

Pulmonary Rehabilitation Setting for Adults With Chronic Obstructive Pulmonary Disease (COPD): An Economic Rapid Review

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All authors in the Evidence Development and Standards branch at Health Quality Ontario are impartial. There are no competing interests or conflicts of interest to declare.

Rapid Review Methodology

Rapid reviews are completed in 2–4-week time frames. Clinical questions are developed by the Evidence Development and Standards branch at Health Quality Ontario, in consultation with experts, end users, and/or applicants in the topic area. A systematic literature search is then conducted to identify relevant systematic reviews, health technology assessments, and meta-analyses. The methods prioritize systematic reviews, which, if found, are rated by AMSTAR to determine the methodological quality of the review. If the systematic review has evaluated the included primary studies using the GRADE Working Group criteria (<http://www.gradeworkinggroup.org/index.htm>), the results are reported and the rapid review process is complete. If the systematic review has not evaluated the primary studies using GRADE, the primary studies in the systematic review are retrieved and the GRADE criteria are applied to 2 outcomes. If no systematic review is found, then RCTs or observational studies are included, and their risk of bias is assessed. All rapid reviews are developed and finalized in consultation with experts.

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Health Quality Ontario strives to promote health care that is supported by the best available scientific evidence. The Evidence Development and Standards branch works with expert advisory panels, clinical experts, scientific collaborators, and field evaluation partners to conduct evidence-based reviews that evaluate the effectiveness and cost-effectiveness of health interventions in Ontario.

Based on the evidence provided by Evidence Development and Standards and its partners, the Ontario Health Technology Advisory Committee—a standing advisory subcommittee of the Health Quality Ontario Board—makes recommendations about the uptake, diffusion, distribution, or removal of health interventions to Ontario's Ministry of Health and Long-Term Care, clinicians, health system leaders, and policy-makers.

Health Quality Ontario's research is published as part of the *Ontario Health Technology Assessment Series*, which is indexed in MEDLINE/PubMed, Excerpta Medica/Embase, and the Centre for Reviews and Dissemination database. Corresponding Ontario Health Technology Advisory Committee recommendations and other associated reports are also published on the Health Quality Ontario website. Visit <http://www.hqontario.ca> for more information.

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To conduct its rapid reviews, the Evidence Development and Standards branch and its research partners review the available scientific literature, making every effort to consider all relevant national and international research; collaborate with partners across relevant government branches; consult with expert advisory panels, clinical and other external experts, and developers of health technologies; and solicit any necessary supplemental information.

In addition, Evidence Development and Standards collects and analyzes information about how a health intervention fits within current practice and existing treatment alternatives. Details about the diffusion of the intervention into current health care practices in Ontario add an important dimension to the review. Information concerning the health benefits, economic and human resources, and ethical, regulatory, social, and legal issues relating to the intervention may be included to assist in making timely and relevant decisions to optimize patient outcomes.

Disclaimer

This report was prepared by the Toronto Health Economics and Technology Assessment (THETA) Collaborative, a research partner of the Division of Evidence Development and Standards at Health Quality Ontario, and is developed from analysis, interpretation, and comparison of published scientific research. It also incorporates, when available, Ontario data and information provided by experts. As this is a rapid review, it may not reflect all the available scientific research and is not intended as an exhaustive analysis. Health Quality Ontario assumes no responsibility for omissions or incomplete analysis resulting from its rapid reviews. In addition, it is possible that other relevant scientific findings may have been reported since completion of the review. This report is current as of the date of the literature search specified in the Research Methods section. Health Quality Ontario makes no representation that the literature search captured every publication that was or could be applicable to the subject matter of the report. This rapid review may be superseded by an updated publication on the same topic. Please check the Health Quality Ontario website for a list of all publications: <http://www.hqontario.ca/evidence/publications-and-ohtac-recommendations>.

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List of Abbreviations

COPD	Chronic obstructive pulmonary disease
QALY	Quality-adjusted life-year

Background

As legislated in Ontario's *Excellent Care for All Act*, Health Quality Ontario's mandate includes the provision of objective, evidence-informed advice about health care funding mechanisms, incentives, and opportunities to improve quality and efficiency in the health care system. As part of its Quality-Based Procedures (QBP) initiative, Health Quality Ontario works with multidisciplinary expert panels (composed of leading clinicians, scientists, and administrators) to develop evidence-based practice recommendations and define episodes of care for selected disease areas or procedures. Health Quality Ontario's recommendations are intended to inform the Ministry of Health and Long-Term Care's Health System Funding Strategy.

