral or negative | 1.00 | | |
| Positive | 0.86 | 0.43 - 1.74 | 0.681 |
| Adherence to training | | | |
| 0-49% | 1.00 | | |
| 50-74% | 6.12 | 1.50 - 25.07 | 0.012 |
| 75-100% | 12.56 | 3.48 - 45.30 | <0.001 |
| 6MWD at baseline | | | |
| Q1 | 1.00 | Reference | |
| Q2 | 0.33 | 0.12 - 0.86 | 0.023 |
| Q3 | 0.37 | 0.13 - 1.03 | 0.056 |
| Q4 | 0.23 | 0.08 - 0.70 | 0.010 |
| Site | | | |
| Site number (1 - 11) | 0.0* | 0.0 - 0.0 | - |

* Constant term from the random-effect. Odds ratios (ORs) were computed using univariable logistic regression and multilevel mixed-effects logistic regression.

## Appendix S7: Baseline characteristics and physical performance of patients with high adherence (75% or more) to the interventions

| | Singing for Lung Health | Physical Exercise Training | P-value |
|---|---|---|---|
| **Baseline characteristics** | | | |
| N | 88 | 71 | |
| Age, mean (SD) | 70.8 (7.8) | 70.0 (7.5) | 0.48 |
| Sex | | | |
| Female | 51 (58%) | 47 (66%) | 0.29 |
| Male | 37 (42%) | 24 (34%) | |
| BMI, mean (SD) | 27.8 (5.9) | 27.8 (5.9) | 0.99 |
| FEV1 (baseline), median (IQR) | 1.1 (0.9, 1.4) | 1.2 (0.9, 1.5) | 0.28 |
| FEV1 % predicted (baseline), median (IQR) | 49.0 (37.0, 62.0) | 51.0 (44.0, 66.0) | 0.11 |
| Expectations towards benefits of singing | | | |
| Negative | 0 (0%) | 2 (3%) | 0.27 |
| Neutral | 26 (30%) | 19 (27%) | |
| Positive | 62 (70%) | 50 (70%) | |
| **Physical performance** | | | |
| 6MWD at baseline, median (IQR) | 406.5 (321.5, 455.5) | 419.0 (355.0, 451.0) | 0.45 |
| 6MWD (follow-up), median (IQR) | 427.0 (367.5, 467.0) | 438.5 (375.5, 480.0) | 0.23 |
| Change from baseline, mean (SD) | 16.3 (40.5) | 19.1 (36.8) | 0.65 |
| MID (30 m) reached | 24 (27%) | 25 (36%) | 0.25 |

## Appendix S8: Factors associated with high adherence (75% or more) to the interventions

| Variable | OR | 95% CI | P-value |
|---|---|---|---|
| Intervention | | | |
| Physical Exercise Training | 1.00 | Reference | 0.41 |
| Singing for Lung Health | 1.24 | 0.74 - 2.08 | |
| Age | | | |
| -60 years | 1.00 | Reference | |
| 61-70 years | 1.41 | 0.63 - 3.16 | 0.41 |
| 71-80 years | 2.01 | 0.89 - 4.56 | 0.09 |
| >80 years | 1.85 | 0.62 - 5.55 | 0.27 |
| Sex | | | |
| Woman | 1.00 | Reference | |
| Male | 1.17 | 0.67 - 2.03 | 0.58 |
| GOLD class | | | |
| 1 | 1.72 | 0.39 - 7.55 | 0.47 |
| 2 | 1.00 | Reference | |
| 3 | 1.51 | 0.85 - 2.68 | 0.16 |
| 4 | 0.63 | 0.27 - 1.46 | 0.28 |
| BMI | | | |
| <18.5 | 0.32 | 0.05 - 1.91 | 0.21 |
| 18.5-24.9 | 1.00 | Reference | |
| 25-29.9 | 0.84 | 0.45 - 1.59 | 0.59 |
| 30 - | 1.08 | 0.56 - 2.06 | 0.82 |
| Expectations towards benefits of singing | | | |
| Neutral or negative | 1.00 | Reference | |
| Positive | 1.65 | 0.95 - 2.89 | 0.08 |

Odds ratios (ORs) were computed using multivariable logistic regression. ORs > 1 indicate an increased probability of high adherence.

