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Physiological changes related to 10 weeks of singing for lung health in patients with COPD

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ABSTRACT

Background Singing for Lung Health (SLH) was non-inferior to physical exercise training in improving 6-minute walking test distance (6MWD) and quality of life (St. George's Respiratory Questionnaire (SGRQ)) within a 10-week pulmonary rehabilitation (PR) programme for COPD in our recent randomised controlled trial (RCT) (NCT03280355). Previous studies suggest that singing improves lung function, respiratory control and dyspnoea, however this has not yet been convincingly confirmed. Therefore, this study aimed to explore the impact of SLH on physiological parameters and the associations with achieving the minimal important difference (MID) in 6MWD and/or SGRQ.

Methods We conducted post hoc, per-protocol analyses mainly of the SLH group of the RCT, exploring associations with 6MWD and SGRQ results by stratifying into achieving versus not-achieving 6MWD-MID (≥30 m) and SGRQ-MID (≤−4 points): changes in lung function, inspiratory muscle strength/control, dyspnoea, and heart rate response using logistic regression models. Further, we explored correlation and association in achieving both 6MWD-MID and SGRQ-MID (or in neither/nor) using Cohen's κ and Cochran-Mantel-Haenszel Test.

Results In the SLH study group (n=108), 6MWD-MID was achieved by 31/108 (29%) and in SGRQ by 53/108 (49%). Baseline factors associated with achieving MID in either outcome included short baseline 6MWD and high body mass index. Achieving 6MWD-MID was correlated with improved heart rate response (OR: 3.14; p=0.03) and achieving SGRQ-MID was correlated with improved maximal inspiratory pressure (OR: 4.35; p=0.04). Neither outcome was correlated with significant spirometric changes. Agreement in achieving both 6MWD-MID and SGRQ-MID was surprisingly insignificant.

Conclusions This explorative post hoc study suggests that SLH is associated with physiological changes after short-term PR for COPD. Future physiological studies will help us to understand the mechanisms of singing in COPD. Our study furthermore raises concern about poor agreement between subjective and objective benefits of PR despite state-of-the-art tools.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Singing for lung health (SLH) as part of community-based pulmonary rehabilitation has shown effects on walking distance and quality of life (QoL) in COPD, but current knowledge on the impact of SLH on physiological parameters is scarce.

WHAT THIS STUDY ADDS

⇒ This study suggests that improvements in 6-minute walking test and QoL during a short-term SLHprogramme is associated with diverse physiological changes in patients with COPD.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE, AND/OR POLICY

⇒ Our findings support that SLH has physiological impact besides being a pleasant leisure time activity in COPD. However, further studies are needed to explore associations and to conclude on benefits of SLH for COPD.

INTRODUCTION

Singing has become widely acknowledged as a beneficial activity for people living with chronic respiratory disease and is proposed to improve physical, psychological, and social health.[1 2] An initial body of research in respiratory disease suggests that singing addresses dyspnoea control,[3–10] improves exercise capacity,[4 11 12] enhances quality of life (QoL),[3 4 13 14] and reduces anxiety and depression.[14] Moreover, singing with peers builds meaningful cohesion and reduces experiences of isolation.[1 3 4 15–20]

However, it is still unknown how singing exerts its effects, that is, which specific physiological parameters may change during an effective singing training course.[2–4] A recent narrative review[2] suggested that singing may improve aspects in breathing pattern, respiratory control, hyperinflation, dyspnoea, health-related QoL, interoception, and physical capacity and activity in COPD. However, the authors concluded that the present evidence suffers from severe between-study heterogeneity including definitions and parameters of effectiveness. The gold standard parameter of effectiveness in pulmonary rehabilitation (PR) research is walking test distance, either 6-minute walking test (6MWT) or incremental shuttle walking test.[21 22] In contrast, the primary outcome of the majority of studies on singing is perceived effect (qualitative or semiquantitative outcomes) and not objective parameters such as exercise capacity and physiological mechanisms.[2–4 12] Thus, there is a lack of research on physiological changes during singing and on the association between achieving objective and subjective improvement.

We recently published results from the so-far largest randomised controlled trial (RCT) on singing compared with physical exercise training (PExT) as part of a 10 weeks' community-based PR programme in COPD.[12] As intervention, we used the current best-practice and disease-specific singing approach, Singing for Lung Health (SLH)[3 10 23 24] and with the comparator (PExT) representing the gold standard training activity within PR. We included 270 patients with COPD and found that SLH was non-inferior to PExT in improving 6MWT distance (6MWD) (primary study outcome) and QoL (St. George's Respiratory Questionnaire, SGRQ) (the first of several secondary study outcomes).[12]

In the present study, we aimed to explore physiological changes related to SLH. Specifically, we aimed to investigate whether SLH was associated with physiological changes in lung function, inspiratory muscle strength and control, dyspnoea and breathing control, and exercise-induced changes in pulse and oxygen saturation. Further, we aimed to investigate associations and overlap between achieving minimal important difference (MID) in 6MWD and/or SGRQ.

To elucidate these aspects, we conducted post hoc analyses of our RCT exclusively focusing on the proportion of SLH study participants with complete data from both baseline and follow-up, thus representing the SLH per-protocol population.[12] We hypothesised that attending SLH would be associated with positive changes in physiological parameters and mostly in persons who achieved either 6MWD-MID or SGRQ-MID. Moreover, we hypothesised that achieving 6MWD-MID and SGRQ-MID would be clearly overlapping.

METHODS

Study design, oversight, participants, randomisation and blinding, and data collection

For this post hoc, explorative study, we included data retrieved from the per-protocol RCT population (n=195), that is, patients who completed both baseline and follow-up assessments. The main focus of this paper is on the SLH group (n=108), but we also included supplementary analyses of the overall RCT per-protocol population (n=195) and of the group receiving the gold standard, PExT, the PExT group (n=87) to assess basic comparability and for transparent reporting and exploratory investigation.

The RCT was conducted between August 2017 and May 2019 (ClinicalTrials.gov; NCT03280355). Details on inclusion criteria, procedures for randomisation, blinding, and data collection are described in our previous paper.[12]

Groups

Participants were stratified accordingly:

Stratum 1: Study group: SLH is the main focus of this paper, with PExT data mainly presented as supplementary data.

Stratum 2: PR outcomes:

1. Objective benefit of PR=achieving 6MWD-MID (≥30 metres)[25] or not, and
2. Subjective benefit of PR=achieving SGRQ-MID (≤−4.0 units)[26] or not.