For more information on Health Quality Ontario's Quality-Based Procedures initiative, visit www.hqontario.ca.

Objective of Analysis

The objective of this analysis was to determine the cost-effectiveness of home-based pulmonary rehabilitation for adults with chronic obstructive pulmonary disease compared with pulmonary rehabilitation in other settings.

Clinical Need and Target Population

Chronic obstructive pulmonary disease (COPD) encompasses a group of irreversible conditions characterized by limited airflow due to lung tissue damage. It affects more than 1.5 million Canadians (1) and is a major cause of illness and death, with patients often experiencing dyspnea (shortness of breath), decreased exercise capacity, and impaired quality of life. Sudden worsening of COPD often leads to hospitalizations and therefore increased health care costs. Due to the long-term effects of the condition, therapy interventions aim to prevent disease progression, relieve symptoms, increase exercise tolerance, and reduce mortality.

Technology/Technique

Pulmonary rehabilitation, consisting of structured exercise and education programs, has been shown to relieve dyspnea and fatigue, improve emotional function, and enhance patients' sense of control over their condition. (2) Rehabilitation can take place in a variety of settings; hospital inpatient, hospital outpatient, and community settings are most common. Home and community pulmonary rehabilitation programs are a possible alternative to hospital programs because they may have the potential to reduce resource use and improve access for patients. However, the comparative cost-utility of pulmonary rehabilitation programs in various settings is unclear.

Rapid Review

Research Question

What is the effectiveness of home-based pulmonary rehabilitation compared to pulmonary rehabilitation in other settings?

Research Methods

Literature Search

Search Strategy

A literature search was performed on December 10, 2013, using Ovid MEDLINE, Ovid MEDLINE In-Process and Other Non-Indexed Citations, and National Health Service Economic Evaluations Database for studies published from January 1, 2008, to December 11, 2013. (Appendix 1 provides details of the search strategies.) Abstracts were reviewed by a single reviewer and, for those studies meeting the eligibility criteria, full-text articles were obtained. Reference lists were also examined for any additional relevant studies not identified through the search.

Inclusion Criteria

- English-language full-text publications
- Published between January 1, 2008, and December 11, 2013
- Cost-utility analyses

Exclusion Criteria

- Abstracts, posters, reviews, letters/editorials, foreign language publications, and unpublished studies

Outcomes of Interest

- Incremental cost per quality-adjusted life-year gained

Expert Panel

In November 2013, an Expert Advisory Panel on Post-Acute Community-Based Care for COPD Patients was struck. Members of the panel included physicians, personnel from the Ministry of Health and Long-Term Care, and representatives from community care organizations.

The role of the expert advisory panel was to provide advice on primary COPD patient groupings; to review the evidence, guidance, and publications related to defined COPD patient populations; to identify and prioritize interventions and areas of community-based care; and to advise on the development of a care pathway model. The role of panel members was to provide advice on the scope of the project, the methods used, and the findings. However, the statements, conclusions, and views expressed in this report do not necessarily represent the views of the expert panel members.

Results of Rapid Review

A total of 199 abstracts were identified in the systematic review. Fourteen full-text articles were retrieved for review. No economic study comparing home-based pulmonary rehabilitation with pulmonary rehabilitation in other settings met the inclusion criteria. But we identified one cost-utility analysis comparing community-based pulmonary rehabilitation with hospital outpatient-based pulmonary rehabilitation in the United Kingdom. One published protocol for an ongoing randomized controlled trial and cost-utility evaluation was also identified; this paper was excluded.

Table 1 summarizes the characteristics and results of the included study, and they are discussed below. Please refer to Appendix 2 for a detailed economic evidence table for the included study.

Waterhouse et al (3) conducted a randomized controlled trial to determine the cost-effectiveness of community- versus hospital-based pulmonary rehabilitation in adults with COPD. The authors also aimed to determine the cost-effectiveness of telephone-based follow-up for each of these programs. This study was undertaken as a 2 x 2 factorial design in which participants were randomized to receive pulmonary rehabilitation in either a hospital or a community setting, then further randomized to receive subsequent standard care or follow-up by telephone. The time horizon of the study was 18 months and analysis was by intention-to-treat. The major inclusion criterion was that patients had a score on the Medical Research Council (MRC) Breathlessness Scale of grade 3 or worse, predominantly due to COPD in the view of a respiratory physician, mirroring guidelines from the National Institute for Health and Clinical Excellence in the United Kingdom.

