

CLINICAL PRACTICE GUIDELINES

Australian and New Zealand Pulmonary Rehabilitation Guidelines

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ABSTRACT

Background and objective: The aim of the Pulmonary Rehabilitation Guidelines (Guidelines) is to provide evidence-based recommendations for the practice of pulmonary rehabilitation (PR) specific to Australian and New Zealand healthcare contexts.

Methods: The Guideline methodology adhered to the Appraisal of Guidelines for Research and Evaluation (AGREE) II criteria. Nine key questions were constructed in accordance with the PICO (Population, Intervention, Comparator, Outcome) format and reviewed by a COPD consumer group for appropriateness. Systematic reviews were undertaken for each question and recommendations made with the strength of each recommendation based on the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) criteria. The Guidelines were externally reviewed by a panel of experts.

Results: The Guideline panel recommended that patients with mild-to-severe COPD should undergo PR to improve quality of life and exercise capacity and to reduce hospital admissions; that PR could be offered in hospital gyms, community centres or at home and could be provided irrespective of the availability of a structured education programme; that PR should be offered to patients with bronchiectasis, interstitial lung disease

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and pulmonary hypertension, with the latter in specialized centres. The Guideline panel was unable to make recommendations relating to PR programme length beyond 8 weeks, the optimal model for maintenance after PR, or the use of supplemental oxygen during exercise training. The strength of each recommendation and the quality of the evidence are presented in the summary.

Conclusion: The Australian and New Zealand Pulmonary Rehabilitation Guidelines present an evaluation of the evidence for nine PICO questions, with recommendations to provide guidance for clinicians and policymakers.

Key words: bronchiectasis, chronic obstructive pulmonary disease, exercise and pulmonary rehabilitation, guidelines, interstitial lung disease.

Abbreviations: 6MWT, 6-min walk test; AGREE, Appraisal of Guidelines for Research and Evaluation; CINAHL, cumulative index to nursing and allied health literature; COPD, chronic obstructive pulmonary disease; CRQ, Chronic Respiratory Disease Questionnaire; EID, exercise-induced oxygen desaturation; EMBASE, Excerpta Medica dataBASE; FEV₁, forced expiratory volume in 1 s; GRADE, Grading of Recommendations, Assessment, Development and Evaluation; HCU, healthcare utilization; HRQoL, health-related quality of life; ILD, interstitial lung disease; IPF, idiopathic pulmonary fibrosis; ISWT, incremental shuttle walk test; LOS, length of stay; MD, mean difference; MID, minimal important difference; mMRC, modified MRC; MRC, Medical Research Council; PAH, pulmonary arterial hypertension; PH, pulmonary hypertension; PICO, Population, Intervention, Comparator, Outcome; PR, pulmonary rehabilitation; QALY, quality-adjusted life year; RCT, randomized controlled trial; SF-36v2, 36-Item Short Form Health Survey version 2; SGRQ, St George's Respiratory Questionnaire; SMD, standardized MD; TSANZ, Thoracic Society of Australia and New Zealand.

SUMMARY OF RECOMMENDATIONS

The Guideline panel recommends that:

1.
 - a. Patients with COPD should undergo pulmonary rehabilitation (PR; strong recommendation, moderate quality evidence).
 - b. PR is provided after an exacerbation of COPD, within 2 weeks of hospital discharge (weak recommendation, moderate quality evidence).
2. Patients with moderate-to-severe COPD (stable or following discharge from hospital for an exacerbation of COPD) should undergo PR to decrease hospitalizations for exacerbations (strong recommendation, moderate-to-low quality evidence).
3.
 - a. Home-based PR be offered to patients with COPD as an alternative to usual care (weak recommendation, moderate-to-low quality evidence).
 - b. Home-based PR, including regular contact to facilitate exercise participation and progression, be offered to patients with COPD as an alternative to hospital-based PR (weak recommendation, moderate-to-low quality evidence).
 - c. Community-based PR, of equivalent frequency and intensity as hospital-based programmes, be offered to patients with COPD as an alternative

to usual care (weak recommendation, moderate quality evidence).

