

Interventions to increase referral and uptake to pulmonary rehabilitation in people with COPD: a systematic review

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Abstract: Pulmonary rehabilitation (PR) reduces the number and duration of hospital admissions and readmissions, and improves health-related quality of life in patients with COPD. Despite clinical guideline recommendations, under-referral and limited uptake to PR contribute to poor treatment access. We reviewed published literature on the effectiveness of interventions to improve referral to and uptake of PR in patients with COPD when compared to standard care, alternative interventions, or no intervention. The review followed recognized methods. Search terms included “pulmonary rehabilitation” AND “referral” OR “uptake” applied to MEDLINE, EMBASE, CINAHL, PsycINFO, ASSIA, BNI, Web of Science, and Cochrane Library up to January 2018. Titles, abstracts, and full papers were reviewed independently and quality appraised. The protocol was registered (PROSPERO # 2016:CRD42016043762). We screened 5,328 references. Fourteen papers met the inclusion criteria. Ten assessed referral and five assessed uptake (46,146 patients, 409 clinicians, 82 hospital departments, 122 general practices). One was a systematic review which assessed uptake. Designs, interventions, and scope of studies were diverse, often part of multifaceted evidence-based management of COPD. Examples included computer-based prompts at practice nurse review, patient information, clinician education, and financial incentives. Four studies reported statistically significant improvements in referral (range 3.5%–36%). Two studies reported statistically significant increases in uptake (range 18%–21.5%). Most studies had methodological and reporting limitations. Meta-analysis was not conducted due to heterogeneity of study designs. This review demonstrates the range of approaches aimed at increasing referral and uptake to PR but identifies limited evidence of effectiveness due to the heterogeneity and limitations of study designs. Research using robust methods with clear descriptions of intervention, setting, and target population is required to optimize access to PR across a range of settings.

Keywords: health services research, service improvement, access to healthcare, evidence-based practice, long-term condition, supervised exercise

Introduction

COPD presents a considerable health challenge. It is estimated that worldwide 328 million people have COPD and 65 million people live with moderate to severe COPD.¹ In 2015, COPD accounted for 5% of all deaths globally,² and in the UK, ~1.2 million people and 4.5% of all people aged over 40 years live with the condition.³ COPD is likely to be underdiagnosed and prevalence in the UK may be rising.³ It compromises individuals’ quality of life and impacts healthcare costs, mostly relating to hospital admissions. In 2012, it was estimated to cost the UK National Health Service £800 million per annum.⁴ Pulmonary rehabilitation (PR), providing supervised

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exercise and education, improves COPD symptoms leading to improvements in exercise capacity and quality of life.⁵ PR reduces the number and duration of respiratory hospital admissions experienced by individuals,⁶ the number of readmissions,^{6,7} and can foster self-management skills.⁸ It is a cost-effective treatment.⁹

Despite a clear evidence base and guidelines recommending PR,^{10,11} it is grossly underutilized in practice worldwide.¹² In England and Wales, for example, the National COPD Audit Programme for 2013/14 estimated the prevalence of COPD patients eligible for PR to be 446,000; however, only 68,000 were referred (15% of normative need) of whom only 69% attended an initial assessment (10% of normative need).¹³ Utilization may be impacted by availability, referral, and uptake but even where places are available they may not be utilized. In the East of England in 2014/15, the number of available PR places represented only 53.8% of the proposed target, but just 73% of these places were taken up.¹⁴ There is an urgent need to improve referral and uptake to PR both in the UK^{6,13} and globally¹² but there is no best practice guidance for doing so.

We set out to conduct a systematic review of published studies on the effectiveness of interventions to increase rates of referral and uptake from primary care or outpatient departments to exercise-based PR programs in patients with COPD compared to standard care, alternative interventions, or no intervention.

Methods

Recognized systematic review methods¹⁵ were adapted to conduct the review. The review protocol was registered on PROSPERO (2016:CRD42016043762)¹⁶ and reported according to PRISMA guidelines.¹⁷

Eligibility

Studies were required to report at least one of the main outcomes of interest: rates of referral to or uptake of exercise-based PR programs in patients with COPD. We defined PR programs as including “multicomponent, multidisciplinary interventions, which are tailored to the individual patient’s needs. The rehabilitation process should incorporate a program of physical training, disease education, and nutritional, psychological, and behavioral intervention.”¹⁸ Uptake was defined as having attended a first appointment with a PR provider including initial assessment.

We included all studies that used established quantitative or mixed methods of data collection, eg, trials, surveys, direct observations, action research, interviews, focus groups

or questionnaires, systematic reviews, and meta-analyses. Interventions could be contrasted with standard care, alternative interventions, or have no comparator or control.

We included studies of i) healthcare professionals who referred COPD patients to PR in primary, secondary, or community care settings; ii) adult patients (≥ 18 years) with a diagnosis of COPD in any setting, who had received a referral to PR (whether taken up or not); and iii) informal adult carers (≥ 18 years) of these patients, defined as spouse or partner, family members, friends, or significant others, who provided physical, practical, transportation, or emotional help to someone with COPD. We excluded professional carers. We also excluded studies that featured mixed participant groups where subgroups with COPD were not described or where studies were conducted in various settings and data from inpatient and outpatient services could not be separated.

Published studies were included. Conference abstracts and opinion papers were not considered for analysis. No language restrictions were applied.

Data sources and search strategy

We searched the following databases: MEDLINE and EMBASE (via OVID), CINAHL and PsycINFO (via Ebsco-Host), ASSIA and BNI (via ProQuest), Web of Science, and Cochrane Library to the end of January 2018. A search strategy was developed on MEDLINE (see Supplementary material) and adapted for other databases. The strategy included “quantitative” OR “mix* method*.” Filters for randomized controlled trials (RCTs) and systematic reviews were adapted from Scottish Intercollegiate Guidelines Network search filters.¹⁹ We also searched “related article” searches in PubMed for all studies included in the review and scanned reference lists of all included studies and key references, searching for relevant papers citing the included papers in the Institute for Scientific Information Web of Science (Science Citation Index and Social Sciences Citation Index). An interim report of this work, searching literature up to June 2016 and without specific search criteria for quantitative and mixed methods studies, was presented at the British Thoracic Society in 2016.²⁰

Study selection and data extraction

Search results were screened on titles and abstracts and then on full text by two independent reviewers (FE and IW), gaining consensus on inclusion with input from a referee (JF) if required.

