CHEST

Effectiveness of a Long-term Home-Based Exercise Training Program in Patients With COPD After Pulmonary Rehabilitation

A Multicenter Randomized Controlled Trial

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BACKGROUND: Most patients with COPD do not maintain exercise training after pulmonary rehabilitation (PR).

RESEARCH QUESTION: Does a 12-month home-based, minimal-equipment strength training program after PR have an effect on dyspnea, exercise capacity, and patient-reported outcomes in patients with COPD?

STUDY DESIGN AND METHODS: In a parallel-arm multicenter study across four Swiss PR clinics, patients with COPD were allocated randomly (1:1 ratio) into an intervention group (IG; home-based strength training program) or control group (CG; usual care). The primary outcome was change in Chronic Respiratory Questionnaire (CRQ) dyspnea scale score from baseline to 12 months. Secondary outcomes were change in exercise capacity (1-min sit-to-stand-test [1MSTST], 6-min walk test [6MWT]), health-related quality of life, exacerbations, and symptoms. We assessed the IG's experience by interviews at study end. Main analyses were based on the intention-to-treat approach, and adjusted linear regression models were used.

RESULTS: One hundred twenty-three patients with COPD (IG, n = 61; CG, n = 62) were randomized, 61 of whom were women and whose mean ± SD age was 66.8 ± 8.1 years and mean ± SD FEV_1 was 39.3 ± 15.3% predicted. One hundred four participants completed 12 months of follow-up (IG, n= 53; CG, n= 51). Of the 53 IG participants, 37 participants (70%) conducted the training until study end. We found no difference in change in CRQ dyspnea scale score over 12 months (adjusted mean difference, 0.28; 95% CI, –0.23 to 0.80; $P = .27$). We found moderate evidence for a difference in 1MSTST repetitions favoring the IG (adjusted mean difference, 2.6; 95% CI, 0.22-5.03; $P = .033$), but no evidence for an effect in other outcomes. Seventy-nine percent of the IG reported positive effects that they attributed to the training.

INTERPRETATION: The home exercise program had no effect on dyspnea, but improved 1MSTST performance and patient-perceived fitness. The supported program was well accepted by patients with COPD and may facilitate continued exercise training at home.

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KEY WORDS: COPD; dyspnea; effectiveness; functional exercise capacity; home-based exercise training; long-term maintenance; minimal equipment; pulmonary rehabilitation; randomized controlled trial; quality of life

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ABBREVIATIONS: 6MWT = 6-min walk test; CG = control group; CRQ = Chronic Respiratory Questionnaire; HOMEX = home exercise; IG = intervention group; ITT = intention-to-treat; 1MSTST = 1-min sit-to-stand test; PP = per-protocol; PR = pulmonary rehabilitation; SA = sensitivity analysis

Take-home Points

Study Question: Does a home-based, minimal-equipment strength training program after pulmonary rehabilitation have an effect on dyspnea, exercise capacity, and other patient-reported outcomes over 12 months in patients with severe and very severe COPD compared with usual care?

Results: The strength training program had no effect on dyspnea or other patient-reported outcomes in patients with COPD after 1 year, but show beneficial effects on functional exercise capacity assessed by the 1-min sit-to-stand test and on patient-experienced well-being and fitness.

Interpretation: Adherence to this long-term training program was surprisingly high. The program was well accepted by patients with COPD and may facilitate continued training at home.

Exercise training is a cornerstone of pulmonary rehabilitation (PR) and the management of COPD.[1,2] The evidence on positive effects of exercise training programs with or without other elements of PR on dyspnea, exercise capacity, and health-related quality of life in people with COPD is overwhelming.[3] However, a great majority of patients with COPD who would benefit do not follow such programs.[4-6] For those who undergo supervised exercise training during PR, it often is challenging to maintain exercising in daily life, and strong effects shown immediately after completion of PR tend to decrease or vanish in the long term.[1,7]

Home-based programs became increasingly popular in recent years and complement traditional center-based inpatient and outpatient PR.[1] Consequently, a rising number of randomized controlled trials have investigated the effectiveness of home-based programs,[8] and the consideration of these alternative models and opportunities and challenges for PR currently are under debate.[9-11] The latest Cochrane review on effectiveness and safety of PR programs delivered by information and communication technology and mostly at home identified 15 studies and showed similar outcomes to those of traditional center-based PR in people with COPD and higher attendance rates, but with low to moderate certainty of evidence.[12]