Outcomes and measures

Baseline characteristics included sociodemographic information, body mass index (BMI), medication usage, smoking history, expectations towards benefits of singing, forced expiratory volume in 1 s (FEV_1 in L, and as percentage predicted (FEV_1%)), forced vital capacity (FVC in L, and as percentage predicted (FVC%)), FEV_1/FVC ratio (FEV_1/FVC as percentage), forced expiratory flow (FEF25%–75% (L/s)), maximum inspiratory pressure (MIP), single breath count test, breath holding test, Modified Medical Research Council Dyspnoea Scale, modified BORG-CR10-Dyspnoea Scale, and baseline performance in 6MWD and SGRQ total score.

Effect was reported as change from baseline to follow-up concerning the following study domains and related parameters:

1. Performance in 6MWD and SGRQ, including achievement of MID (yes/no).[25 26]
2. Lung function: FEV_1 and FVC, both reported in litres (MID: ≥120 mL).[27]
3. Inspiratory muscle strength and control: MIP (MID: ≥17 cm H_2O;[28–31] ≥10% change also explored).
4. Dyspnoea and breathing control: single breath count test (≥10% and ≥50% change).[19 32 33]
5. Exercise-induced changes in pulse and saturation: pulse (beats/min) and heart rate response (highest pulse reached minus baseline pulse) (≥10% and ≥50% change), and Oxygen Saturation Response and Chronotropic Index (exercise-induced oxygen desaturation (EID)).[34]

See online supplemental table S1 for details and interpretation of study outcomes and measures.

Trial interventions

Information on content and delivery of the 10 weeks' trial interventions and additional patient education as part of the PR programme are reported in our previous paper and appertaining supplementary files.[12] Content, delivery and approach of SLH have also been described previously.[2 12 23 24]

Patient and public involvement

Participants were not involved in study development, recruiting or execution. We intend to enlist the support of participants in developing and implementing our dissemination strategy.

Statistics

To investigate comparability, the overall per-protocol population (n=195) was compared (SLH vs PExT). Subsequently, the SLH group (and supplementary, the PExT group) was stratified according to the two study outcomes, 6MWD and SGRQ, comparing achieved versus not achieved MID for each outcome. We used *Student's* t-test in the primary analyses to test independence within continuous data (described results as mean±SD) regarding baseline, follow-up, and change values (=computed change from baseline to follow-up). Level of significance was reported as p value, and changes were presented with 95% CI. Pearson's χ^2 test (or Fisher's test) was used to test independence in distribution within categorical data (results reported as number and percentage). Within-group changes from baseline to follow-up were analysed using paired-samples tests with level of significance reported as: no star: p>0.05, *: p<0.05, **: p<0.01; ***: p<0.001.

Explanatory factors were explored in relation to the two study outcomes using logistic regression models. At first, significance was explored in all relevant variables using univariable models. Continuous variables were transposed into categories: age (transposed into tertiles), sex (male/female), BMI (transposed into tertiles), 6MWD at baseline (transposed into tertiles) and MID yes/no in FEV_1. Change in MIP was explored in categories (yes/no): ≥17 cm H_2O and ≥10% improvement. Change in single breath count test was explored in categories: ≥10% and ≥50% improvement, and changes in EID were explored in categories (yes/no): ≥10% and ≥50% improvement in heart rate and resolvement of baseline EID at follow-up (yes/no) (see online supplemental table S1 for elaborated outcomes and measures). Subsequently, multilevel mixed-effects logistic regression models were conducted and comprised variables displaying significance in the univariable regression models.

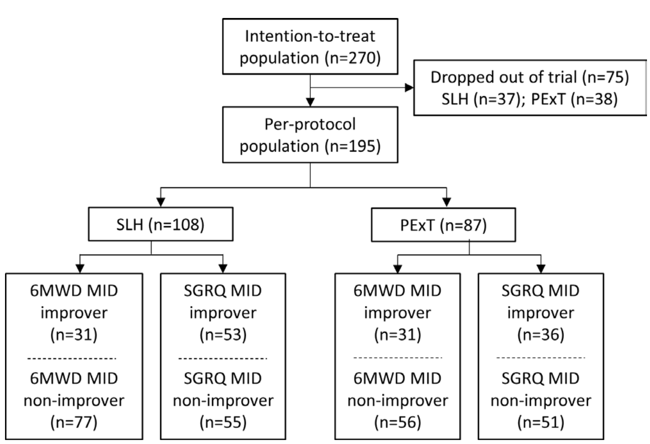

Figure 1 Consort flow diagram. 6MWD, 6-minute walking test distance; MID, minimal important difference; PExT, physical exercise training; SGRQ, St. George's Respiratory Questionnaire; SLH, singing for lung health.

To investigate correlation and association in achieving MID in both study outcomes (or in neither) in SLH, likelihood and chance-corrected proportional agreement were analysed using Cohen's κ. Further, the Cochran-Mantel-Haenszel test for 2×2 xK tables was used to assess association and independence between 6MWD and QoL; this analysis included both overall study groups (SLH and PExT).

Statistical analyses were performed using SPSS V.27.0 (IBM, Chicago, USA); and STATA/IC V.16.1 (StataCorp, Texas, USA). Statistical significance was reached at p<0.05.

The STrengthening the Reporting of OBservational studies in Epidemiology[35] research checklist was used in accordance with recommendations for conduct and dissemination of observational studies.

RESULTS

Participants

The SLH study group (n=108) was retrieved from the RCT per-protocol population (n=195; representing 72% of the RCT intention-to-treat population (n=270)). 6MWD-MID was achieved by 31/108 (29%) and SGRQ-MID by 53/108 (49%) (see figure 1).

Baseline characteristics

The per-protocol populations of SLH and PExT were comparable. Overall, most were women (n=122; 62.2%), mean age was 68.9 (SD 7.9) years; mean pack years was 40.5 (SD 22.9); mean BMI was 28.2 (SD 5.9); and mean FEV_1% predicted was 51.3 (SD 15.8). Both the SLH and the PExT groups showed comparability when stratified in outcomes: 6MWD and SGRQ (MID achieved vs MID not achieved), but differed in size (SLH: n=108; PExT: n=87). Online supplemental table S2 depicts supplementary analyses of baseline data for SLH vs PExT. Online supplemental tables S3 and S4 depict supplementary analyses of baseline characteristics in SLH and PExT, analysed in stratum 6MWD (online supplemental table S3) and stratum SGRQ (online supplemental table S4).