A data extraction form was piloted and two reviewers (FE and IW) independently extracted data from eligible

papers. Data included study setting, sample size, recruitment method, study design, study objectives, participant/patient characteristics, methods of data collection, data analysis, recorded outcomes, limitations, and conflict of interests. We planned to tabulate data and carry out a meta-analysis using Review Manager ([RevMan], Version 5.3; The Cochrane Collaboration, The Nordic Cochrane Centre, Copenhagen, 2014) statistical software according to our prespecified protocol if this was appropriate.

Quality assessment

The same reviewers independently appraised study quality to assess the risk of bias in individual studies using the Cochrane Collaboration's tool for assessing risk of bias in RCTs,²¹ the ACROBAT-NRSI (A Cochrane Risk Of Bias Assessment Tool for Non-Randomized Studies of Interventions),²² and AMSTAR (A Measurement Tool to Assess systematic Reviews)²³ depending on the type of study.

Results

Searches identified 5,328 potentially relevant articles of which 14 met our inclusion criteria (Figure 1). All were in English language. Six studies were conducted in the UK,^{24–29}

four in Denmark,^{30–33} two in Australia,^{34,35} and one in USA.³⁶ One was a systematic review.³⁶ Study characteristics and findings are summarized in Table 1.

Ten studies included rates of referral to PR as an outcome^{24,25,27–33,36} of which eight^{24,27,29–33,36} reported the number of patients or patient records studied, in total 44,720. This total included five large audits capturing data from 43,098 patient records (range 1,211–32,018).^{30–33,36} Five studies assessed rates of uptake to PR of which three reported the number of patients studied, in total 1,426 (range 126–600).^{26,34,35} One study reported only percentages.²⁵ A systematic review by Jones et al³⁷ found no eligible studies of uptake.

Populations and settings

Descriptions of patient populations were limited. Age and sex were most commonly reported and no studies reported ethnicity. Age and sex were reported by six studies that measured referral^{24,27,30–33} and three that measured uptake.^{26,34,35} The number and/or roles of clinicians involved were reported by seven studies that measured referral^{24,25,28,30,31,33,36} and two that measured uptake.^{25,35} Overall, patients were older (mean age ≥ 69 years) and 44%–64% of the samples were males.

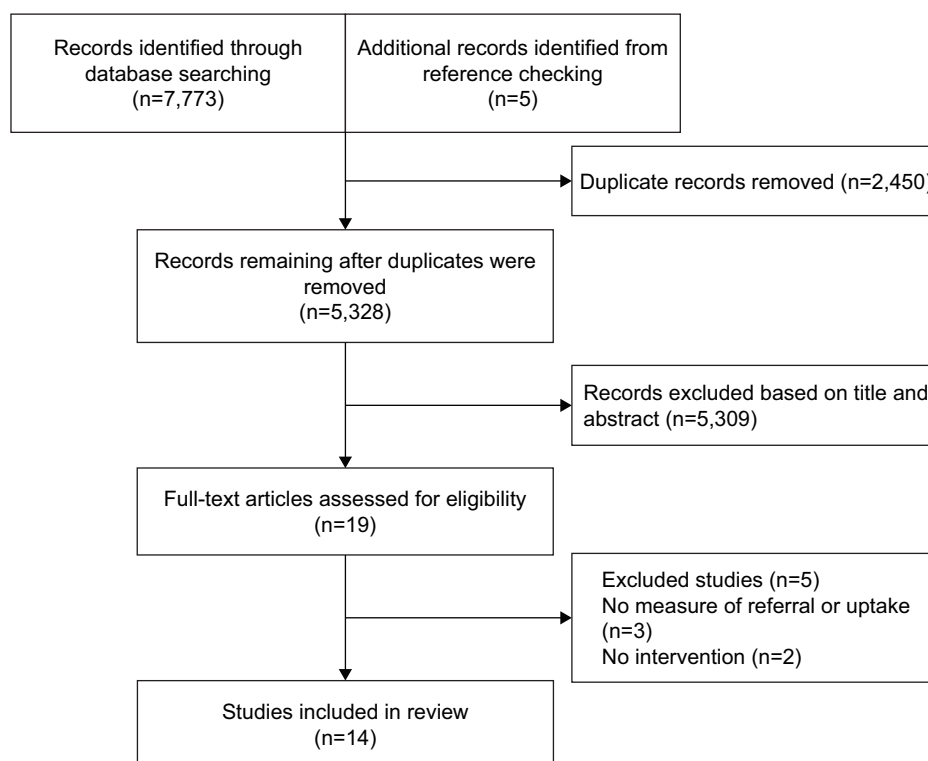


Figure 1 Study flow diagram.