The programs assessed in these studies varied largely regarding the type of exercise training and required equipment (eg, cycle ergometers[13] or minimal equipment[14]), the technological methods (eg, telephone calls,[14,15] websites,[16] or remote monitoring with videoconferencing[17]), and the content and degree of supervision, education, and self-management elements. The programs usually lasted between 6 and 10 weeks and assessed midterm outcomes after 6 months. One study with 12 months of follow-up assessment showed that gains in exercise capacity and dyspnea could not be maintained in the long term.[14] An effective home-based maintenance PR program that lasted for 1 year required elaborated technological devices.[17] Similarly, studies that assessed home-based exercise training without additional PR elements showed short-term improvements in exercise capacity and patient-reported outcomes right after program completion.[18,19] Others comprised home-based elements, but also center-based training.[20,21]

Against this background, we developed a structured, home-based strength training home exercise (HOMEX) program for patients with COPD that can be provided right after PR, aiming to maintain exercise training effects elicited during PR, or as a stand-alone program. We deliberately focused on the strength component of exercise training because skeletal muscle dysfunction is prevalent in COPD[22] and os associated with lower daily physical activity and poor prognosis,[1,2] and we did not consider self-management or education PR elements. Our emphasis was on the long-term aspect and that the training becomes a habit in the people's usual environment.[23,24] The aim of this study was to assess the effectiveness of the program and the experience after 12 months in patients with COPD who completed PR.

Study Design and Methods

Study Design

In this multicenter, randomized, parallel-group controlled trial, we recruited participants at the end of PR in four Swiss PR clinics and

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The results of this study were presented at the American Thorax Society virtual meeting, May 18, 2021 and the European Respiratory Society Congress virtual meeting, September 7, 2021.

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randomly allocated them to the HOMEX group (intervention group [IG]) or to no intervention and usual care (control group [CG]). The study took place between January 2018 and March 2020. It was approved by the local ethics committees (Identifier: BASEC No. 2017-02092) and is registered at ClinicalTrials.gov (Identifier: NCT03461887). All participants gave written informed consent.

Participants, Recruitment, Randomization, and Blinding

We included individuals with COPD (Global Initiative for Chronic Obstructive Lung Disease stages II-IV) who understood and spoke German and completed PR no longer than 1 month previously. Exclusion criteria were not being able to exercise because of physical, cognitive or safety reasons, as judged by investigators.

All individuals admitted to the clinics were screened for eligibility and recruited consecutively (January 2018-February 2019). After baseline assessments, the assessors randomized the participants (1:1 ratio) over the Research Electronic Data Capture[25] system. We used block randomization with varying block sizes, stratified by 1-min sit-to-stand test (1MSTST) repetitions ($\leq$ 19 vs $>$ 19 repetitions) and study center. One independent statistician created the randomization list using R software (R Foundation for Statistical Computing) and another uploaded it into the Research Electronic Data Capture system. Neither participants nor assessors were masked to group assignment. The data analyses and used models were predefined in the study protocol.[26]

Intervention

The HOMEX training program requires a chair and resistance bands. It consists of trunk and upper and lower limb exercises at different intensity levels. The exercises are presented in 38 cards including pictures, performance instructions, training volume and intensity, and a gain when conducted regularly (e-Fig 1). We instructed the participants to perform the training during 6 days each week for about 20 min/d over 12 months. The participants also were provided with an exercise training book to record the daily trainings, individualized goals, and rewards (e-Fig 2). A health care professional also trained in motivational interviewing techniques (referred to herein as the *coach*) visited the participants at home at the study start, after 8 weeks, and after 3 months and conducted 17 structured phone calls during the year (Fig 1). Additional intervention elements were the involvement of a close person as a sparring partner and the information of the general practitioner.[26,27]

Outcome Measures

The main outcomes were assessed at baseline and at the end of the intervention after 12 months in the PR clinics, the primary outcome, and health care use variables additionally at the 3- and 6-month follow-up via questionnaires and telephone interviews (Fig 1).

The primary outcome was change in dyspnea after 12 months, measured by the standardized, self-administered version of the Chronic Respiratory Questionnaire (CRQ) dyspnea domain.[28,29] Secondary outcomes were functional exercise capacity (6-min walk test [6MWT][30] and 1MSTST[31]), health-related quality of life (CRQ subscales for fatigue, emotional functioning, and mastery[28,29]; EuroQol 5-Dimension Questionnaire[32]), COPD symptoms (COPD Assessment Test[33]), depression and anxiety symptoms (Hospital Anxiety and Depression Scale),[34] and event-based exacerbations (increase in symptoms and increase in dosage of or new prescription of systemic corticosteroids, antibiotics, or both).