At baseline, SLH participants achieving 6MWD-MID had higher BMI and lower 6MWD compared with those not achieving MID (online supplemental table S3A), and those achieving SGRQ-MID had higher BMI, higher SGRQ (=lower QoL), and had lower performance in 6MWD, single breath count test, and MIP (online supplemental table S3B).

Comparing the SLH and PExT groups, we found no significant difference except that SLH participants achieving 6MWD-MID had higher BMI, lower FEV_1/FVC ratio, and lower 6MWD (online supplemental table S3A), and SLH-participants achieving SGRQ-MID had lower BMI and lower value parameters related to lung function, inspiratory control and function, and dyspnoea control (online supplemental table S4A). In the PExT group, only educational level differed in those achieving SGRQ-MID (online supplemental table S4B).

Physiological changes in SLH

Table 1 depicts values and effects stratified by 6MWD and SGRQ in SLH (n=108) and substratified in MID achieved/not-achieved.

No significant between-group differences were observed in the 6MWD stratum (table 1). However, we observed a tendency favouring the proportion achieving SGRQ-MID and in physiological variables related to lung function, inspiratory control and function, dyspnoea and breathing control, and heart rate response, although not reaching statistical significance. Several significant within-group differences favouring the proportion achieving MID were further observed in both subgroups (SGRQ, single breath count test, and MIP).

In the SGRQ stratum (table 1), we observed that the SLH group improved significantly in 6MWD and in physiological variables related to inspiratory control and function and to dyspnoea and breathing control. We observed several within-group changes favouring the proportion achieving MID in variables related to inspiratory control and function and to dyspnoea and breathing control.

Values and effects for supplementary analyses of the PExT group are available in the supplementary files (online supplemental table S5). Briefly, in those achieving 6MWD-MID (online supplemental table S5A), we observed a tendency towards increased difference in change in QoL. Similarly, in those achieving SGRQ-MID (online supplemental table S5B), we observed a tendency towards improved EID. Compared with the SLH group, we observed fewer significant within-group differences in parameters related to inspiratory control, function, and dyspnoea or breathing control.

Relationship between SLH and physiological changes in 6MWD and SGRQ MID strata

The multivariable logistic regression analysis (table 2) included selected variables (oligo variables) based on display of significance in the initial univariable analyses, for each of the two strata: achieved 6MWD-MID (table 2) *respectively* SGRQ-MID (table 3).

Achieving 6MWD-MID was associated with short baseline 6MWD (OR: 6.07; 95% CI 1.4 to 0.5; p=0.01) and older age (OR: 0.13; 95% CI 0.1 to 0.6; p=0.01). We observed no baseline factors associated with achieving SGRQ-MID.

Concerning changes from baseline to follow-up in physiological parameters, achieving 6MWD-MID was associated with ≥50% improvement in heart rate response, and achieving SGRQ-MID was associated with achieving ≥10% improvement in MIP.

We found no associations in any study domain in the multivariable models PExT (online supplemental table S6).

Agreement and association between 6MWD and QoL response

Table 4 shows that achieving MID in both or neither 6MWD and SGRQ was observed in 57.4% in both the SLH and in the PExT groups, resulting in *slight agreement* using Cohen's κ (SLH group: κ=0.14; p=0.14; PExT group: κ=0.11; p=0.32). In both groups, it was numerically more common to perceive an effect without improving 6MWD than to improve both.

Using the Cochran-Mantel-Haenszel test to assess association across overall study groups (SLH and PExT), we observed a tendency towards an association. The chance-corrected proportional agreement between achieving 6MWD-MID and SGRQ-MID is depicted in online supplemental table S7.

DISCUSSION

In this post hoc explorative study, we used per-protocol data from our recent RCT[12] where we compared SLH with PExT within a 10 weeks community-based PR programme. We found that SLH provided physiological improvement in patients who achieved 6MWD-MID (=physical exercise capacity) and/or SGRQ (=QoL); however, we observed more improvements in those achieving SGRQ-MID. Specifically, SLH was associated with improved MIP and single breath count test. We found no significant overlap and/or close association between achieving 6MWD-MID and/or SGRQ-MID.

Achieving 6MWD-MID and/or SGRQ-MID in SLH participants

We observed that less than a third of SLH participants (31/108) achieved 6MWD-MID, whereas almost a half (53/108) achieved SGRQ-MID (table 1). Impact of singing/SLH on exercise capacity has not yet been established, and no previous studies have reported on the proportion of participants achieving MID in walking distance tests.[19 36–40] The improvement in SGRQ, though, falls in line with reporting of impact of singing/SLH on QoL in previous studies.[3 13 14 41 42] Interestingly, the change found in this study was much larger in the 6MWD stratum and in those achieving 6MWD-MID (61.8 m (SD 41.9)) than in the intention-to-treat analysis of the RCT.[12] For the SGRQ stratum, change was also higher (24.8 m (SD 43.2)) but did not reach MID. Regarding SGRQ, however, MID was achieved in both outcomes (6MWD stratum: −6.7 (SD 12.0); SGRQ stratum: −11.8 (SD 7.5)).

The SLH participants achieving 6MWD-MID had lower BMI, FEV_1/FVC ratio, and 6MWD at baseline compared with those who did not achieve MID (online supplemental table S3A). Those achieving SGRQ-MID had lower BMI and lower parameters related to lung function, inspiratory control and function, and dyspnoea control (online supplemental table S4A). Evidently, it is

Table 1 Effect in SLH (n=108) (baseline/post/change): (1A) 6MWD-MID (≥30 m) achieved versus not achieved and (1B) SGRQ-MID total score (≤−4 units) achieved versus not achieved