Table 1 Study characteristics

Study and setting	Sample size	Demographics ^a	Source of participants	Study design	Intervention	Comparator group	Outcome measures	Findings relevant to this review
Studies measuring referral								
Angus et al; ²⁴ primary care, urban, semirural, and rural, UK	16 General practices; 18 practice nurses; 293 patients	Age: mean 69.7 (SD 10.1) Male: 55.6%	COPD registers	Descriptive observational study	Computer-guided review, based on NICE guidance, by practice nurses during routine COPD review	None	Change to primary diagnosis. Percentage of patients recommended for inhaler prescription, smoking cessation support, oxygen assessment, PR referral	24% (47/191) of patients with confirmed COPD diagnosis were referred to PR
Deprez et al; ²⁶ primary care, rural, USA	18 General practices (>25 primary care physicians and mid-level providers); 1,210 patient records	Not reported	Samples of records from each participating practice	Before and after audit of patient charts	1) Team-based model. Three collaborative learning sessions to educate and empower clinical staff with ideas to implement and sustain practice changes 2) On-site visits, email, and telephone support from faculty 3) Change tools: COPD flow sheet, COPD registry, patient self-management worksheet 4) Feedback from patient focus groups	None	Percentage of patients with documented spirometry results, COPD stage, annual influenza vaccine, pneumonia vaccine, diet, exercise counseling, PR referral. Percentage of visits with documented smoking status, self-management goals, respirator education, smoking cessation counseling (smokers only)	5% Increase in PR referral (7%–12%, 16 practices) (P=0.048)*
Hopkinson et al; ²⁷ respiratory ward, acute hospital, London, UK	1 Respiratory ward; 94 patients	Age: mean 74.6 (11.2) Male: 64%	Patients on ward from October 2009 to September 2010	Before and after study of process indicators	1) Ward-based staff education 2) Discharge care bundle with referral for PR assessment 3) Patient offered phone call 48–72 hours postdischarge to check if they were improving, if not then community input expedited 4) PDSA cycles to refine the process 5) Prize draw for staff completing checklist 6) Ward staff attended hospital PR sessions 7) PR patient information leaflet	Usual care (historical)	Compliance with smoking cessation advice. PR referral. Self-management plan administered. Inhaler technique reviewed. Follow-up arrangements documented	54.4% Increase in PR referral (13.6%–68%)

Hull et al; ²⁸ primary care trust, inner London, UK	36 General practices	Not reported	COPD management data routinely collected from participant practices	Longitudinal audit, borough- wide quality improvement project	1) Eight networks of 4-5 general practices 2) Financially incentivized KPIs 3) Care package based on NICE guidance 4) IT infrastructure to monitor networks and KPIs 5) Support from community respiratory team 6) Network boards to review practice performance against targets, supported by clinical leads 7) Quarterly community COPD multidisciplinary team meeting 8) Rapid email/phone advice from respiratory consultant Educational program: individual meeting with consultant from sponsoring company focused on GOLD guidelines; regional meetings with 30 GPs and staff, pulmonary specialist, and GP from steering committee to discuss the guidelines; symposium for all GPs and staff, plenary sessions, workshops, practical issues	COPD management data from two neighboring PCTs. UK- wide QOF for national performance comparison	Number of COPD cases on network registers. Completed care plans. Referral to community-based PR. Flu immunization. Smoking prevalence. Stop smoking attempts. Rates of emergency hospital admission for COPD	25% Increase in PR referral (45%-70%, between 2010 and 2013). No comparative data reported
Lange et al; ³⁰ primary care, Denmark	186 GPs; 4,943 patients	1st audit: Age: mean 70.7 (8.7) Male: 44.2% Current smoker: 42.3% FEV ₁ %: 56.4 (23.3)	20 Consecutive patients visiting each GP over two 4-month periods 1 year apart	Before and after audit of GP patient notes	None	None	Proportion of patients having spirometry testing (primary parameter). Secondary parameters: compliance with inhaler technique, smoking cessation advice (current smokers), referral to COPD rehabilitation, physical exercise advice, dietary instruction, influenza vaccination, inhaled corticosteroids in mild and severe COPD	3.5% Increase in referral for COPD rehabilitation (16.7%-20.2%) (P<0.01)*
Lange et al; ³¹ outpatient clinics, Denmark	1,868 Patients; 22 hospitals with outpatient departments	1st audit: Age: mean 69.2 (10.7) Male: 45% Current smoker: 29.2% FEV ₁ %: 43.6 (17.7)	30-50 Consecutive patients from each department over two 3-month periods 1 year apart	Before and after audit of hospital records	None	None	Care quality indicators recorded: height, weight, BMI, smoking status, pack-years, FEV ₁ % predicted, FVC % predicted, pulse oximetry, smoking cessation advice (current smokers), PR referral, nutritional advice if relevant, inhaler technique checked	6.4% Increase in PR referral (56.3%-62.7%) (P=0.006). Not significant in weighted analysis due to considerable variation between hospitals, 95% CI (-2%, 22%)

(Continued)

Table 1 (Continued)

Study and setting	Sample size	Demographics ^a	Source of participants	Study design	Intervention	Comparator group	Outcome measures	Findings relevant to this review
Roberts et al, ²⁹ primary care, North East London, UK	20 General practices (10 intervention, 10 control); 1,235 patients (640 intervention, 595 control)	Not reported	Patients on practice lists with COPD diagnosis	Quasi-experimental, pragmatic nonrandomized controlled study	1) Patient-held scorecard containing six care quality indicators comparing patient's care to the standard. Sent to patient with letter advising patient to discuss scorecard at the next COPD review 2) Telephone helpline for patients	Usual care	Compliance with care quality indicators: diagnosis confirmed by postbronchodilator spirometry, annual review performed, self-management plan received, PR referral for patients with MRC score ≥ 3 , patients quit smoking	7.4% Increase in PR referral for intervention group (1.2%–8.6%) compared to 1.3% increase for control group (0.9%–2.2%). Difference between groups of 6.1% ($P=0.03$)*
Tottenborg et al, ³² hospital outpatients, Denmark	56 Hospitals; 32,018 patients	Reported by year (2008–2011); 2008 outpatients: Age: median 70.1 Male: 45% Current smoker: 32.6% FEV ₁ %: median 41	All patients aged ≥ 30 seen at hospital outpatient clinic from January 2008 to December 2011	Before and after audit. Nationwide, population-based quality improvement initiative	Continuous mandatory monitoring of quality of hospital-based COPD care via Danish Clinical Register of COPD. Focus on six care quality indicators. Patient data prospectively registered as part of clinical routine	None	Fulfillment of care quality indicators for each year: lung function (FEV ₁ % predicted), BMI, MRC dyspnea score, smoking status, smoking cessation (current smokers), PR offer where MRC score ≥ 3	36% Increase in PR referral (55%–91%) (RR 2.78, 95% CI, 2.65; 2.90)*
Ulrik et al, ³³ primary care, Denmark	124 GPs; 3,058 patients	1st audit: Age: mean 68 (range 35–95) Male: 44%	20 Consecutive patients visiting each GP during two 4-month periods 1 year apart	Before and after audit surveys	Educational program for GPs and staff: individual meeting with consultant from sponsoring company focused on GOLD guidelines; meetings with GPs and staff with steering committee, pulmonologist, and a GP to discuss GOLD guidelines; regional symposiums for GPs and staff; individual meeting with consultant from a sponsoring company focusing on GP's data	None	Proportion of patients with spirometric data (primary parameter). Secondary parameters: BMI, dietary instruction given, instruction for inhaler technique, smoking cessation advice, monitoring of MRC dyspnea score, referral to COPD rehabilitation	4% Increase in referral to COPD rehabilitation (12% vs 16%) (NS)