The IG's adherence to the HOMEX program was evaluated according to their daily reports in the training books. The coaches regularly discussed these reports with them to minimize information bias and recorded training interruptions of more than 3 consecutive days in coaching protocols. Self-efficacy (scale, 1-10) was assessed at the 3-, 6-, and 12-month follow-ups. Satisfaction and experience with the intervention was assessed at the 12-month follow-up by a standardized questionnaire (using a Likert-type scale) and structured interview with open-ended questions.

Sample Size and Statistical Analyses

Considering for the primary outcome of CRQ dyspnea scale score (for which we hypothesized maintenance for the IG and decline for the CG) the well-established minimum important difference of 0.5[35] and an SD of 0.9 detected in the same population with COPD in a previous study,[36] for 80% power and 5% significance level (two-sided), a sample size calculation resulted in 52 patients per group. Anticipating a 15% dropout rate, we targeted a required total sample size of 122 individuals.

We analyzed differences of change between the IG and CG from baseline to the 12-month follow-up in primary and secondary outcomes by linear regression models, adjusted for age, sex, and stratification variables. To assess the course of the primary outcome over time, considering 3- and 6-month follow-up data, we used linear mixed-effects models. We used an intention-to-treat (ITT) approach for the main analyses. We conducted three per-protocol (PP) approaches in which we restricted the analyses to adherent participants (PP approach 1), additionally excluded CG participants with high training volumes (PP approach 2) or adjusted with prognostic factors for the primary outcome (PP approach 3), and two sensitivity analyses (SAs; adjusting for prognostic factors of the

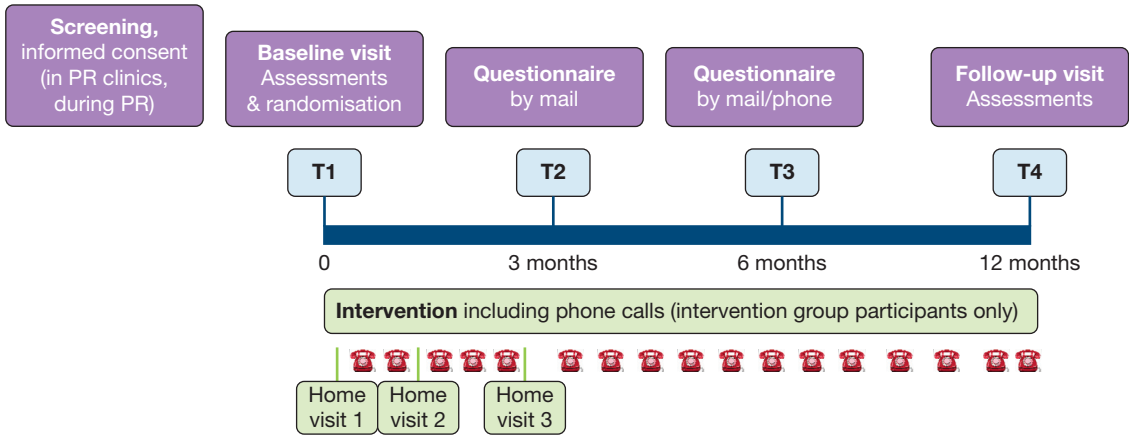

Figure 1 – *Graph showing time schedule on assessments and study visits (purple and blue) and the delivery of the intervention (light green; intervention group participants only). PR = pulmonary rehabilitation.*

primary outcome [SA 1][37] and using multiple imputation [SA 2]). PP approach 1, PP approach 3, and SA 1 were prespecified in the protocol. The approach to considered training volumes of CG participants (PP approach 2) was reported, but not prespecified. SA 2 was specified a posteriori. We conducted multiple imputation using the multivariate imputation by chained equations technique with 10 imputed data sets.

We classified a week to be adherent if the participants documented at least two exercises on at least 3 days. Associations among adherence, demographics, and outcome variables were assessed via Spearman correlation coefficients and Mann-Whitney-Wilcoxon tests. Satisfaction questionnaire data were analyzed descriptively and satisfaction interviews were analyzed with conventional content analysis using a data-driven category development.[38] For health care use and cost-effectiveness analyses, we compared the distribution of hospitalizations, hospitalization days, physician visits, inpatient rehabilitation days, workdays lost, and usefulness (EuroQol 5-Dimension Questionnaire index value) between IG and CG participants. More detailed information on intervention, assessments, and analyses is provided in e-Appendix 1.