	Table 1A				Table 1B			
	6MWD				SGRQ			
	6MWD-MID achieved (n=31)	6MWD-MID not achieved (n=77)	Between-group difference (P value)	95% CI for the difference	SGRQ-MID achieved (n=53)	SGRQ-MID not achieved (n=55)	Between-group difference (P value)	95% CI for the difference
Age, years	68.4 (8.2)	71.4 (8.4)	0.09		69.6 (7.6)	71.4 (9.1)	0.12	
Sex, female, n (%)	18 (58%)	43 (56%)	0.83		31 (60.8%)	30 (52.6%)	0.39	
BMI								
Baseline	30.9 (6.2)	27.3 (5.4)	**0.003**		29.7 (6.2)	27.1 (5.2)	**0.01**	
Follow-up	30.9 (6.2)	27.3 (5.3)	**0.002**		29.9 (6.2)	26.9 (5.2)	**0.005**	
Change (follow-up - baseline)	0.1 (0.8)	−0.04 (0.6)	0.29	(−0.4 to 0.3)	0.2 (0.9)	−0.2 (1.1)	0.051	(−0.7 to 0.1)
6MWT distance								
Baseline	337.2 (119.9)	407.4 (91.2)	**0.01**		363.5 (115.8)	410.2 (87.8)	**0.01**	
Follow-up	399.0 (108.7)	406.7 (90.9)	0.71		388.2 (104.6)	420.1 (84.7)	**0.04**	
Change (follow-up - baseline)	61.8 (41.9)***	−0.8 (22.7)	**<0.001**	(−78.7 to −46.5)	24.8 (43.2)***	9.9 (37.4)*	**0.02**	(−32.0 to −1.1)
MID (≥30 metres) achieved, n (%)	31 (28.7%)	77 (71.3%)	**<0.001**		18 (35.3%)	13 (22.8%)	0.15	
SGRQ total score								
Baseline	47.6 (17.53)	42.9 (16.6)	0.10		50.7 (16.1)	38.1 (15.4)	**<0.001**	
Follow-up	40.9 (15.0)	39.9 (16.1)	0.38		38.9 (14.3)	41.5 (17.0)	0.19	
Change (follow-up - baseline)	−6.7 (12.0)***	−3.0 (9.0)***	0.07	(−1.2 to 8.5)	−11.8 (7.5)***	3.4 (5.4)***	**<0.001**	(12.8 to 17.9)
MID (- four units) achieved, n (%)	18 (58.1%)	33 (42.9%)	0.15		53 (47.2%)	55 (50.9%)	**<0.001**	
FEV_1, litres								
Baseline	1.3 (0.5)	1.2 (0.5)	0.36		1.2 (0.5)	1.2 (0.4)	0.90	
Follow-up	1.4 (0.6)	1.2 (0.5)	0.16		1.3 (0.6)	1.2 (0.5)	0.89	
Change (follow-up - baseline)	0.1 (0.2)	−0.0 (0.2)	0.09	(−1.5.-0.01)	0.0 (0.2)	0.0 (1.3)	0.92	(−0.1 to 0.1)
FVC, Litres								
Baseline	2.5 (0.9)	2.6 (0.9)	0.66		2.5 (0.7)	2.3 (0.7)	0.33	

Continued

Table 1 Continued

	Table 1A				Table 1B			
	6MWD				SGRQ			
	6MWD-MID achieved (n=31)	6MWD-MID not achieved (n=77)	Between-group difference (P value)	95% CI for the difference	SGRQ-MID achieved (n=53)	SGRQ-MID not achieved (n=55)	Between-group difference (P value)	95% CI for the difference
Follow-up	2.6 (0.9)	2.6 (0.9)	0.90		2.5 (0.8)	2.4 (0.7)	0.40	
Change (follow-up - baseline)	0.1 (0.5)	0.0 (0.4)	0.20	(−0.3 to 0.1)	−0.0 (0.2)	0.0 (0.2)	0.92	(−0.1 to 0.1)
Single breath count test								
Baseline	27.5 (10.2)	26.9 (8.8)	0.74		24.9 (7.5)	29.0 (10.1)	**0.03**	
Follow-up	31.3 (10.1)	28.9 (8.4)	0.21		28.8 (8.5)	30.5 (9.4)	0.24	
Change (follow-up - baseline)	3.8 (7.2)**	1.9 (5.3)***	0.09	(−4.8 to 1.0)	3.5 (5.8)***	1.4 (5.9)*	**0.03**	(−4.4 to −0.1)
Maximum inspiratory pressure (MIP,≥17 cm H_2O)								
Baseline	55.8 (24.0)	50.6 (19.3)	0.24		48.1 (19.9)	55.9 (23.9)	**0.03**	
Follow-up	62.5 (26.7)	54.4 (19.2)	0.08		55.7 (23.6)	57.9 (20.1)	0.29	
Change (follow-up - baseline)	6.7 (12.6)**	3.1 (10.6)**	0.08	(−8.8 to 1.6)	6.9 (12.9)***	1.47 (8.8)	**0.007**	(−9.6 to −1.1)
≥10% improvement, n (%)	15 (48.0%)	30 (40.0%)	0.43		25 (52.0%)	18 (33.0%)	0.053	
Pulse								
Baseline	84.7 (13.6)	85.1 (14.6)	0.88		85.6 (15.1)	84.4 (13.6)	0.67	
Follow-up	85.2 (13.4)	84.9 (16.1)	0.94		84.5 (13.4)	85.5 (16.8)	0.74	
Maximum heart rate during 6MWT								
Baseline	111.2 (13.1)	117.5 (18.4)	0.09		115.8 (16.2)	115.6 (18.2)	0.94	
Follow-up	116.2 (14.2)	115.9 (17.4)	0.95			116.5 (17.1)	0.78	
Heart rate response (ΔHR)								
Baseline	26.5 (13.9)	32.4 (16.8)	0.09		30.2 (18.4)	31.1 (14.1)	0.77	
Follow-up	31.0 (13.8)	31.0 (17.6)	0.99		31.1 (16.1)	30.9 (16.9)	0.97	
Change (follow-up - baseline)	4.5 (12.9)*	−1.2 (20.1)	0.09	(−12.4 to 0.9)	0.8 (21.4)	0.3 (15.5)	0.89	(−7.6 to 7.1)
Lowest oxygen saturation during 6MWD								
Baseline	87.3 (6.5)	88.9 (6.6)	0.25		88.1 (6.2)	87.4 (6.8)	0.56	