Both programs were designed to be identical in content and were supervised by 1 of 2 physiotherapy teams. Each program consisted of twice weekly classes for 6 weeks. One hour of each class was spent on review, warm-up, exercise, and cool-down, and 1 hour on education. Participants were encouraged to exercise between classes. They kept an exercise diary at home between sessions, were given an individualized exercise booklet at the end of the course of rehabilitation, and were encouraged to maintain their level of exercise. Access to the sessions was designed to reflect participants' real lives: both venues were chosen for their proximity to public transport links and parking facilities, and participants were expected to make their own way to each session.

The results of the analysis showed that over 18 months, the hospital-based pulmonary rehabilitation strategy was £867 more costly and resulted in a gain of 0.03 QALYs, compared to the community-based strategy. The resulting incremental cost-effectiveness ratio was £28,820. Adherence to the programs was similar in each setting: 62.5% completed the community-based program and 64.6% completed hospital-based rehabilitation. However, only 103 patients (43%) of 240 originally enrolled provided data at 18 months' follow-up.

The difference in mean costs was largely driven by a £824 difference in prescription costs (Table 2). Program costs were similar for each group, an average of £28.67 per session for hospital-based participants and £33.14 for community-based participants. The cost of the rehabilitation program accounted for only 5% of the total cost for each group.

The reason for the difference in QALYs between groups was unclear. The hospital-based group reported a greater improvement from baseline in walking distance (109%), compared with the community-based group (91%), as measured by the endurance shuttle walking test. However, the difference in change between groups was not statistically significant. A large but not significant difference by physiotherapy team was noted, but because teams alternated between locations, possible differences in the teams

themselves did not explain this variability. No difference in quality of life was observed when measured with the EQ-5D index rather than the SF-36 questionnaire.

The results of probabilistic sensitivity analysis showed that there was a 56% probability that community-based rehabilitation would fall below a threshold of £20,000 per QALY gained, and a 50% probability that community-based rehabilitation was cost-effective at a threshold of £30,000 per QALY gained.

The authors concluded that pulmonary rehabilitation in both community-based and hospital-based settings have similar efficacy with significant improvements in exercise capacity and quality of life. From an economic perspective, neither pulmonary rehabilitation program was greatly favoured over the other. Thus, the choice to adopt pulmonary rehabilitation in either setting will depend on local factors.

Table 1: Study Characteristics and Results

Study Design	Time Horizon	Perspective	Comparators	Results
RCT	18 months	United Kingdom National Health Service	<ol style="list-style-type: none"> 1) Hospital program with telephone follow-up 2) Hospital program without follow-up 3) Community program with telephone follow-up 4) Community program without follow-up <p>Programs were supervised by 2 physiotherapy teams who each worked across both sites. Classes were 2 hours each (1 hour exercising, 1 education), twice per week for 6 weeks.</p>	<p>Hospital, mean: £4,511; 1.54 QALYs Community, mean: £3,644; 1.51 QALYs</p> <p>Hospital-based rehab was £867 more costly and 0.03 QALYs more effective than community rehab, with a cost per QALY gained of £28,820.</p> <ol style="list-style-type: none"> 1) £4,832; 1.54 QALYs 2) £4,218; 1.55 QALYs <p>For hospital-based rehab, no telephone follow-up was more expensive and more effective.</p> <ol style="list-style-type: none"> 3) £3,230; 1.55 QALYs 4) £3,952; 1.48 QALYs <p>For community-based rehab, telephone follow-up was less expensive and more effective.</p>

Abbreviations: QALY, quality-adjusted life-year; RCT, randomized controlled trial.
 Source: Waterhouse et al, 2010. (3)