Results

Figure 2 shows the flow of participants through the study. One hundred twenty-three individuals, with one exception all from the inpatient PR setting, were included and randomized (61 patients to the IG and 62 patients to the CG). About half of the participants were women, the mean ± SD age was 66.8 ± 8.1 years, and 75% had a diagnosis of severe or very severe COPD (Table 1). All participants, except one, had comorbidities, most frequently cardiovascular (75%) and musculoskeletal (41.5%) diseases (e-Table 1).

One hundred four participants completed 12-month follow-up assessments (53 participants in the IG, 51 participants in the CG). Reasons for loss to follow-up were death (n = 8), loss of contact (n = 5), withdrawal of consent (n = 5), and unrelated serious adverse event

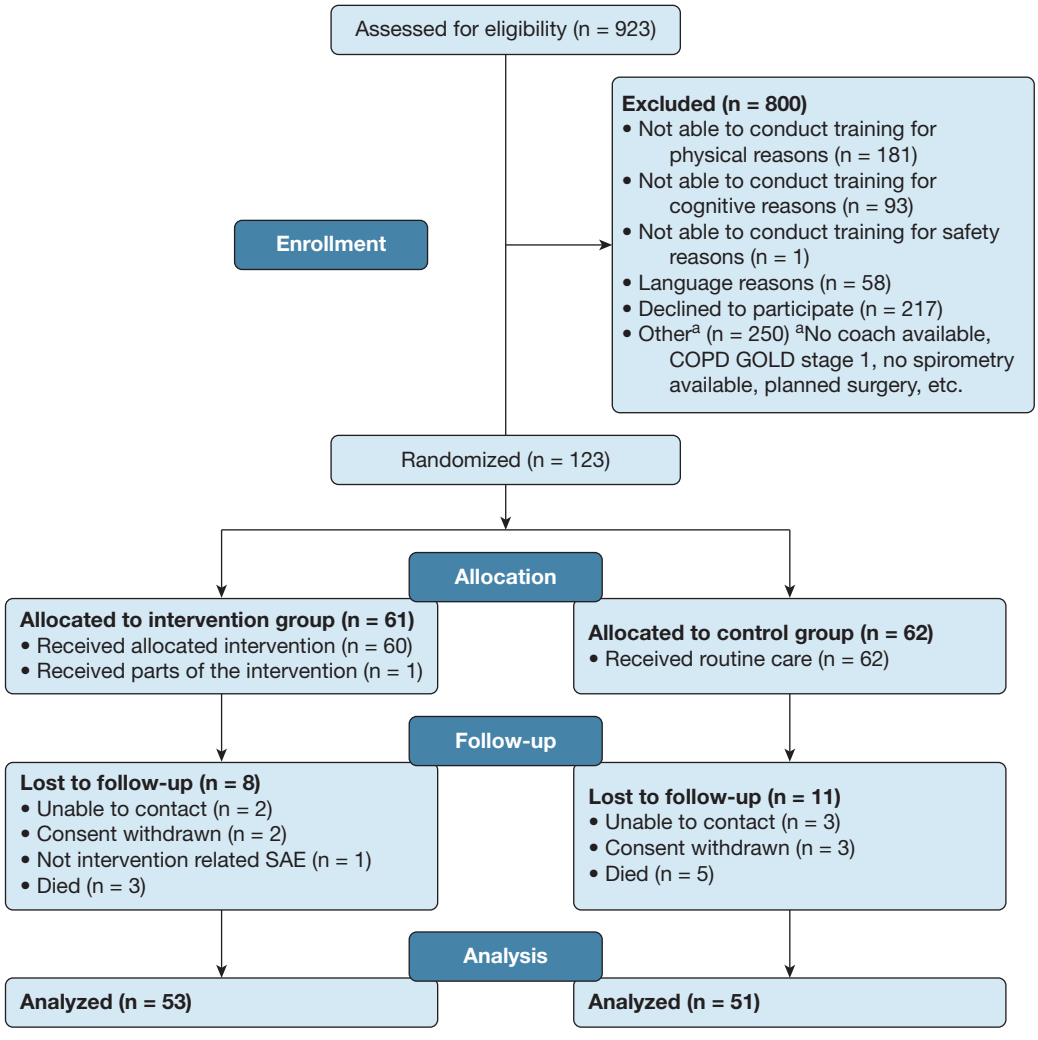

Figure 2 – *Diagram showing flow of participants through the trial. GOLD = Global Initiative for Chronic Obstructive Lung Disease.*