Continued

Table 1 Continued

	Table 1A				Table 1B			
	6MWD				SGRQ			
	6MWD-MID achieved (n=31)	6MWD-MID not achieved (n=77)	Between-group difference (P value)	95% CI for the difference	SGRQ-MID achieved (n=53)	SGRQ-MID not achieved (n=55)	Between-group difference (P value)	95% CI for the difference
Follow-up	88.2 (7.4)	87.7 (7.6)	0.77		88.6 (7.7)	87.2 (7.3)	0.34	
Exercise-induced oxygen desaturation during 6MWT (SpO_2≤88 %)								
Baseline	11 (35%)	36 (47%)	0.29		20 (39%)	27 (47%)	0.39	
Follow-up	11 (35%)	31 (44%)	0.41		18 (38%)	24 (44%)	0.53	
EID (0=No EID to 1=EID only at baseline to 2=EID only at follow-up to 3=EID at baseline)								
0	15 (48%)	30 (43%)	0.56		22 (47%)	23 (43%)	0.73	
1	5 (16%)	9 (13%)			7 (15%)	7 (13%)		
2	5 (16%)	8 (11%)			7 (15%)	6 (11%)		
3	6 (19%)	23 (33%)			11 (23%)	18 (33%)		
Adherence, number of attended sessions	14.8 (5.1)	14.7 (5.8)	0.92		14.02 (5.8)	15.6 (85.3)	0.22	
Adherence to the intervention, n (%)								
0%–49%	5 (16.1%)	12 (15.6%)	0.53		10 (19.6%)	7 (12.3%)	0.58	
50%–74%	7 (22.6%)	11 (14.3%)			8 (15.7%)	10 (17.5%)		
75%–100%	19 (61.3%)	54 (70.1%)			33 (64.7%)	40 (70.2%)		
Smoking status, yes, n (%)								
Baseline	11 (35.5%)	15 (19.5%)	0.17		13 (25.5%)	13 (22.8%)	0.34	
Follow-up	10 (32.3%)	14 (18.2%)	0.08		12 (23.5%)	12 (21.1%)	0.91	
Quit smoking during training, n (%)	2 (6.5%)	1 (1.3%)			2 (3.9%)	1 (1.8%)		

Data are presented as mean±SD unless otherwise stated. 6MWD: (MID: ≥30 m); SGRQ total score: Item (MID ≤−4 units); FEV_1: (MID:≥120 mL); single breath count (MID:≥10% change); MIP (MID≥17 cm H_2O. Here, ≥10% improvement is reported). EID: (SpO_2≤88%). Within-group significance is shown as: No star: p>0.05, *:p<0.05, **: p<0.01; ***: p<0.001.
BMI, body mass index; EID, exercise-induced oxygen desaturation; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; MID, minimal important difference; MIP, maximum inspiratory pressure; 6MWD, 6-minute walking test distance ; 6MWT, 6-minute walking test; SGRQ, St. George's Respiratory Questionnaire; SLH, singing for lung health.

Table 2 Univariable and multivariable logistic regression in SLH: baseline factors and change factors (change from baseline to post): factors associated with achieving SLH (6MWD-MID, n=31)

2A: SLH (6MWD-MID achieved: n=31)																			
Univariable logistic regression: baseline factors					**Multivariable logistic regression: selected baseline factors**					**Univariable logistic regression: change factors (change from baseline to post)**					**Multivariable logistic regression: selected change factors**				
Variable		**OR**	**95% CI**	**P value**	**Variable**		**OR**	**95% CI**	**P value**	**Variable**		**OR**	**95% CI**	**P value**	**Variable**		**OR**	**95% CI**	**P value**
Age					**Age**														
	–65 years	Base				–65 years	Base												
	66-75 years	0.53	(0.2 to 0.6)	0.21		66-75 years	0.44	(0.1 to 1.4)	0.16										
	>75 years	0.17	(0.1 to 0.6)	**0.008**		>75 years	0.13	(0.03 to 0.6)	**0.01**										
Sex																			
	Female	1.09	(0.5 to 2.5)	0.83															
	Male	Base																	
BMI					**BMI**														
	<18.5	Empty				<18.5	Empty												
	18.5-24.9	Base				18.5-24.9	Base												
	25-29.9	1.97	(0.6 to 6.4)	0.26		25-29.9	1.46	(0.4 to 5.7)	0.54										
	30 -	3.55	(1.1 to 11.3)	**0.03**		30 -	2.03	0.5 to 8.3)	0.99										
6MWD					**6MWD**														
	1	5.31	(1.7 to 16.5)	**0.004**		1	6.07	(1.4 to 0.5)	**0.01**										
	2	1.98	(0.58 to 6.8)	0.28		2	2.10	(0.5 to 0.1)	0.32										
	3	Base				3	Base												
GOLD class																			
	1	Empty																	
	2	Base																	
	3	0.88	(0.4 to 2.1)	0.77															
	4	0.47	(0.1 to 2.4)	0.37															
FEV1										**FEV1 MID (≥120 mL)**					**FEV1 MID (≥120 mL)**				
	1	0.62	(0.2 to 1.7)	0.36							No	Base				0 (no)	Base		

Continued

Table 2 Continued

2A: SLH (6MWD-MID achieved: n=31)															
Univariable logistic regression: baseline factors				Multivariable logistic regression: selected baseline factors				Univariable logistic regression: change factors (change from baseline to post)				Multivariable logistic regression: selected change factors			
Variable	OR	95% CI	P value	Variable	OR	95% CI	P value	Variable	OR	95% CI	P value	Variable	OR	95% CI	P value
2	0.87	(0.3 to 2.4)	0.79					Yes	2.57	(1.0 to 6.4)	**0.04**	1 (yes)	2.04	(0.7 to 5.8)	0.18
3	Base														
FVC				**FVC**				**FVC≥10% change**							
1	2.23	(0.7 to 7.0)	0.17	1	1.18	(0.3 to 4.8)	0.82	No	Base						
2	2.62	(0.9 to 7.8)	0.09	2	1.70	(0.5 to 6.2)	0.42	Yes	1.36	(0.6 to 3.4)	0.51				
3	Base			3	Base										
MIP								**MIP MID (≥17 cm H2O)**				**MIP MID (≥17 cm H2O)**			
1	Base							No	Base			0 (no)	Base		
2	1.55	(0.2 to 1.6)	0.26					Yes	2.44	(0.8 to 7.5)	0.12	1 (yes)	1.65	(0.5 to 6.0)	0.45
3	1.81	(0.7 to 5.0)	0.25												
Single breath count								**Single breath count≥10% change**							
1	1.12	(0.4 to 3.0)	0.83					No	Base						
2	1.21	(0.4 to 3.5)	0.72					Yes	1.22	(0.5 to 2.8)	0.64				
3	Base							**Single breath count≥50% change**				**Single Breath Count 50% change**			
								No	Base			0 (no)	Base		
								Yes	2.77	(0.7 to 10.4)	0.13	1 (yes)	2.16	(0.5 to 9.1)	0.30
Heart rate response				**Heart rate response**				**Heart rate response ≥10% change**							
1	3.04	(1.1 to 8.4)	0.003	1	1.46	(0.4 to 5.6)	0.58	No	Base						
2	0.83	(0.2 to 3.0)	0.78	2	0.74	(0.2 to 3.1)	0.68	Yes	2.05	(0.9 to 4.8)	0.10				
3	Base			3	Base										
								Heart rate response≥50% change				**Heart rate 50% change**			
								No	Base			0 (no)	Base		
								Yes	3.68	(1.4 to 9.9)	**0.01**	1 (yes)	3.14	(1.1 to 8.8)	**0.03**
EID)(SpO2≤88 %)								**EID (SpO2≤88 %)**							