Studies measuring referral and uptake								
Foster et al. ²⁵ primary care, Stoke on Trent, UK	8 Primary care practices; 126 patients	Current smoker: 34.9%	Patients on COPD registers eligible for PR	Before and after audit of practice data. Survey of practitioners and patients	Participatory action research: clinician questionnaire to assess knowledge and attitudes about PR and ideas for increasing referrals; briefing note based on questionnaire feedback and literature review with suggestions for standardizing PR knowledge and increasing referral (in- house education, practice protocols, "pop-ups," and memory aids to prompt discussion about PR)	None	Audit data: COPD register size, number of patients eligible for PR, number of eligible patients coded for conversation about PR, outcome of conversation about PR (referred, referral declined, completed, not completed). Cross-sectional survey of patients eligible for PR: PR referral accepted, reasons for declining referral, whether a conversation about PR had taken place	Patients with PR code and PR referral ranged from 27% to 100% across 6/8 practices; proportion coded as attending PR ranged from 0% to 25% (data collected at one time point only). 25.7% (126/490) of patients returned the survey: 66% (84/126) had discussed PR with a clinician, of which 70.2% (59/84) had accepted PR referral
Studies measuring uptake								
Graves et al. ²⁶ setting unclear, North Bristol, UK	600 Patients (400 inter- vention, 200 noninter- vention)	Intervention group who opted in (n=235):	Patients invited to PR program	Observational study	GOIS (1.5 hours) prior to assessment for PR; run by physiotherapist and clinical psychologist; discussion of patient case study, self- management, PR information, alternatives to PR Patient manual summarizing Cochrane evidence on COPD treatments, related topics, and suggested questions to ask the doctor	Usual care including single sheet information pamphlet about COPD	Rates of attendance at GOIS. Attendance at PR assessment. Starting PR. PR drop out. PR graduation	16.3% Fewer patients in the intervention group attended pre-course assessment compared to usual care (58.7% vs 75%) (P<0.001)*
Harris et al. ³⁴ secondary and outpatient, Adelaide, Australia	3 Respiratory outpatient clinics; 249 patients (125 intervention, 124 control)	Intervention group: Age: mean 73.6 Male: 55% Current smoker: 18%	Patients with moderate to severe COPD identified through inpatient admission for COPD and at respiratory outpatient clinics	Controlled before and after			Main outcomes: PR enrollment, rates of influenza vaccination, bone density testing. Secondary outcomes: COPD mastery, COPD knowledge, communication with usual doctor, satisfaction with disease-related information, anxiety	18% Increase in PR enrollment for the most socioeconomically disadvantaged patients in the intervention group compared to 0% in the control group (P=0.05)*. 12% Increase for the least socioeconomically disadvantaged patients in the intervention group compared to 7% in the control group (NS)

(Continued)

Table 1 (Continued)

Study and setting	Sample size	Demographics ^a	Source of participants	Study design	Intervention	Comparator group	Outcome measures	Findings relevant to this review
Jones et al; ²⁷ no restriction on setting	0	N/a	N/a	Systematic review	Review of RCTs of interventions to improve patient uptake and/or completion of PR in COPD	Any concurrent control group referred to and/or enrolled on to PR but not receiving an intervention aimed to improve uptake and/or completion	Uptake of PR: received baseline assessment and/or enrolled on to PR. Completion of PR: received discharge assessment; total number of sessions attended	No studies of uptake identified
Zwar et al; ³⁵ community, Sydney, Australia	44 General practices; 56 GPs; 451 patients (234 intervention, 217 control)	Intervention group: Age: mean 65.8 (10.3) Male: 47% Current smoker: 31.6%	Patients in participant practices with COPD diagnosis	Cluster RCT	Individualized care plan based on clinical practice guidelines delivered by nurses in patient's home over 6 months. Partnership model of working between nurses and GPs	GPs provided with a copy of COPD guidelines. Patients received usual care	Primary outcome: health-related quality of life. Secondary outcomes: overall quality of life, lung function, smoking status, immunization status, attendance at PR, patient knowledge of COPD	21.5% Difference in the number attending PR in the intervention group compared to the control group (31.1% vs 9.6%) (OR 5.16 (2.40–11.10)) (P=0.002)*

Notes: Studies varied in their reporting of patient characteristics. Here, we present age, sex, smoking status, and lung function where reported. Some studies also reported other patient characteristics. *Statistically significant at P<0.05. **Abbreviations:** BMI, body mass index; FEV₁, forced expiratory volume; GOIS, group opt-in session; GP, general practitioner; IT, information technology; KPI, key performance indicator; MRC, score on Medical Research Council Dyspnea Scale; NICE, National Institute for Clinical Excellence (UK); NS, not significant; PCT, primary care trust; PDSA, plan, do study, act; PR, pulmonary rehabilitation; QOF, Quality and Outcomes Framework; RCT, randomized controlled trial.