TABLE 1] Characteristics of Participants at Baseline by Group

Characteristic	Intervention Group (n = 61)	Control Group (n = 62)
Age, y	66.1 ± 8.3	67.4 ± 7.9
Female sex	31 (50.8)	30 (48.4)
Living alone	27 (44)	27 (44)
Still working	6 (10)	5 (8)
BMI, kg/m^2	24.6 ± 6.2	25.1 ± 5.9
FEV_1 (L)	1.14 ± 0.54	1.05 ± 0.50
FEV_1, % predicted	41 ± 16	38 ± 15
FVC, L	2.24 ± 0.78	2.23 ± 0.84
FVC, % predicted	63 ± 18	62 ± 18
FEV_1 to FVC ratio	0.51 ± 0.13	0.47 ± 0.11
GOLD stage		
II	18 (30)	13 (21)
III	22 (36)	25 (40)
IV	21 (34)	24 (39)
Smoking status		
Current	9 (14.8)	4 (6.5)
Former	51 (83.6)	56 (90.3)
Never	1 (1.6)	2 (3.2)
Pack-years smoking	46 (22)	49 (24)
No. of comorbidities	4.1 ± 2.2	4.3 ± 2.1
Exacerbations previous 12 mo[a] (at least 1)	50 (81)	53 (86)
Inpatient treated (at least 1)	42 (69)	39 (62)
Outpatient treated (at least 1)	23 (37)	29 (47)
Total No.	1.8 ± 1.7	2.1 ± 1.8
Inpatient PR during previous 12 mo[b]	35 (57)	45 (73)
Long-term oxygen therapy	34 (56)	39 (63)
Use of walking aid	14 (23)	19 (31)
6MWT distance, m	386 ± 124	379 ± 131
1MSTST, repetitions	17 ± 6	17 ± 9
CRQ subscale score, 1-7		
Dyspnea	4.61 ± 1.28	4.56 ± 1.27
Fatigue	5.11 ± 0.92	4.98 ± 1.08
Emotional function	5.53 ± 0.92	5.26 ± 1.15
Mastery	5.48 ± 1.01	5.26 ± 1.18
CAT score, 0-40	14.8 ± 6.3	15.3 ± 6.7
HADS subscale score, 0-21		
Depression	4.1 ± 2.8	4.2 ± 3.1
Anxiety	4.6 ± 2.8	4.7 ± 3.7
EQ VAS score, 0-100	63.6 ± 17.0	66.0 ± 18.7
EQ-5D-5L index value	0.84 ± 0.13	0.81 ± 0.18
Motivation to conduct program scale score, 1-10	8.5 ± 1.5	8.5 ± 1.5

Data are presented as No. (%) or mean ± SD, unless otherwise indicated. CAT = COPD Assessment Test; CRQ = Chronic Respiratory Questionnaire; EQ VAS = EuroQol Visual Analogue Scale; EQ-5D-5L = 5-level EuroQol-5D version; GOLD = Global Initiative for Chronic Obstructive Lung Disease; HADS = Hospital Anxiety Depression Scale; 1MSTST = 1-min sit-to-stand test; PR = pulmonary rehabilitation; 6MWT = 6-min walk test; VAS = visual analog scale.
[a]In the 12 mo before the start of the study.
[b]Not including current PR.

(n = 1). Fifteen 12-month follow-up visits were conducted at the participants' home because they were not able or willing to travel to the clinics; for two participants, the visit was conducted by phone, mail, or both.

Primary and Secondary Outcomes

In the IG, the mean ± SD CRQ dyspnea scale score decreased from 4.65 ± 1.33 to 4.42 ± 1.49, and in the CG, it decreased from 4.61 ± 1.27) to 4.06 ± 1.45 from baseline to 12 months. The ITT analysis showed no evidence for a between-group difference in change of CRQ dyspnea scale score after 12 months (0.28; 95% CI, –0.23 to 0.80; $P = .27$). The mixed-linear model on changes in CRQ dyspnea scale score considering 3- and 6-month assessments showed no evidence for a difference between the groups (e-Table 2, e-Fig 3).

No evidence was found for a difference between the two groups in change in 6MWT distance after 12 months (1.37; 95% CI, –35.06 to 37.79; $P = .94$), but moderate evidence for a between-group difference for the change of repetitions in the 1MSTST favoring the IG (2.6; 95% CI, 0.22-5.03; $P = .033$). In all other outcomes, no evidence for differences between the two groups was found (Table 2).