Continued

Table 2 Continued

2A: SLH (6MWD-MID achieved: n=31)															
Univariable logistic regression: baseline factors				**Multivariable logistic regression: selected baseline factors**				**Univariable logistic regression: change factors (change from baseline to post)**				**Multivariable logistic regression: selected change factors**			
Variable	**OR**	**95% CI**	**P value**	**Variable**	**OR**	**95% CI**	**P value**	**Variable**	**OR**	**95% CI**	**P value**	**Variable**	**OR**	**95% CI**	**P value**
No	Base							1	Base						
Yes	0.63	(0.3 to 1.5)	0.29					2	1.11	(0.3 to 3.9)	0.87				
								3	1.25	(0.4 to 4.5)	0.73				
								4	0.52	(0.2 to 1.6)	0.24				
								Resolvement of baseline EID at folloiw-up							
								No	Base						
								Yes	1.45	(0.5 to 4.7)	0.54				
Adherence															
0%–49%	Base														
50%–74%	0.58	(0.1 to 4.6)	0.60												
75%–100%	0.59	(0.1 to 3.8)	0.58												
Expections towards benefits of singing															
Neutral or negative	Base														
Positive	0.95	(0.4 to 2.3)	0.91												

BMI, body mass index; EID, exercise-induced oxygen desaturation; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; MID, minimal important difference; MIP, maximum inspiratory pressure; 6MWD, 6-minute walking test distance ; SLH, singing for lung health.

Table 3 Univariable and multivariable logistic regression in SLH: baseline factors and change factors (change from baseline to post): factors associated with achieving SGRQ-MID Total Score (n=53)

Univariable logistic regression: Baseline factors				Multivariable logistic regression: Selected baseline factors regression model 1				Multivariable logistic regression: Selected baseline factors regression model 2 (as FEV_1 and FVC are correlated)				Univariable logistic regression: Change factors (change from baseline to post)				Multivariable logistic regression: Selected change factors regression model 1				Multivariable logistic regression: Selected change factors regression model 2 (as FEV1 and FVC are correlated)			
Variable	OR	95% CI	p-value	Variable	OR	95% CI	p-value	Variable	OR	95% CI	p-value	Variable	OR	95% CI	p-value	Variable	OR	95% CI	p-value	Variable	OR	95% CI	p-value
Age				**Age**				**Age**															
−65 years	Base			−65 years	Base			−65 years	Base														
66-75 years	1.07	(0.4 to 2.8)	0.90	66-75 years	1.04	(0.4 to 3.1)	0.94	66-75 years	1.06	(0.4 to 3.2)	0.92												
>75 years	0.44	(0.2 to 1.3)	0.14	>75 years	0.46	(1.1 to 1.7)	0.25	>75 years	0.35	(0.1 to 1.3)	0.12												
Sex																							
Female	1.37	(0.6 to 2.9)	0.42																				
Male	Base																						
BMI				**BMI**				**BMI**															
<18.5	Empty			<18.5	Empty			<18.5	Empty														
18.5-24.9	Base			18.5-24.9	Base			18.5-24.9	Base														
25-29.9	1.17	(0.5 to 3.1)	0.75	25-29.9	0.87	(0.3 to 2.5)	0.80	25-29.9	0.70	(0.2 to 2.1)	0.52												
30 -	2.92	(2.9 to 7.9)	**0.03**	30 -	2.42	(1.7 to 8.2)	0.16	30 -	1.31	(0.4 to 4.6)	0.67												
6MWD				**6MWD**				**6MWD**															
1	3.16	(1.2 to 8.1)	**0.02**	1	2.34	(1.7 to 7.4)	0.15	1	2.61	(0.9 to 7.9)	0.09												
2	1.47	(0.6 to 3.9)	0.43	2	1.33	(0.4 to 4.0)	0.62	2	1.66	(0.6 to 5.1)	0.37												
3	Base			3	Base			3	Base														
GOLD class																							
1	1.30	(0.1 to 22.0)	0.85																				
2	Base																						
3	1.84	(0.8 to 4.2)	0.15																				
4	0.75	(0.2 to 2.9)	0.67																				
FEV1				**FEV1**								**FEV MID (≥120 mL)**				**FEV1 MID (≥120 mL)**							

Continued

Table 3 Continued

Univariable logistic regression: Baseline factors				Multivariable logistic regression: Selected baseline factors regression model 1				Multivariable logistic regression: Selected baseline factors regression model 2 (as FEV_1 and FVC are correlated)				Univariable logistic regression: Change factors (change from baseline to post)				Multivariable logistic regression: Selected change factors regression model 1				Multivariable logistic regression: Selected change factors regression model 2 (as FEV1 and FVC are correlated)			
Variable	OR	95% CI	p-value	Variable	OR	95% CI	p-value	Variable	OR	95% CI	p-value	Variable	OR	95% CI	p-value	Variable	OR	95% CI	p-value	Variable	OR	95% CI	p-value
1	2.71	(1.1 to 7.0)	**0.04**	1	2.99	(0.9 to 9.6)	0.07					No	Base			0 (no)	Base						
2	1.67	(0.6 to 4.4)	0.30	2	2.31	(0.7 to 7.3)	0.15					Yes	2.19	(0.9 to 5.4)	0.09	1 (yes)	1.51	(0.6 to 4.0)	0.41				
3	Base			3	Base																		
FVC								**FVC**				**FVC≥10% change**								**FVC 10% change**			
1	2.65	(1.0 to 7.1)	0.053					1	2.71	(0.9 to 8.8)	0.09	No	Base							0 (no)	Base		
2	2.71	1.0 to 7.1)	**0.04**					2	2.64	(0.9 to 8.2)	0.09	Yes	2.24	(0.9 to 5.3)	0.07					1 (yes)	1.98	(0.8 to 4.9)	0.14
3	Base							3	Base														
Maximum Inspiratory Pressure (MIP)												**MIP MID (≥17 cm H2O)**				**MIP MID (≥17 cm H2O)**				**MIP MID (≥17 cm H2O)**			
1	Base											No	Base			0 (no)	Base			0 (no)	Base		
2	0.86	(0.4 to 2.1)	0.75									Yes	5.10	(1.4 to 19.3)	**0.02**	1 (yes)	4.35	(1.1 to 17.6)	**0.04**	1 (yes)	4.58	(1.2 to 17.6)	**0.03**
3	0.56	(0.2 to 1.5)	0.24																				
Single breath count				**Single breath count**				**Single breath count**				**Single breath count≥10% change**											
1	2.94	(1.2 to 7.4)	**0.02**	1	2.09	(0.6 to 7.8)	0.28	1	2.22	(0.6 to 8.2)	0.23	No	Base										
2	2.56	(0.9 to 7.0)	0.07	2	1.63	(0.5,5.2)	0.41	2	1.99	(0.6 to 6.3)	0.24	Yes	1.35	(0.6 to 2.9)	0.44								
3	Base			3	Base			3	Base			**Single breath count≥50% change**											
												No	Base										
												Yes	1.63	(0.4 to 6.1)	0.47								
Heart rate response												**Heart rate response≥10% change**											
1	1.53	(0.6 to 3.7)	0.35									No	Base										
2	0.56	(0.2 to 1.5)	0.26									Yes	1.81	(0.8 to 3.9)	0.13								
3	Base											**Heart rate response≥50% change**											