Study designs

Study designs were heterogeneous and most were observational. Of the referral studies, two captured referral data at one time point only,^{24,25} six reported before and after longitudinal data,^{28,30–33,36} one reported before and after results using a historical comparison group,²⁷ and one conducted a pragmatic non-RCT.²⁹ Of the uptake studies, one captured uptake data at one time point only,²⁵ one reported before and after results using a historical comparison group,²⁶ one used a controlled before and after design,³⁴ and there was one cluster RCT.³⁵ The systematic review by Jones et al²⁷ searched for RCTs evaluating uptake and identified none.

Interventions

Most studies measured referral or uptake to PR in the context of multifaceted evidence-based management of COPD. Only one study focused specifically on referral²⁵ and one on uptake.²⁶ Interventions ranged from clinician education to system-wide change.

Studies measuring referral in primary care included a computer-guided COPD review,²⁴ educational programs for healthcare providers (HCPs),^{30,33} collaborative team-based education and empowerment,³⁶ an action research study which generated a range of interventions including education and memory aids,²⁵ general practice networks with specialist support and financial incentives,²⁸ and a patient-held scorecard comparing the patient's own care against care quality indicators.²⁹ Secondary care interventions included education for HCPs,³¹ education for HCPs plus a discharge bundle,²⁷ and quality monitoring through a clinical register.³² Studies measuring uptake included a group opt-in session for patients prior to PR assessment,²⁶ a patient-held manual summarizing evidence on COPD treatments with questions to ask the physician,³⁴ individualized care planning supported by partnership working between general practitioners (GPs) and nurses,³⁴ and the action research study by Foster et al.²⁵

Referral was reported at the level of individual patients,²⁴ practice/department,^{25,29,36} and system level or GP network.^{28–33} Uptake was reported at individual patient levels.^{26,34,35}

Table 1 illustrates the range of characteristics of the studies. Primary care was the most common setting. Most interventions targeted clinicians. Patients were targeted in two studies measuring referral^{27,29} and three measuring uptake.^{26,34,35} Two interventions were at the level of healthcare systems, both measuring referral.^{28,32} Education and learning support were the most common features of interventions that targeted clinicians.^{25,27,30,31,33,36} Regarding design, three out of four

studies measuring uptake had a comparison group design^{26,34,35} compared to three out of 10 measuring referral.^{27–29} All studies of interventions that included elements aimed at patients had a comparison group design.^{26,27,29,34,35}

Outcomes

Referral to PR was the main outcome in eight out of 10 studies^{24,25,27–29,31,32,36} and uptake was the main outcome in three out of four studies.^{25,26,34} There was limited detail about procedures for data collection. Most referral outcomes were measured by audits of patient records.^{25,28–33,36} Graves et al,²⁶ Harris et al,³⁴ and Zwar et al³⁵ measured uptake for individual patients though terms such as “enrollment”³⁴ and “attendance”²⁵ were not defined. Foster et al²⁵ asked patients about their decision to attend PR in a survey.

Conflicts of interest

Potential conflicts of interest were noted in four studies where the authors developed and owned the computer software being assessed²⁴ and where consultants from funding organizations were involved in intervention delivery and quality control.^{30,31,33}

Assessment of methodological quality of included studies

All studies had areas of high risk of bias. In the RCT by Zwar et al,³⁵ this related to the unavoidable lack of blinding of participants (Table 2). The risk of attrition bias was unclear. Furthermore, 52 out of 234 patients allocated to the intervention group did not receive the intervention. No reasons were given for this and the risk of bias is unclear in this regard (Other bias in Table 2). All remaining studies were considered to have a high risk of bias due to a critical risk of confounding that was associated with the study designs (Table 3). The systematic review by Jones et al³⁷ was of high methodological quality (Table 4).

Study findings

Due to study heterogeneity, we considered it inappropriate to summarize results using a meta-analysis. The reported outcomes can only be understood in the context of each study

and are not readily comparable across studies. Furthermore, when considering the study outcomes in light of the various characteristics shown in Table 5 there were no discernible patterns to link study characteristics and outcomes.

Referral to PR

Four studies reported statistically significant increases in PR referral. In primary care, Roberts et al²⁹ reported an increase for the intervention group following use of a patient-held quality scorecard, which was 6.1% ($P=0.03$) greater than that for the control group. Following a collaborative model of education and change implementation, mean referral to PR across 16 general practices increased by 5% (from 7% to 12%) ($P=0.048$),³⁶ and a 3.5% increase in referrals (from 16.7% to 20.2%) ($P<0.01$) followed an education program in primary care.³⁰ Tøttenborg et al³² reported a 36% increase in referrals (from 55% to 91%) (relative risk 2.78, 95% CI, 2.65; 2.90) across hospital outpatient departments during mandatory monitoring of quality indicators.

Positive but statistically nonsignificant results followed an educational program in primary care³³ and an education program across outpatient departments.³¹ Two studies reported increases based on descriptive data following use of a COPD discharge care bundle in a hospital ward²⁷ and a quality improvement intervention across primary care.²⁸ A computer-guided COPD review²⁴ and an action research study²⁵ did not collect comparative data.

Uptake of PR

Two studies reported statistically significant increases in uptake. Harris et al³⁴ evaluated a patient manual summarizing evidence on COPD treatments and reported an increase of 18% in PR enrollment among participants in the most socioeconomically disadvantaged stratum compared to no increase in the matched control group ($P=0.05$). Zwar et al³⁵ reported a 21.5% difference in the number of intervention group patients attending PR ($P=0.002$) compared to controls where the intervention group had received an individualized care plan supported by partnership working between nurses and GPs.

Table 2 Risk of bias assessment (Cochrane RCT) for randomized studies

Study	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Incomplete outcome data (attrition bias)	Blinding of outcome assessment (detection bias)	Selective reporting (reporting bias)	Other bias
Zwar et al ³⁵	Low	Low	High	Unclear	Low	Low	Unclear

Abbreviation: RCT, randomized controlled trial.