In the three PP approaches, the IG sample size decreased from 53 to 36 participants, in the PP approach 2, the CG sample size additionally decreased from 51 to 39 participants. No PP approach showed evidence for differences between the two groups, consistent with the ITT analyses (e-Tables 3-5). However, both sensitivity analyses that considered the entire sample confirmed the ITT results, that is, moderate evidence for a between-group difference for the change of repetitions in the 1MSTST favoring the IG (additional adjustment for FEV_1 and initial motivation to perform the exercises and other trainings during the study period: 2.88 [95% CI, 0.47-5.30; $P = .02$]; multiple imputation: 2.88 [95% CI, 0.41[5.35; $P = .023$]; e-Tables 6, 7).

Adherence to the Intervention and Satisfaction

Overall, 37 participants (70%) performed the HOMEX training until study end and 42 participants (79%) performed the HOMEX training for at least 10 months. Sixteen participants stopped the training on average after 28 weeks (SD, 14.6 weeks; range, 1-46 weeks), 11 participants for health reasons and five participants for other reasons. We excluded one participant who did not start the training for more detailed adherence analyses. According to our definition of an adherent week (at least two exercises on at least 3 days of a week conducted), the 52 participants adhered to the training for a mean ± SD of 38 ± 14 weeks overall (73%) and for a mean ± SD of 42 ± 12 weeks when their health state basically allowed them to train (healthy weeks; 79%). Adherence was reduced for periods in which participants reported adverse events ($P = .007$) and in healthy weeks for periods in which participants reported vacations ($P = .01$). Adherence was not associated with changes in CRQ dyspnea scale score or other outcomes. It was not associated with baseline characteristics or motivational aspects of the program (goal setting, designating a sparring partner). Self-efficacy scores were associated with intervention adherence (e-Table 8).

In the satisfaction survey, 81% of the IG indicated that they liked much or very much participating in the program (e-Table 9). The satisfaction interviews (e-Table 10) showed that 41 participants (79%) reported that they experienced positive effects that they attributed to the training. Most frequently, they experienced improvements in general fitness or endurance (n = 17 [40%]), strength (n = 14 [34%]), capacity in daily life or household activities (n = 13 [31%]), and climbing stairs (n = 11 [27%]; e-Table 11a-b). Additional results of adherence patterns and the participants' experience, assessed by additional in-depth interviews conducted later, are reported in a separate publication.[27]

Health Care Use and Cost-Effectiveness Analysis

Eight participants died and 57 experienced at least one hospitalization (121 hospitalizations in total); 33 patients in the IG (62.3%) and 24 patients in the CG (47.0%; $P = .119$). No hospitalization or serious adverse event was related to the study intervention. Health care use data are presented in Table 3. The cost-effectiveness analysis suggested that the intervention had an incremental cost-effectiveness ratio of Swiss Francs 146,395 per quality-adjusted life-year gained. Regardless of the threshold value for willingness to pay, the probability that the intervention would be cost-effective compared with usual care was less than 50% (e-Figs 4-8, e-Tables 12, 13).

Discussion

This study showed that the HOMEX strength training program had no effect on dyspnea after 12 months in patients with COPD who completed PR. However, the program improved functional exercise capacity assessed by the secondary outcome 1MSTST, and many participants reported having perceived positive effects that they attributed to the training. The program was

TABLE 2] Between-Group Differences in Primary and Secondary Outcomes at 12-Mo Follow-up in the Intention-to-Treat Analysis

Variable	Intervention Group (n = 53[a])		Control Group (n = 51[a])		Adjusted Between-Group Difference (Intervention Minus Control Group)	
	Baseline	12 Mo	Baseline	12 Mo	Mean Difference (95% CI)	*P* Value
Primary end point						
CRQ dyspnea scale score, 1-7	4.65 ± 1.33	4.43 ± 1.49	4.61 ± 1.27	4.06 ± 1.45	0.28 (−0.23 to 0.80)	.27
Secondary end points						
6MWT distance, m[b]	396 ± 110	379 ± 143	417 ± 125	393 ± 133	1.37 (−35.06 to 37.79)	.94
1MSTST, repetitions[c]	16.9 ± 5.8	18.9 ± 8.1	18.2 ± 8.9	17.8 ± 11.4	2.62 (0.22-5.03)	.033
CRQ scale score, 1-7						
Fatigue	5.17 ± 0.93	4.76 ± 1.33	5.07 ± 1.07	4.67 ± 1.28	0.02 (−0.47 to 0.50)	.95
Emotional function	5.58 ± 0.92	5.10 ± 1.23	5.37 ± 1.08	5.01 ± 1.25	−0.12 (−0.56 to 0.31)	.58
Mastery	5.56 ± 1.05	5.50 ± 1.33	5.35 ± 1.06	5.25 ± 1.30	0.03 (−0.42 to 0.49)	.90
CAT score, scale 0-5	14.3 ± 6.1	15.3 ± 7.8	15.3 ± 6.7	16.5 ± 7.2	−0.01 (−2.25 to 2.24)	.99
HADS scale score, 0-21						
Depression	4.0 ± 2.7	4.2 ± 3.6	4.0 ± 3.0	4.8 ± 3.7	−0.43 (−1.57 to 0.71)	.46
Anxiety	4.5 ± 2.7	4.8 ± 3.4	4.5 ± 3.5	5.3 ± 3.4	−0.49 (−1.64 to 0.66)	.40
EQ VAS, 0-100	65.3 ± 16.6	62.6 ± 19.0	66.8 ± 18.1	60.7 ± 20.0	2.53 (−5.10 to 10.17)	.51
EQ-5D-5L index value	0.85 ± 0.13	0.78 ± 0.19	0.82 ± 0.17	0.76 ± 0.19	−0.017 (−0.08 to 0.05)	.62
No. of exacerbations over 12 mo	1.8 ± 1.7	2.1 ± 1.3	2.0 ± 1.8	2.6 ± 1.9	−0.29 (−0.89 to 0.31)	.34