Continued

Table 3 Continued

Univariable logistic regression: Baseline factors				Multivariable logistic regression: Selected baseline factors regression model 1				Multivariable logistic regression: Selected baseline factors regression model 2 (as FEV_1 and FVC are correlated)				Univariable logistic regression: Change factors (change from baseline to post)				Multivariable logistic regression: Selected change factors regression model 1				Multivariable logistic regression: Selected change factors regression model 2 (as FEV1 and FVC are correlated)			
Variable	OR	95% CI	p-value	Variable	OR	95% CI	p-value	Variable	OR	95% CI	p-value	Variable	OR	95% CI	p-value	Variable	OR	95% CI	p-value	Variable	OR	95% CI	p-value
												No	Base										
												Yes	1.18	(0.5 to 3.1)	0.74								
EID (SpO2≤88 %)												**EID (SpO2≤88 %)**											
No	Base											1	Base										
Yes	0.73	(0.3 to 1.6)	0.42									2	0.96	(0.3 to 3.2)	0.94								
												3	1.12	(0.3 to 3.9)	0.86								
												4	0.68	(0.3 to 1.7)	0.41								
												Resolvement of baseline EID at folloiw-up											
												No	Base										
												Yes	1.04	(0.3 to 3.2)	0.94								
Adherence																							
0%–49%	Base																						
50%–74%	0.95	(0.1 to 7.2)	0.96																				
75%–100%	1.61	(0.3 to 10.1)	0.26																				
Expections towards benefits of singing																							
Neutral or negative	Base																						
Positive	0.95	(0.4 to 2.1)	0.90																				

Tables 2 and 3 depict univariable and multivariable logistic regression models of baseline factors and change factors, respectively, in the SLH group stratified in 6MWD (table 2) and SGRQ (table 3). Variables for baseline were computed into tertiles, and variables for change from baseline to post were computed into defined change achieved yes/no. FEV (MID: 120 ml). MID:≥17 cm H_2O. ORs were computed using multivariable logistic regression. ORs>1 indicate an increased probability of achieving 6MWD-MID or SGRQ-MID, respectively. The multivariable logistic regression models (2A and 2B) included selected variables showing significance in the univariable analyses, leading to two different regression models. Table 3 depicts two separate multivariable models, as FEV_1 and FVC are correlated and should not be included in the same model.

BMI, body mass index; EID, exercise-induced oxygen desaturation; FEV_1, forced expiratory volume in 1 s; MID, minimal important difference; MIP, maximum inspiratory pressure; 6MWD, 6-minute walking test distance ; SGRQ, St. George's Respiratory Questionnaire ; SLH, singing for lung health.

Table 4 Association between achieving MID in both 6MWD and SGRQ (or in neither/nor) across overall study groups (SLH and PExT)

OR:1.78 p=0.065			SGRQ-MID total score achieved Yes	SGRQ-MID total score achieved No
SLH	6MWD-MID achieved	Yes	19 (17.6%)	12 (11.1%)
		No	34 (31.5%)	43 (39.8%)
PExT		Yes	15 (17.2%)	16 (18.4%)
		No	21 (24.1%)	35 (40.2%)

Table 4 depicts results from the Cochran-Mantel-Haenszel test for 2×2 xK tables to assess association and independence between achieving 6MWD-MID and/or SGRQ-MID across both study groups (SLH and PExT).
MID, minimal important difference; 6MWD, 6-minute walking test distance ; PExT, physical exercise training; SGRQ, St. George's Respiratory Questionnaire ; SLH, singing for lung health.

easier to improve from a poorer and more challenged starting point, for example either with a very high or a very low BMI.[43] Yet, interestingly, the same pattern was not present in the supplementary analyses of the PExT group, which, notably, however, represented a smaller sample size and, thus, this observation may not be valid. It would be interesting to investigate predictors associated with improvements as this might guide which activity a specific patient phenotype should be referred for and, thus, potentially might help to overcome usual barriers, for example regarding attendance.

Physiological changes in 'effective' SLH

A key element in singing is a controlled and coordinated breathing pattern with diaphragmatic breathing and extended expiration to support vocalisation.[3 10 13 14 42]

The recent narrative review[2] suggested that singing may improve aspects in breathing pattern, respiratory control, hyperinflation, dyspnoea, health-related QoL, and interoception. Improved physical capacity and activity has likewise been reported in some previous studies besides enhanced respiratory well-being.[20 36 41 44] However, specific physiological changes have not been convincingly confirmed.[2 4 20 42] In accordance with formerly posed requests,[2] the present study explored whether SLH might be associated with change in any detectable physiological parameters specifically focusing on measures reflecting lung function, inspiratory muscle strength and control, dyspnoea and breathing control, and exercise-induced changes in pulse and saturation.

Previous studies have reported that studies on singing lack consistency when addressing lung function, perception of dyspnoea, and improved breathing pattern, ranging from self-reported perception of improved lung function to guideline-based measurement of spirometry and inspiratory pressure.[2] This lack of consistency in perceptions and clinical effects has also been addressed in previous studies[4 20 42] and a more holistic view on effects may be relevant to consider due to the complex nature of SLH and other approaches to singing. For example, the notion of lung function may also need to include evaluation of dyspnoea, MIP and physical capacity.[42] Previously, it has been suggested that singing improves lung function[9 41 42] which we, however, did not observe in the present study - when measured solely by spirometry.