Table 2: Costs by Study Arm

Included Resources	Hospital-Based Programs, Mean (SD), £ (n = 47)	Community-Based Programs, Mean (SD), £ (n = 43)	Difference, mean (95% CI), £
GP phone	91.06 (187.75)	43.72 (111.03)	47.34 (–16.79 to 111.47)
GP surgery	337.79 (224.69)	318.14 (205.00)	19.65 (–75.39 to 114.68)
GP home visit	178.72 (428.18)	121.12 (328.57)	57.61 (–103.38 to 218.59)
Walk-in centre	9.96 (34.95)	21.77 (82.21)	–11.81 (–38.92 to 15.30)
NHS direct	4.26 (22.91)	7.00 (31.96)	–2.72 (–14.30 to 8.86)
District nurse visits	25.87 (95.12)	27.40 (84.70)	–1.52 (–39.39 to 36.34)
Health visitor visits	7.15 (49.01)	3.91 (25.62)	3.24 (–13.00 to 19.49)
Social worker visits	18.04 (86.51)	14.80 (97.00)	3.25 (–35.19 to 41.69)
Home help	39.32 (245.74)	149.77 (565.96)	–110.45 (–297.64 to 76.75)
Other services	54.43 (286.33)	42.05 (195.30)	12.38 (–89.67 to 114.43)
Average total costs per individual	755.98 (796.91)	739.36 (813.67)	16.63 (–320.94 to 354.20)
Prescriptions	1,752.77 (2,254.94)	928.32 (1,119.26)	824.45 (67.73 to 1,581.16)
PR sessions	262.91 (95.34)	327.55 (86.15)	–64.94 (–102.27 to –27.01)
OP/A&E costs	727.59 (967.77)	650.69 (934.84)	76.90 (–322.42 to 476.22)
Inpatient costs	1,011.96 (2,493.00)	997.83 (2,066.68)	14.13 (–950.17 to 978.44)
Average total costs for all resources per individual	4,511.21 (3,794.69)	3,643.74 (3,314.43)	867.47 (–631.17 to 2,366.11)

Abbreviations: A&E, accident and emergency; GP, general practitioner; NHS, National Health Service; OP, outpatient; PR, pulmonary rehabilitation; SD, standard deviation.

Source: Waterhouse et al, 2010. (3)

Conclusions

This literature review could not determine whether hospitals or home and community locations are the most cost-effective setting for pulmonary rehabilitation programs for adults with COPD.

We identified only one published study that compared the costs and QALYs of pulmonary rehabilitation across different settings. The study showed that hospital-based pulmonary rehabilitation is more costly and more effective than community-based pulmonary rehabilitation. The resulting cost per QALY gained was £28,820 (equivalent to \$65,800 in 2013 Canadian dollars).

The study was designed to be pragmatic, without overly strict inclusion criteria. Approximately 60% of patients in each arm completed each rehabilitation program. The cost of each program was similar and comprised a small proportion of the total cost for each group. The main difference in total cost was attributed to prescriptions, which were £824 more expensive in the hospital-based group. No reason for this difference was proposed.

The cause of the difference in QALYs is unclear. Improved quality of life in the hospital-based group could be due to a small increase in walking ability compared with the community-based group. However, it may also be due to the fact that quality of life was included as a secondary outcome and therefore the study was not powered to detect changes between groups for this outcome.

Acknowledgements

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Health Quality Ontario's Expert Advisory Panel on Post-Acute Community-Based Care for COPD Patients

Panel Members	Affiliation(s)	Appointment(s)
Co-Chairs		
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Lisa Droppo	Ontario Association of Community Care Access Centers (OACCAC)	Chief Care Innovations Officer
Primary Care		
Dr Kenneth Hook	Ontario College of Family Physicians STAR Family Health Team	Past-President Senior Physician
Dr Alan Kaplan	Family Physicians Airway Group of Canada	Chair, Family Physicians Airway Group of Canada
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Nursing		

Panel Members	Affiliation(s)	Appointment(s)
Cheryl Lennox	South West Community CCAC, Intensive Home Care Team	Nurse Practitioner-Primary Health Care Certified Respiratory Educator
Andrea Roberts	Toronto Central CCAC	Rapid Response Transition Nurse
Mary-Jane Herlihey	ParaMed Home Health Care Ottawa	Clinical Consultant
Suzy Young	St. Mary's General Hospital	Nurse Practitioner Primary Health Care SWCCAC Intensive Health Care Team Certified Respirator Educator