Data are presented as mean ± SD or coefficient (95% CI) from linear models, unless otherwise indicated. Linear models were adjusted for age, sex, and the stratification of the variables No. of repetitions on the 1MSTST (≤ 19 vs > 19 repetitions) and study center. CAT = COPD Assessment Test; CRQ = Chronic Respiratory Questionnaire; EQ VAS = EuroQol Visual Analogue Scale; EQ-5D-5L = 5-level EuroQol-5D version; HADS = Hospital Anxiety Depression Scale; 1MSTST = 1-min sit-to-stand test; 6MWT = 6-min walk test; VAS = visual analog scale.

[a]Unless stated otherwise.

[b]n = 44 in the intervention group; n = 37 in the control group.

[c]n = 49 in the intervention group; n = 46 in the control group.

safe and most of the multimorbid and severely ill study participants adhered to the training during the study year.

The intervention did not show evidence for an effect on the primary outcome CRQ dyspnea scale score or on other patient-reported outcomes after 12 months. Thus, the program was not able to maintain the gains of PR against the expected natural course of decline.[1,7] However, some interesting trends were noted. The mean deterioration in CRQ dyspnea scale score was larger in the CG compared with the IG (−0.55 vs −0.23). Similar patterns emerged for the Hospital Anxiety and Depression Scale and EuroQol visual analog scale, where the changes favored consistently the IG, albeit without showing statistical evidence for such an effect.

The positive effect of the intervention on 1MSTST repetitions (mean difference, 2.6; 95% CI, 0.22-5.03) almost reached the established minimal important difference of three repetitions[31] and was confirmed robustly in the sensitivity analyses. The loss of statistical evidence in the PP analyses is probably attributable to the reduced sample size. One explanation for why the intervention showed no effect on functional exercise capacity measured by 6MWT may be the high number of missing follow-up assessments, especially for CG participants (nine in the IG vs 14 in the CG). This could have introduced selection bias because more severely ill CG participants than IG participants did not carry out the 6MWT. Another explanation is that the HOMEX training specifically improved the strength, intramuscular coordination, or both of the lower leg muscles because repetitive sit-to-stand exercises are a program component. In particular, sitting down on a chair requires eccentric contractions of the quadriceps muscle and postural control,[39] which is less relevant during walking.

Although we were not able to demonstrate statistical evidence for an effect of the HOMEX program on

TABLE 3] Health Care Use During the Study Year by Group

Variable	Intervention Group (n = 53)				Control Group (n = 51)				*P* Value[a]	SMD	*P* Value[b]
	Mean	SD	Median	IQR	Mean	SD	Median	IQR			
Days of hospitalization[c]	6.74	12.3	0	7.50-0.00	5.14	10.34	0	9.00-0.00	.476	0.141	.305
No. of pneumologist visits	3.96	3.61	3	4.00-2.00	3.53	3.71	3	6.00-2.00	.548	0.118	.618
Days of work lost	2.79	13.14	0	0.00-0.00	0.86	3.35	0	0.00-0.00	.311	0.201	.39
No. of specialist visits	4.13	8.65	2	5.50-1.00	4.08	6.91	3	4.00-1.00	.972	0.007	.681
No. of general practitioner visits	7.70	5.81	6	9.50-4.00	7.61	6.65	6	12.00-4.00	.941	0.014	.847
Days of inpatient rehabilitation	2.77	18.4	0	0.00-0.00	6.06	19.97	0	0.00-0.00	.385	0.171	.873

SMD = standardized mean difference.
[a]Mann-Whitney *U* test.
[b]Kruskal-Wallis test.
[c]COPD exacerbation hospitalization.

most objectively assessed outcomes, a vast majority of the IG participants reported that they experienced positive changes in daily life that they attributed to the training. They not only reported having perceived general and specific improvements in overall strength, but interestingly also in general fitness and endurance, ability to perform daily activities, walking, and climbing stairs, which is in line with the improvement in the 1MSTST. However, the question remains why these patient-experienced changes were not reflected by the well-established outcomes.