Table 3 Cochrane Risk of Bias Assessment Tool for nonrandomized studies of interventions (ACROBAT-NRSI)

Study	Bias due to confounding	Bias in selection of participants into the study	Bias in measurement of interventions	Bias due to departures from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported results
Angus et al ²⁴	Critical	Serious	Serious	Serious	Serious	Moderate	Moderate
Deprez et al ³⁶	Critical	Serious	Low	No information	Moderate	Moderate	Low
Foster et al ²⁵	Critical	Serious	Serious	Serious	Serious	Moderate	Moderate
Graves et al ²⁶	Critical	Low	Low	Serious	Low	Moderate	Moderate
Harris et al ³⁴	Critical	Serious	Low	Moderate	Moderate	Moderate	Moderate
Hopkinson et al ²⁷	Critical	Serious	Low	Serious	Low	Moderate	Moderate
Hull et al ²⁸	Critical	Moderate	Serious	Moderate	Low	Moderate	Moderate
Lange et al ³⁰	Critical	Serious	Low	Moderate	Moderate	Moderate	Moderate
Lange et al ³¹	Critical	Serious	Low	Moderate	Moderate	Moderate	Moderate
Roberts et al ²⁹	Critical	Serious	Low	Moderate	Moderate	Moderate	Moderate
Tøttenborg et al ³²	Critical	Low	Low	Moderate	Moderate	Moderate	Moderate
Ulrik et al ³³	Critical	Serious	Low	Moderate	Moderate	Moderate	Moderate

One study did not collect comparative data²⁵ and a statistically significant decrease in uptake followed a group opt-in patient information session compared to usual care (58.7% vs 75%, $P < 0.001$).²⁶

Discussion

Our carefully conducted systematic review identified a heterogeneous group of studies. Most reported some positive results but only six out of 14 demonstrated statistically significant improvements. Statistically significant increases in referral followed educational sessions for clinicians in primary care,³⁰ collaborative learning sessions for HCPs,³⁶ use of a patient-held COPD care scorecard in primary care,²⁹ and continuous monitoring of care quality indicators in hospital settings.³² Statistically significant increases in uptake followed use of a patient-held summary of COPD research

evidence in secondary care³⁴ and a nurse/GP partnership model of care.³⁵ Significantly fewer patients who attended a group opt-in information session subsequently attended PR assessment compared to patients for whom no opt-in session was offered, although subsequent completion rates improved among those who attended.²⁶ Only three studies focused specifically on referral²⁵ or uptake^{26,37} and we are unable to accurately evaluate the impact of a targeted approach to increase referral or uptake to PR.

The potential for generalizability from the studies is limited by four factors. Firstly, most study designs carried areas of high risk of bias. Secondly, some interventions were not well defined. For example, in two studies the terms “enrollment”³⁴ and “attendance”³⁵ were not explained and it was not possible to distinguish between attendance at pre-course assessment and the first PR class, which are separate stages in the PR pathway. Thirdly, there was limited reporting of patient and clinician populations which may be potentially nonrepresentative. Fourthly, the studies were conducted in high income countries and there were no interventions in low-to-middle income countries where over 90% of deaths globally from COPD occur.²

Two of the studies performed spirometry and confirmed a COPD diagnosis in 57.8%³⁵ and 81%²⁴ of patients. Jones et al³⁷ included only participants with a diagnosis of COPD confirmed by spirometry in their systematic review and identified no studies of uptake. Evidence shows that patients on COPD registers do not always have a confirmed diagnosis with proportions varying from 73%³⁸ to 90%.³⁹ The question remains as to whether this is problematic for drawing conclusions from intervention studies. If studies do not confirm a COPD diagnosis it is possible that the COPD population

Table 4 Quality assessment of Jones et al³⁷ against the AMSTAR (A MeaSurement Tool to Assess systematic Reviews) measurement tool”

Was an “a priori” design provided?	Yes
Was there duplicate study selection and data extraction?	Yes
Was a comprehensive literature search performed?	Yes
Was the status of publication (ie, gray literature) used as an inclusion criterion?	Yes
Was a list of studies (included and excluded) provided?	Yes
Were the characteristics of the included studies provided?	Yes
Was the scientific quality of the included studies assessed and documented?	Yes
Was the scientific quality of the included studies used appropriately in formulating conclusions?	Yes
Were the methods used to combine the findings of studies appropriate?	N/a
Was the likelihood of publication bias assessed?	Yes
Was the conflict of interest stated?	Yes

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Table 5 Summary of intervention characteristics

	Clinician-focused intervention elements										Patient-focused intervention elements		
	Comparator group	Study of wider COPD care	System level intervention	Primary care setting	Guideline support tools and methods	Decision support	Protocol guidance	Education and learning	Expert support	Clinician collaborative working	Individual financial incentive	Patient information	Personal support for patients
Angus et al ²⁴ (R)		◆		◆	◆	◆							
Deprez et al ³⁶ (R)*		◆		◆				◆	◆				
Hull et al ²⁸ (R)	◆	◆	◆	◆	◆		◆						
Lange et al ³⁰ (R)*		◆		◆									
Lange et al ³¹ (R)		◆		◆									
Hopkinson et al ²⁷ (R)		◆		◆	◆		◆				◆		◆
Roberts et al ²⁹ (R)*	◆	◆		◆							◆		◆
Tøttenborg et al ³² (R)*		◆	◆										
Ulrik et al ³³ (R)		◆		◆									
Foster et al ²⁵ (R) (U)		◆		◆	◆	◆							
Graves et al ²⁶ (U)	◆											◆	
Harris et al ³⁴ (U)*	◆	◆										◆	
Zwar et al ³⁵ (U)*	◆	◆		◆									◆

Notes: *Study reported statistically significant increase in referral or uptake ($P < 0.05$). R, study including referral measure; U, study including uptake measure.

is overestimated and that effect sizes are therefore over or underestimated. However, Zwar et al³⁵ provided a pragmatic argument for including patients with a clinical diagnosis of COPD that did not require confirmation by spirometry, indicating that this reflects practice in primary care, where diagnosis is often made and treatment initiated on clinical grounds.