Appendices

Appendix 1: Literature Search Strategies

Search date: December 11, 2013

Limits: 2008-current; English

MEDLINE SEARCH

Databases searched: Ovid MEDLINE, Ovid MEDLINE In-Process and Other Non-Indexed Citations,

Limits: English, 2008-Present

Filters: Health Technology Assessment Filter: EconEval_Filter_NHS EED MEDLINE best sensitivity from Glanville2009

Database(s): Ovid MEDLINE(R) 1946 to November Week 3 2013, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations December 10, 2013

Search Strategy:

#	Searches	Results
1	exp Pulmonary Disease, Chronic Obstructive/ or exp Emphysema/ or (copd or coad or chronic airflow obstruction* or (chronic adj2 bronchitis) or emphysema or (chronic obstructive adj2 (lung* or pulmonary or airway* or airflow* or respiratory or bronchopulmonary) adj (disease* or disorder*))).ti,ab.	75602
2	exp Pneumonia/ or (pneumoni* or peripneumoni* or pleuropneumoni* or lobitis or ((pulmon* or lung*) adj inflammation*)).ti,ab.	169371
3	exp Exercise Tolerance/ or exp Exercise/ or exp Rehabilitation/ or exp Rehabilitation Nursing/ or exp "Physical and Rehabilitation Medicine"/ or exp Rehabilitation Centers/ or exp Physical Therapy Modalities/ or (rehabilitat* or (physical* adj (fit* or train* or therap* or activit*)) or ((exercise* or fitness) adj3 (treatment or intervent* or program*)) or (train* adj (strength* or aerobic or exercise*)) or wellness program* or ((pulmonary or lung* or respirat* or cardiac) adj2 (physiotherap* or therap* or rehabilitat*)) or angina plan* or heart manual*).ti,ab.	494803
4	1 or 2	239449
5	4 and 3	8779
6	economics/ or exp "costs and cost analysis"/ or economics, dental/ or exp "economics, hospital"/ or economics, medical/ or economics, nursing/ or economics, pharmaceutical/ or (economic\$ or cost or costs or costly or costing or price or prices or pricing or pharmaco-economic\$).ti,ab. or (expenditure\$ not energy).ti,ab. or (value adj1 money).ti,ab. or budget\$.ti,ab.	601403
7	((energy or oxygen) adj cost) or (metabolic adj cost) or ((energy or oxygen) adj expenditure).ti,ab.	20932
8	6 not 7	596650
9	(letter or editorial or historical article).pt.	1475635
10	8 not 9	567988
11	Animals/ not (Animals/ and Humans/)	3974352
12	10 not 11	534257
13	5 and 12	603
14	limit 13 to english language	531
15	limit 14 to yr="2008 -Current"	253
16	remove duplicates from 15	199