## Appendix S9: Baseline characteristics of Per protocol population ("Completers" vs. "Non-completers")

| | Completers (both study groups) (n=195) | | Non-completers (both study groups) (n=75) | | Between-group difference (*p*-value) |
|---|---|---|---|---|---|
| **Age** | 69.9 | ±8.0 | 68.7 | ±9.5 | 0.35 |
| **Sex (female), n (%)** | 122 | (62.6%) | 46 | (62.6%) | 0.89 |
| **BMI** | 28.2 | ±5.9 | 27.1 | ±6.3 | 0.23 |
| **Educational level, n (%)** | | | | | 0.07 |
| Low education | 71 | (36.4%) | 32 | (42.7%) | |
| Medium education | 72 | (36.9%) | 33 | (44.0%) | |
| High education | 34 | (23.4%) | 28 | (22.4%) | |
| **Occupational status, n (%)** | | | | | 1.00 |
| Full- or part time job | 22 | (11.3%) | 8 | (10.7%) | |
| Unemployed/retired | 173 | (88.7%) | 67 | (89.3%) | |
| **Income, n (%)** | | | | | 0.08 |
| Low income | 143 | (73.3%) | 65 | (86.7%) | |
| Medium income | 42 | (21.5%) | 8 | (10.7%) | |
| High income | 10 | (5.1%) | 2 | (2.7%) | |
| **Living place, n (%)** | | | | | 0.10 |
| Urban | 8 | (4.1%) | 8 | (10.7%) | |
| Medium | 60 | (30.8%) | 18 | (24.0%) | |
| Rural | 127 | (65.1%) | 49 | (65.3%) | |
| **Marital status, number, n (%)** | | | | | 0.03 |
| Married/co-habiting | 123 | (63.1%) | 43 | (57.3%) | |
| Single/widowed | 72 | (36.9%) | 32 | (42.7%) | |
| **Smoking Status, n (%)** | | | | | 0.004 |
| Current | 38 | (19.5%) | 29 | (38.7%)) | |
| Former | 144 | (73.8%) | 41 | (54.7%) | |
| Never | 13 | (6.7%) | 5 | (6.7%) | |
| **Pack years** | 40.5 | ±16.8 | 40.5 | ±22.9 | 1.00 |
| **FEV1 (% of predicted)** | 51.3 | ±15.8 | 51.6 | ±19.4 | 0.91 |
| **mMRC, n (%)** | | | | | 0.01 |
| 0 | 11 | (5.6%) | 2 | (2.7%) | |
| 1 | 68 | (34.9%) | 17 | (22.7%) | |
| 2 | 67 | (34.4%) | 21 | (28.0%) | |
| 3 | 19 | (9.7%) | 9 | (12.0%) | |
| 4 | 30 | (15.4%) | 26 | (34.7%) | |
| **GOLD classification, n (%)** | | | | | 0.01 |
| Class 1 | 5 | (2.6%) | 4 | (5.4%) | |
| Class 2 | 97 | (50.0%) | 37 | (50.0%) | |
| Class 3 | 76 | (24.3%) | 18 | (39.2%) | |
| Class 4 | 16 | (8.2%) | 15 | (20.3%) | |
| **Medication, n (%)** | | | | | |
| LAMA | 138 | (70.8%) | 53 | (70.7%) | 1.00 |
| LABA | 148 | (75.9%) | 61 | (81.3%) | 0.42 |
| ICS | 93 | (47.7%) | 37 | (49.3%) | 0.86 |
| OCS | 7 | (3.6%) | 6 | (8.0%) | 0.20 |
| Roflumilast | 0 | (0.0%) | 1 | (1.3%) | 0.28 |
| Theophylline | 1 | (0.5%) | 1 | (1.3%) | 0.48 |
| **Medication, number of all COPD controller drugs** | | | | | 0.89 |
| None | 27 | (13.8%) | 8 | (10.7%) | |
| Usage of 1 type of medication | 25 | (12.8%) | 8 | (10.7%) | |
| Usage of 2 types of medication | 72 | (36.9%) | 29 | (38.7%) | |
| Usage of 3 types of medication | 66 | (33.8%) | 27 | (36.0%) | |
| Usage of 4 types of medication | 5 | (2.6%) | 3 | (4.0%) | |
| **Home-oxygen therapy, n (%)** | 7 | (3.6%) | 2 | (2.7%) | 0.74 |

| | | | | | |
|---|---|---|---|---|---|
| **Positive expectations towards benefits of singing, n (%)** | 135 | (69.2%) | 44 | (58.7%) | 0.11 |
| **Baseline test performance** | | | | | |
| **6MWD, metres** | 393.1 | ±101.0 | 352.5 | ±101.2 | 0.004 |
| **BORG CR 10 - after 6MWD** | 6.8 | ±2.7 | 7.1 | ±3.1 | 0.53 |
| **St. George's Respiratory Questionnaire (SGRQ)** | | | | | |
| Total score | 43.2 | ±16.5 | 50.1 | ±17.7 | 0.004 |
| Symptoms score | 46.8 | ±22.4 | 52.5 | ±22.5 | 0.07 |
| Activity score | 62.2 | ±20.5 | 71.5 | ±20.8 | 0.01 |
| Impact score | 31.2 | ±17.4 | 37.2 | ±19.4 | 0.02 |
| **Hospital Anxiety and Depression Scale (HADS)** | | | | | |
| Anxiety score | 4.8 | ±3.7 | 5.1 | ±3.7 | 0.65 |
| Depression score | 2.9 | ±2.9 | 3.8 | ±3.4 | 0.03 |

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