Health care use in both groups was high, which was not surprising given the severely ill and comorbid patient population. The cost-effectiveness analyses suggested that the intervention showed an incremental cost-effectiveness ratio. Nevertheless, the results are highly uncertain because of the small sample size, the large variation in resource use among patients with COPD, and the short follow-up period. Although IG participants reported slightly more hospitalization days and doctor visits that contributed to the higher cost estimates, no statistical evidence for these differences was found.

Our results are in contrast to two recent maintenance programs that showed an effect for exercise capacity assessed by 6MWT[13,17] and health-related quality of life[17] after 1 year. However, both interventions required technological devices or additional equipment.[13,17] Maintenance programs differ in terms of delivery, intensity, and supervision, and adherence is crucial for effectiveness. In our study, around two-thirds of the patients adhered over the year according to our definition. It is unclear whether the restriction on adherent patients in a larger sample would have resulted in more favorable outcomes.

Besides assessing this intervention in a larger sample, we suggest that further research should identify characteristics of patients who are able to maintain long-term adherence to such minimal-equipment, home-based programs and for whom other programs are more appropriate. We did not find associations of adherence with outcomes or patient characteristics, but our sample likely was underpowered. Furthermore, a better understanding of the gap between the participants' perceived improvements and the failure of most outcomes to demonstrate an effect is needed. The implications of our results for clinicians are that the training was

safe, that many severely ill patients with COPD were motivated and able to follow the program, and that many patients perceived positive changes.

One limitation of the study is that some participants did not travel to the rehabilitation clinics for the follow-up assessment visit. So as not to lose them and to prevent selection bias, our assessors conducted home visits. We do not expect that this influenced the standardized questionnaire assessments, but the 6MWT could not be performed. However, during most home visits, it was possible to conduct the 1MSTST, which supports the practical value of this test. Another limitation is that assessors were not masked. Although we do not expect an effect on the standardized primary and secondary outcomes assessments, we cannot rule out the possibility that the satisfaction interviews were biased in favor of the intervention. One possible explanation for why the effect of the intervention on dyspnea was not statistically significant is that our study was underpowered. Although our assumed SD of 0.9 was based on previous studies in exactly the same patient population,[36] the current SD was higher (1.3). An additional limitation is that we did not measure changes in muscle strength objectively to quantify self-reported improvement in strength. Finally, our results are generalizable to those who completed inpatient PR. We currently are assessing the effectiveness of HOMEX in a sample of patients with COPD who did not conduct PR within the previous year.

One strength of our study is the rigorous study design. Furthermore, our study population reflects "real" patients with COPD from the Swiss PR setting, and our results are generalizable to this group of patients with severe and very severe COPD, frequent exacerbations, and additional comorbidities. Although we included people with predominantly advanced COPD, the dropout rate of 15% was moderate. Another strength is the long-term perspective of the study and that we assessed the effect of a low-threshold strengthening program on subjective perception of dyspnea.

Interpretation

This study showed that the 12-month HOMEX exercise program had no effect on dyspnea, but provided benefits in functional exercise capacity assessed by the 1MSTST. Most of the IG participants subjectively experienced positive effects that they attributed to the training. Adherence to this long-term training program was surprisingly high. It was well accepted by patients with COPD and may facilitate continued training at home.

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Author contributions: A. F. is the guarantor of the content of the manuscript, including the data and analysis. A. F., M. A. P., T. R., and K. D. L. developed the concept and overall design of the trial and the intervention. K. D. L. and T. R. piloted the HOMEX program. J. B. developed the analysis plan, prepared the randomization list, and conducted the statistical analyses. R. K. contributed to the assessment strategy of the annual training data. A. P. developed and conducted the analysis of the adherence data. Y. T. and M. S. B. developed and conducted the cost-effectiveness analysis. T. F. R. and T. C. monitored the data. A. F. drafted the manuscript. All authors provided input for the manuscript and read, revised, and approved the final version.

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