Strengths and limitations

Strengths of this review are the use of recognized systematic methods and a search without language or date restriction, which reduced the risk of bias in conducting the review. A limitation is that it was not possible to verify the content of the reported PR programs to ensure that they matched the definition adopted for this review.¹⁸ Due to heterogeneity among the studies and poor quality assessments relative to evidence-based medicine quality criteria it is not possible to provide clear evidence-based recommendations for practice. The scope of this review, inclusive of different study designs, provides a novel and broad insight into the extent and type of evidence in the field and can provide a useful stimulus for intervention developers and researchers.

Comparison with other studies

Our review supplements that of Jones et al³⁷ by including a broad range of study designs and not requiring spirometry-confirmed diagnosis. A Cochrane review of referral, uptake, and adherence to PR has been registered recently and will add knowledge to this field.⁴⁰

Whilst we cannot draw clear conclusions from our review about the efficacy of the interventions to increase referral and uptake to PR, these studies do address some of the known barriers and facilitators to referral and uptake.

Referral is impacted by accessibility of PR programs, HCPs' knowledge of who and how to refer, the administrative burden of making a referral, successful previous referral of other patients, the influence of the referring doctor (either positive or negative), and by patients knowing what PR involves and how it will help their health.⁴¹ Interventions in this review supported clinicians through education and guidance to improve their knowledge of referral and PR,^{24,25,27,28,30,31,33,36} use of reminders and prompts,^{24,25} and the inclusion of PR referral in a discharge care bundle.²⁷ Education and learning support were the most common features of interventions directly targeting clinicians though it is unclear whether the education programs addressed the nature of the conversation between the HCP and the patient about PR referral or supported clinician skills in this regard. None of the

interventions addressed accessibility of PR programs and it can only be assumed that sufficient capacity was available.

Barriers to patient uptake include transport and location,^{42–44} inconvenient timing,^{42,44} disruption to routine/other priorities,^{41–43} influence of the referring doctor,⁴² lack of explanation of benefits,⁴⁴ lack of perceived benefit,^{41,42,44} believing oneself to be too disabled⁴⁴ or that one's conditions is not serious enough,^{41,44} negative past experience with PR or exercise,⁴⁴ and burden of COPD and other health conditions.⁴¹ Reasons for attending include a trusted, enthusiastic doctor who explained the benefits, perceived increased severity of the condition, perceiving that PR would help increase control and independence and improve health, and perceived social benefits.⁴⁴ Positive reinforcement of PR by HCPs during the referral process is important.⁴¹ The study by Zwar et al,³⁵ in which attendance at PR increased, provided individualized care plans and nurse support in patients' homes, a model which could accommodate a personalized discussion over time about the benefits of PR to the patient and presumably establish a trusting relationship. However, Zwar et al³⁵ noted that although more patients in the intervention group attended PR this was still less than a third of the group. Interestingly, the information session provided in the study by Graves et al,²⁶ which informed patients about the benefits of PR, was associated with reduced attendance at assessment but did improve attendance of those who started PR. Whilst perhaps not providing motivational support for patients who were unsure about attending, it could nevertheless improve service efficiency and highlights the importance of considering the whole PR pathway. The manual of COPD evidence-based treatments provided by Harris et al³⁴ was helpful for more socioeconomically disadvantaged patients and may have facilitated a constructive clinician–patient interaction for this group. The authors also noted that more patients in this group reported actually using the manual, which would clearly influence any impact assessment. This highlights the need for good understanding of *how* interventions work as well as whether they work. Practical factors such as transport, travel, and timing were not addressed by the interventions.

Strategies to improve referral and uptake have also been studied in cardiac rehabilitation (CR) with some success. A systematic review of interventions to promote uptake and adherence in CR reported improvements in eight out of 10 studies of uptake but, as in our review, the authors could not make clear practice recommendations due to heterogeneity and risk of bias in the studies.⁴⁵ Another systematic review of interventions around referral and uptake to CR found 11

studies of referral and 13 studies of enrollment in the US, Canada, and the UK.⁴⁶ The highest rates of referral (up to 85%) were found in studies that implemented automatic referral orders (eg, from healthcare records or data) whereas the highest rates of enrollment (up to 86%) were achieved with a combination of automatic and liaison methods, including discussion with an HCP. Enrollment and uptake to CR can also be improved by referral and structured follow-up by nurses or therapists and early outpatient education.^{45,47,48} Whether findings from CR might be translated to PR is worthy of further research. The rehabilitation pathway differs for CR because referrals typically occur at the time of hospitalization for an acute event or procedure, whereas in the UK, for example, most PR referrals occur in primary care at the time of stable disease.¹³

Implications for practice and research

There is a call to provide recommendations to increase the delivery of PR worldwide to validate novel techniques for doing so, and to enhance evidence-based policy.¹² While more evidence is needed to establish the efficacy and effectiveness of different approaches, the studies reviewed here provide a useful platform for further work. The variety of interventions they represent, from one-off information sessions to system-wide improvement projects, reflects the complex nature of COPD care management and the potential value of a range of evidence building approaches.

Firstly, there is an urgent need for high quality study designs to determine the efficacy, effectiveness, and causal mechanisms of interventions. There is a lack of evidence from RCTs and we identified only one ongoing RCT to test a method not previously evaluated: a video to increase PR uptake following hospitalized exacerbations of COPD.⁴⁹ Whilst RCTs are the gold standard for establishing a generalizable evidence base, they may not be the only relevant evaluation design in this field. There is a need to recognize contextual factors and the diversity of PR delivery and settings across the world.⁵⁰ In this regard, quality improvement approaches are well suited to learn what works in a local context, particularly where rapid testing of novel interventions is needed. In contrast to research methods which aim to generate new knowledge, the aim of these approaches is to achieve positive and practical change in an identified service through focus on a well-defined problem.⁵¹ These methods are accessible to service providers in “real-world” settings. Two studies reviewed here, Hull et al²⁸ and Hopkinson et al,²⁷ utilized quality improvement methods. In addition, for the researcher, realist approaches that seek to identify what

works, in which circumstances, and for whom could help to recognize and accommodate contextual complexity within the evaluation design and provide more transferable learning about the impact of contextual factors.⁵² Such methods have value in real-world settings where multiple variables cannot be controlled.