4. Patients with mild COPD (based on symptoms) undergo PR (weak recommendation, moderate-to-low quality evidence).
5. The panel is unable to make a recommendation due to lack of evidence evaluating whether programmes of longer duration are more effective than the standard 8-week programmes.
6.
 - a. More research is needed to determine the optimal model of maintenance exercise programmes ('in-research' recommendation).
 - b. Supervised maintenance programmes of monthly, or less frequently, are insufficient to maintain the gains of PR and should not be offered (weak recommendation, low quality evidence).
7. PR be offered to all patients with COPD, irrespective of the availability of a structured multidisciplinary group education programme (weak recommendation, moderate-to-low quality evidence).
8. Further research of oxygen supplementation during training is required in patients with COPD who have exercise-induced desaturation to reduce the uncertainty around its lack of effect to date ('in-research' recommendation).
9.
 - a. Patients with bronchiectasis undergo PR (weak recommendation, moderate quality evidence).
 - b. Patients with interstitial lung disease undergo PR (weak recommendation, low quality evidence).
 - c. Patients with pulmonary hypertension undergo PR (weak recommendation, low quality evidence).

INTRODUCTION

COPD affects 1.5 million Australians, including 1 in 13 individuals over 40 years of age,¹ with major consequences for participation in work and societal contexts.² The cost of COPD in Australia was estimated at \$8.8 billion in 2008/2009 (most recent figures), with \$929 million in direct health system expenditure, largely due to hospital admissions.³ Indigenous Australians (Aboriginal and Torres Strait Islander Peoples) bear an unequal burden of disease in relation to COPD. Compared with non-Indigenous Australians, the prevalence of COPD is 2.5 times higher, with the death rate being three times higher and the hospitalization rate five times higher in Indigenous Australians.⁴ In New Zealand, COPD affects approximately 200 000 of the population with 14% of adults over 40 years of age having COPD.⁵ The cost of COPD in New Zealand is estimated as \$NZ 5.6 billion with \$NZ 484 million in direct health system expenditure.⁵ Indigenous New Zealanders (Māori) have a higher prevalence of COPD, a 4.4 times higher rate of hospital admissions and 2.2 times more deaths associated with the condition compared with non-Māori.^{5,6}

Pulmonary rehabilitation (PR) is considered a key component of the management of patients with COPD⁷ and has been shown to reduce symptoms of breathlessness and fatigue, improve health-related quality of life (HRQoL)⁸ and reduce hospital

readmissions after an exacerbation.⁹ However, uptake of PR is estimated to be only 5–10% of those patients with moderate-to-severe COPD who could benefit,^{10,11} related to lack of available programmes, poor referral rates and poor patient uptake of existing programmes. While international societies have published a number of documents to guide practice in PR,^{12–15} none has specifically addressed the provision of PR for patients with COPD in the healthcare contexts of Australia or New Zealand. In addition, a growing number of patients with other chronic lung conditions such as bronchiectasis, interstitial lung disease (ILD) and pulmonary hypertension (PH) are referred to Australian and New Zealand PR programmes. Evidence for the benefits of PR in these conditions also needs to be evaluated.

SCOPE AND PURPOSE

These Australian and New Zealand Pulmonary Rehabilitation Guidelines are primarily written for health practitioners providing PR and for the much wider group of health professionals who refer patients to PR in Australia or New Zealand. The patient populations to whom the Guidelines apply are those with chronic respiratory disease, primarily COPD, with some evidence presented for patients with bronchiectasis, ILD and PH. PR for patients with cystic fibrosis or lung cancer was considered outside the scope of the Guidelines due to the smaller body of evidence pertaining to structured PR for these groups.

METHODOLOGY

Members of the Australian Pulmonary Rehabilitation Network of Lung Foundation Australia and members of the Thoracic Society of Australia and New Zealand (TSANZ) were invited to submit an expression of interest to be considered for the Guideline panel. Participants were required to demonstrate expertise in PR and ability to review literature. In total, 28 healthcare professionals were appointed, with 11 of these forming the lead panel members. The Guideline panel had the following representation: 22 physiotherapists, 2 respiratory physicians, 1 health psychologist, 2 nurses and 1 exercise physiologist. Two members of the lead writing group (S.C.J. and A.E.H.) had specific expertise in guideline methodology.