Appendix 2: Economic Evidence Table

Waterhouse et al, 2010 (3)		
Methods		
Study details	Population	Interventions
<p>Type of economic analysis: Cost-utility analysis</p> <p>Study design: RCT</p> <p>Perspective: UK NHS and PSSRU</p> <p>Time horizon: 18 months</p>	<p>People diagnosed with COPD according to Global Initiative for Chronic Obstructive Lung Disease guidelines. Participants were recruited from respiratory clinics within the Sheffield Teaching Hospitals, NHS Foundation Trust, community sources, physiotherapy clinics and self-referrals.</p> <p>N: 240 at baseline (90 at 18-month follow-up) Mean age: 69 years Male: 52% Actual FEV₁: 46.7%</p>	<p>Intvn 1: Hospital-based pulmonary rehabilitation program with telephone follow-up.</p> <p>Intvn 2: Hospital-based pulmonary rehabilitation program without telephone follow-up.</p> <p>Intvn 3: Community-based self-monitored pulmonary rehabilitation program with telephone follow-up.</p> <p>Intvn 4: Community-based self-monitored pulmonary rehabilitation program without telephone follow-up.</p>
Results		
Costs	Health outcomes	Cost-effectiveness
<p>Currency and cost year: British pounds, 2003/2004</p> <p>Intvn 1&2 (avg): £4,511 Intvn 2&3 (avg): £3,644 Intvn 1&2 – 2&3: £867</p> <p>Total mean costs (SD): Intvn 1: £4,832 (£4,566) Intvn 2: £4,218 (£2,946) Intvn 3: £3,230 (£3,035) Intvn 4: £3,952 (£3,530)</p> <p>Discount rate: None/NA</p>	<p>Primary outcome: QALYs Intvn 1&2 (avg): 1.54 (SD, 0.23) Intvn 2&3 (avg): 1.51 (SD, 0.25)</p> <p>Total QALYs, mean (SD): Intvn 1: 1.54 (0.25) Intvn 2: 1.55 (0.21) Intvn 3: 1.55 (0.24) Intvn 4: 1.48 (0.26)</p> <p>Other outcome: Mean increase in distance walked relative to baseline Intvn 1&2: 109% (SD, 137%) Intvn 3&4: 91% (SD, 133%) Intvn 1&2 – 2&3: 17.8% (95% CI, -24.3 to 59.9, $P = 0.405$).</p> <p>Discount rate: None/NA</p>	<p>Primary ICER: Hospital-based pulmonary rehabilitation cost £28,820 per QALY gained compared with community pulmonary rehabilitation.</p> <p>At a threshold of £20,000 to £30,000 per QALY gained, the probability that hospital-based rehabilitation is cost effective is between 44% and 50%.</p>
Interpretation		
Sensitivity analyses	Limitations and applicability	
<p>Adjusting costs by resource use, gender, and age resulted in a decrease in the incremental cost saving associated with community programs (from £867 to £463). QALYs were adjusted according to baseline utility, age, and gender. This did not change the incremental QALYs gained. Both changes resulted in a decreased probability that community-based pulmonary rehabilitation is cost-effective.</p> <p>An analysis was undertaken to assess the cost-effectiveness of telephone follow-up when the location cannot be changed. The results indicate that in the community, follow-up has an 87% probability of being cost-effective at a cost of \$20,000 per QALY. However, follow-up only has a 31% probability of being cost-effective in hospital-based pulmonary rehabilitation. Adjusting costs and QALYs as above reduces the probability of community follow-up to 82% and increases the likelihood that hospital follow-up will be cost-effective to 72%.</p>	<p>This analysis was undertaken from a UK perspective; resource use and unit costs are not directly applicable to Ontario.</p> <p>Although rehabilitation program components are well described, program settings are not, making it difficult to compare applicability to rehabilitation programs in Ontario.</p> <p>The study was powered to detect a change in walking distance as measured by the endurance shuttle walking test. A minimum clinically important difference in quality of life was not established a priori and the power calculations were not conducted to take quality of life into account.</p> <p>The authors did not hypothesize or conduct further analyses into the difference in pharmaceutical costs between settings.</p>	

Data sources

Clinical effectiveness: The primary outcome was the endurance shuttle walking test. Secondary outcomes were health-related quality of life, measured using the following questionnaires and indexes: SF-36, EQ-5D, SF-6D, and Chronic Respiratory Questionnaire (CRQ).

Costs: The cost of the rehabilitation program included staff time, facilities hire, and equipment costs. Staff costs were based on Department of Health pay scales. The Sheffield Teaching Hospitals NHS Foundation Trust finance department provided cost of equipment and local rental. The cost of a portable oxygen cylinder was also included. Cost per session was calculated assuming 208 sessions per year with equipment lifespan of 4 years and 3.5% annuity. With 8 individuals attending each pulmonary rehab session, the cost per session per individual amounts to £28.67 for hospital and £33.14 for community pulmonary rehab, respectively. Other estimates of resource use were collected from patient questionnaires. Baseline drug and resource use were not included. Telephone follow-up costs were added at the end of the trial. Total costs were aggregated to obtain average total cost per patient.

Quality of life: Patients completed the SF-6D questionnaire at baseline, 8 weeks, 6 months, 12 months, and 18 months post-intervention. Scores were calculated using the UK tariff.

Funding

UK National Institute for Health Research

Abbreviations: avg, average; COPD, chronic obstructive pulmonary disease; EQ-5D, EuroQOL 5 Dimension Questionnaire; FEV₁, forced expiratory volume in 1 second; ICER, incremental cost-effectiveness ratio; Intvn, intervention; NA, not available; NHS, National Health Service; PSSRU, Personal Social Services Research Unit; RCT, randomized controlled trial; SF-36, Short Form 36 Health Survey; SF-6D, Short Form 6 Dimension Questionnaire; SD, standard deviation; QALY, quality-adjusted life-year; UK, United Kingdom.

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