Secondly, there is a need to improve reporting of study populations as a factor to enhance external validity. Results from Harris et al³⁴ suggest differential effects across subgroups of patients and this is worthy of further investigation. None of the studies in this review reported the ethnicity of patients. In an area of East London in the UK members of some Black and minority ethnic populations have lower rates of referral to PR compared to White patients⁵³ and there is a need to understand more about how to support PR access in ethnically diverse communities. There may also be specific issues in resource poor countries⁵⁴ which are not represented among the studies in this review.

Thirdly, in their study of a group opt-in session prior to assessment, Graves et al²⁶ reported that, despite no impact on uptake, fewer intervention patients who started PR dropped out for reasons other than illness and significantly more graduated. This indicates the importance of considering the whole PR pathway. Following the patient through the entirety of their PR journey will lead to a greater understanding of how to improve service efficiency. Only two studies in this review intervened at the system level^{28,32} and there is scope for more research in this area. More studies measured referral than uptake and more patients were included in referral studies than in uptake studies, suggesting a differential focus on these two stages.

Fourthly, interventions may benefit from theory-based design. Cox et al⁴¹ used the Theoretical Domains Framework to analyze factors affecting referral and participation in PR and we have highlighted above how some of the reviewed studies addressed these factors, although it was not possible to assess this accurately without access to more detailed intervention descriptions. However, we believe that the work by Cox et al⁴¹ provides a useful theoretical framework for intervention designers. Interventions could focus on specific constructs that have been shown to have relevance and then assess the impact on those constructs to generate a theoretically informed understanding of what works and why.

Conclusion

This review demonstrates the broad range of approaches aimed at increasing referral and uptake to PR across primary

and secondary care. Some positive results have been demonstrated but there is limited generalizable evidence because interventions and methods are heterogeneous and descriptions of populations are limited. Further theory-based testing of promising interventions using robust methods in various populations and settings is required to draw clear conclusions about how to optimize access to PR across a range of settings.

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Author contributions

JF, FE, IW, and CD conceived and designed the review. IK provided expert support and conducted the literature search. FE and IW reviewed the titles and abstracts, selected the papers, and extracted and analyzed the data. All authors were involved in drafting and revision of the manuscript for important intellectual content and approved the final version to be published. All authors agree to be accountable for aspects of the work. JF is the guarantor of the paper.

Disclosure

The authors report no conflicts of interest in this work.

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Supplementary material

MEDLINE search strategy

- 1 (((pulmonary rehabilitation.ti,ab.) or (((emphysema or copd or chronic obstructive pulmonary disease or chronic bronchitis or chronic asthma).ti,ab. or exp Pulmonary Disease, Chronic Obstructive/ or exp Bronchitis, Chronic/ or exp Asthma/ or exp Emphysema/) and ((exercis* or rehab* or physiotherap* or “physical therap*”).ti,ab. or exp Exercise Therapy/ or exp Exercise/ or exp rehabilitation/ or exp Physical Therapy Modalities/))) and ((refer* 1 or referring or referred or referral* or assess*).ti,ab. Or exp “Referral and Consultation”/) And ((rate* or number* or audit* or percentage or barrier* or facilitat* or frequen* or infrequent* or rare* or common* or uncommon or standard* or influenc* or reluctant* or barrier* or obstacle or (meet* adj3 criter*)),ti,ab. Or exp practice patterns, physicians/ or exp guideline adherence or exp data collection/))
- 2 ((pulmonary rehabilitation.ti,ab.) or (((emphysema or copd or chronic obstructive pulmonary disease or chronic bronchitis).ti,ab. or exp Pulmonary Disease, Chronic Obstructive/ or exp Bronchitis, Chronic/ or exp Emphysema/) and ((exercis* or rehab* or physiotherap* or “physical therap*”).ti,ab. or exp Exercise Therapy/ or exp Exercise/ or exp rehabilitation/ or exp Physical Therapy Modalities/))) and ((uptake or up-take or (up adj3 take*) or non-attend* or nonattend* or attend* or engag* or (treat* adj3 refus*) or decline* or concordan* or complian* or barrier* or obstacle* or adher* or accept*).ti,ab. Or exp treatment refusal/ or exp patient compliance/ or exp patient acceptance of healthcare/)
- 3 1 or 2
- 4 (((Meta-Analysis as Topic/ or Meta-Analysis/ or exp Review Literature as Topic/) or ((meta analy\$ or (metaanaly\$) or ((systematic adj (review\$1 or overview\$1))))).tw. or (Cochrane or embase or psychlit or psychlit or psychinfo or psycinfo or cinahl or cinhal or (science citation index) or bids or cancerlit or reference list\$ or bibliograph\$ or hand-search\$ or (relevant journals) or (manual search\$)).ab. or ((selection criteria or data extraction).ab. and review/)) NOT (Comment/ or Letter/ or Editorial/)) Or (((Randomized Controlled Trials as Topic/ or randomized controlled trial/ or Random Allocation/ or Double Blind Method/ or Single Blind Method/ or clinical trial/ or exp Clinical Trials as topic/ or PLACEBOS/) or ((clinical trial, phase i) or (clinical trial, phase ii) or (clinical trial, phase iii) or (clinical trial, phase iv) or (controlled clinical trial) or (randomized controlled trial) or (multicenter study) or (clinical trial)).pt or ((clinical adj trial\$) or ((singl\$ or doubl\$ or treb\$ or tripl\$) adj (blind\$3 or mask\$3)) or (placebo\$) or (randomly allocated) or (allocated adj2 random\$)).tw) NOT (case report.tw or letter/ or historical article/)) or (quantitative or (mix* adj method*)).mp.
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