The proposal for writing the Australian and New Zealand Pulmonary Rehabilitation Guidelines was endorsed by the Clinical Care and Resources Subcommittee of the TSANZ and the process was supported and coordinated by Lung Foundation Australia. The Guideline methodology adhered to the Appraisal of Guidelines for Research and Evaluation (AGREE) II criteria.¹⁶

The research questions addressed in the Guidelines were based on the Guideline panel's considered view of the most important questions related to PR in Australia and New Zealand, with the intention of limiting the number of questions to <10. The questions were constructed in accordance with the PICO

(Population, Intervention, Comparator, Outcome) format. There were nine main questions (Table 1), with PICO questions 1–8 relating specifically to patients with COPD and PICO question 9 addressing PR for patients with bronchiectasis, ILD and PH. The questions were reviewed by a COPD consumer group (Australian COPD and Patient Advocate Group) which agreed that the questions were appropriate.

Systematic literature searches

The definition of PR agreed by the Guideline panel, to set the parameters for the minimum duration of PR for the literature search, was that used in the most recent Cochrane review: '*Any in-patient, out-patient, community-based or home-based rehabilitation programme of at least four weeks' duration that included exercise therapy with or without any form of education and/or psychological support delivered to patients with exercise limitation attributable to COPD*'.⁸

Systematic reviews were undertaken for each PICO question using standard methodology,¹⁷ except for questions 1 and 9. As the updated Cochrane review of PR had recently been published,⁸ the data from that review were used as the basis to answer question 1a and the data from the updated Cochrane review on hospital readmissions⁹ were used as a basis to answer question 1b. Recently published systematic reviews of PR for bronchiectasis,¹⁸ ILD¹⁹ and PH²⁰ were used to underpin question 9. Literature searches for all other questions were undertaken with the assistance of university librarians. The databases searched were Medline, PreMedline, EMBASE, OVID, CINAHL, Cochrane and Scopus. The search terms for each question are presented in Table S1 (Supplementary Information). Tables of the studies reviewed for each question are presented in Table S2 (Supplementary Information). Studies were selected for inclusion in the review if they were randomized controlled trials (RCTs) or systematic reviews that directly addressed the questions. To be included, studies had to report at least one of the pre-specified outcomes of interest, such as exercise capacity, HRQoL, healthcare utilization (HCU), anxiety and depression or mortality.

Appraisal of literature

For each question, at least two members of the Guideline panel read the title and/or abstract of each article from the literature search and decided whether to include the article for full review. At least two reviewers for each question independently extracted data from the same studies. Additional information from authors was requested if necessary. Risk of bias (high, low or unclear risk) for each included study was evaluated based on the following domains: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting or any other bias. Where relevant, a meta-analysis was performed to quantify effect size and certainty (Fig. S1, Supplementary Information). Data and meta-analyses from relevant, recent systematic reviews were used when available. The quality of the body of evidence for

Table 1 PICO questions

PICO question	Population	Intervention	Comparator	Outcome
1. Is PR effective compared with usual care in patients with COPD?	1a. Stable COPD	PR	Usual care	HRQoL (including dyspnoea and fatigue) Exercise capacity Mortality Anxiety and depression
	1b. Following an exacerbation of COPD	PR (non-inpatient) within 2–4 weeks of hospital discharge	Usual care	HRQoL (including dyspnoea and fatigue) Exercise capacity Hospital readmissions Mortality
2. Does PR affect HCU?	Stable COPD or following an exacerbation of COPD	PR	Usual care	Hospital admissions Length of stay Total bed days Exacerbations Emergency department presentations General practitioner visits
3. Is a home-based or community-based PR programme as effective as a hospital-based PR programme?				
3a. Is home-based PR more effective than usual care for patients with COPD?	Stable COPD or following an exacerbation of COPD	Home-based PR	Usual care	HRQoL (including dyspnoea and fatigue) Exercise capacity Mortality
3b. Is home-based PR as effective as hospital-based PR for patients with COPD?	Stable COPD or following an exacerbation of COPD	Home-based PR	Hospital-based PR	HCU Anxiety and depression
3c. Is community-based PR more effective than usual care for patients with COPD?	Stable COPD or following an exacerbation of COPD	Community-based PR	Usual care	HRQoL (including dyspnoea and fatigue) Exercise capacity Mortality Anxiety and depression HCU
4. In patients with mild disease severity, is PR more effective than usual care?	Stable COPD	PR	Usual care	HRQoL (including dyspnoea and fatigue) Exercise capacity Mortality Anxiety and depression HCU
5. Are programmes of longer duration more effective than the standard 8-week programmes?	Stable COPD or following an exacerbation of COPD	PR of longer than 8 weeks	PR of 8 weeks	HRQoL (including dyspnoea and fatigue) Exercise capacity Mortality Anxiety and depression HCU