Interestingly, in this study, achievement of SGRQ-MID was associated with improved MIP and single breath count test (table 1) which we did not observe in the proportion of patients achieving 6MWD-MID. Furthermore, achieving SGRQ-MID was associated with a more pronounced 6MWD improvement (table 1) than the corresponding improvement in SGRQ observed in patients achieving 6MWD-MID (table 1). Surprisingly, we observed no significant associated physiological changes in PExT neither when achieving 6MWD-MID nor SGRQ-MID (online supplemental tables S5 and S6). This could suggest that SLH might provide more benefits which, however, is only speculative, not at least as the overall study groups differed in size and as it was not the aim of this study to compare SLH and PExT. We are not aware of other PR studies measuring agreement and association between objectively and subjectively defined outcomes, but several previous studies on singing[3 4 20] have addressed a discrepancy between physiological and psychosocial benefits and, further, between perceived and clinically observed benefits.

MIP may express inspiratory muscle strength and control and may be correlated to detect changes in general muscle strength and physical capacity (6MWD).[45] MIP has earlier been included in studies of singing and positive effects have been observed in diseases where respiratory function is also profoundly affected (for example cystic fibrosis;[46] Parkinson's disease),[47 48] but not in COPD.[13 42] This study found significant between-group changes in MIP, however, only in the SGRQ stratum.

Changes in the single breath count test might be an indication of strength, control, and coordination in the respiratory muscles, tolerance of CO_2 retention, efficiency and stability of subglottal pressure, and operating lung volumes.[2] In our present study, single breath count test was included to indicate dyspnoea and breathing control and has previously been used in assessment of hyperventilation.[19] Positive changes in single breath count test have been reported in some studies of singing in COPD,[32] but not all.[19 41 42] We observed significant improvements in both MIP and single breath count test in the SGRQ stratum (table 1) suggesting that SLH may improve inspiratory muscle strength and control and may lead to an experience of less dyspnoea and enhanced breathing control. This may be explained by the systematic training of the inspiratory and expiratory muscles during singing and the SLH programme's focus on prolonging the expiration which may increase tolerance of hypoventilation. This training may induce lower operating volume with lower setting of tidal volume—closer to ideal resting position—and, thus, to reduction of hyperinflation and perception of dyspnoea. In any case, both the MIP and the single breath count tests would be easily implementable and might be considered relevant to supplement standard assessment in COPD.[33]

It has been suggested that participants experience that singing/SLH provides similar effects as PExT.[24 49] In the present study, we observed an association between achieving 6MWD-MID and improving heart rate response. This may reflect an increase in overall fitness and dynamics which may be in line with a recent study suggesting that physiological demands in SLH correspond to those of 'brisk pace' walking, however observed in healthy people.[40]

Additional tendencies (in case of exploratory acceptance of p values between 0.05 and 0.10 and/or tendencies related to within-group changes) were observed in the proportion of participants achieving 6MWD-MID regarding measures FEV_1, MIP, single breath count, and heart rate response (table 1). More observations and sufficiently powered studies are needed to clarify whether the observed trends are true effects with a type II error or not.

To sum up, our study does not convincingly support that singing improves lung function as previously indicated. Rather, the study may support previous suggestions that singing/SLH may be associated with improved inspiratory muscle strength and control, dyspnoea and breathing control, and QoL. Furthermore, our study may support previous indications of SLH being associated with improved physical fitness and exercise capacity.

Strengths and limitations

The present study has both strengths and weaknesses. Previous studies on singing in respiratory disease have mainly focused on perceived effect, and studies focusing on objective parameters have largely failed to confirm these perceived benefits.[1 3 4 20]

Our study was based on data from a large-scale and rigorous RCT with well-described interventions and real-life delivery of community-based PR and with validated and established outcome variables commonly used in PR trials. Data were analysed and reported with transparent and basic methods,[12] thus aiming to minimise selection, detection and reporting bias.

We strived for transparent analyses, reporting and discussion aiming to reduce risk of reporting and publication bias. However, the present study was obviously not powered to detect changes being an explorative study based on post hoc analyses in a selected population and, thus, with low rating in the evidence hierarchy. There are several aspects that may cause measurement and reporting bias. The small and selected population, the difference between overall study group sizes, and potential overexaggerating of findings may lead to type I error. A type II error is also possible due to different samples between the 6MWD and SGRQ strata with a smaller subgroup of participants achieving 6MWD-MID than SGRQ-MID. Furthermore, the study reflected observations from a short-term, proof-of-concept study without long-term data and without potential to address persistence of any of the observed changes. The study did not include comprehensive assessment measurements of advanced lung function measurement,[50] for example static lung volumes (total lung capacity, expiratory reserve volume, residual volume), diffusion capacity for carbon monoxide, impulse oscillometry, arterial or capillary blood gas measurement, or helium dilution lung volume measurement. Neither did we include assessment of biomarkers, high-resolution chest CT, body plethysmography or ultrasound-measurement of diaphragmatic thickness or mobility to assess emphysema, hyperinflation, airway resistance, small airways involvement, or diaphragmatic strength. Neither of these are, however, standard in assessment of outcome of PR for COPD yet; however, it would be interesting and relevant to include such parameters in future research on SLH besides testing of physical activity (although challenging to measure),[51] EKG, and exercise stress test, for example chair stand test, in future studies.

The study did not investigate SLH as an add-on to PExT, a combination that may likely be superior to each modality alone in providing benefits and effects and which should also be addressed in future studies. Lastly, several findings and aspects in our study remain to be sufficiently explained and are rather to be regarded as observations. Further studies are needed to investigate these aspects.

CONCLUSION

This study suggests that SLH as part of PR for COPD confers positive physiological changes besides being a pleasant leisure time activity. Future studies focusing on physiology may help us to better understand how singing works and how SLH can be used to improve the lives of patients with COPD. There is also a need to explore the apparent gap between subjective and objective benefits of SLH.

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Collaborators Not applicable.

Contributors MK (study investigator), UB (principal investigator and guarantor), DBR and OH designed the scope and plan for this study. Statistical analyses and were performed by MK and DBR, and UB and OH gave feedback. MK drafted the manuscript, and UB, DBR, OH, AL and PV provided important intellectual input and feedback and approved the final version of the manuscript.

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Competing interests 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 experience of—or knowledge within—singing.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval Ethical approval for the overall RCT 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 Declaration and according to the Act on Processing of Personal Data. Trial protocol is available at ClinicalTrials.gov (number NCT03280355).

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. All data relevant to the study are included in the article or uploaded as supplementary information. Consent forms will not be available according to Danish legislation. De-identified data collected for the study will be available from 1 January 2023, upon reasonable request. Contact study investigator (MK), mk@clin.au.dk.

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