Table 1 Continued

PICO question	Population	Intervention	Comparator	Outcome
6. Does ongoing supervised exercise at a lower frequency than the initial PR programme, maintain exercise capacity and quality of life to 12 months?	Stable COPD	Maintenance exercise programme	Usual care	HRQoL (including dyspnoea and fatigue) Exercise capacity Mortality Anxiety and depression HCU
7. Does a structured education programme enhance the benefits of PR?	Stable COPD or following an exacerbation of COPD	PR with a structured education programme	PR without a structured education programme	HRQoL (including dyspnoea and fatigue) Exercise capacity Mortality Anxiety and depression HCU Disease knowledge Self-efficacy
8. Do patients who experience oxygen desaturation during exercise have greater improvements if oxygen supplementation is provided during training?	COPD with exercise-induced oxygen desaturation	PR with oxygen supplementation	PR without oxygen supplementation	HRQoL (including dyspnoea and fatigue) Exercise capacity Mortality Anxiety and depression HCU
9. Is PR effective in chronic respiratory diseases other than COPD?				
9a. Is PR effective in patients with bronchiectasis?	Bronchiectasis	PR	Usual care	HRQoL (including dyspnoea and fatigue) Exercise capacity HCU Anxiety and depression Mortality
9b. Is PR effective in patients with ILD?	ILD	PR	Usual care	HRQoL (including dyspnoea and fatigue) Exercise capacity HCU Anxiety and depression Mortality
9c. Is PR effective in patients with PH?	PH	PR	Usual care	HRQoL (including dyspnoea and fatigue) Exercise capacity HCU Anxiety and depression Mortality

HCU, healthcare utilization; HRQoL, health-related quality of life; ILD, interstitial lung disease; PICO, Population, Intervention, Comparator, Outcome; PH, pulmonary hypertension; PR, pulmonary rehabilitation.

each recommendation was evaluated using the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) system²¹ which considered within-study risk of bias, directness of evidence, heterogeneity, precision of effect estimates and risk of publication bias (GRADE evidence tables are presented in Table S3 (Supplementary Information)). The strength of each recommendation was formulated based on the GRADE criteria which considered the quality of the evidence and trade-offs between desirable and undesirable outcomes, confidence in effect estimates, patient values and preferences and resource implications.²² In GRADE methodology, 'strong' and 'weak' recommendations are considered as categorical terminology on an underlying continuum, with anchor categories of 'strong against', 'weak against', 'weak for' and 'strong for'.²² The evidence to recommendation tables that detail the items considered when making the decision regarding the strength of the recommendations are presented in Table S4 (Supplementary Information) and these tables should be read in conjunction with each recommendation to provide the reader with the reasoning behind the decision regarding the strength of each recommendation. A 'strong' recommendation means that *all or almost all* informed patients would choose the recommended intervention as described; adherence to this recommendation could be used in clinical practice as a quality criterion or performance indicator. A 'weak' recommendation means that *most* informed patients would choose the recommendation as described; clinicians must help each patient arrive at a management decision consistent with his or her values and preferences.²³ An 'in-research' recommendation means that there is insufficient evidence to recommend the intervention and more research could clarify the effects of the intervention and would be worthwhile.²²

All members of the Guideline panel ($n = 28$) were asked to vote on each recommendation as 'agree', 'disagree' or 'abstain'. The voting results are shown at the end of each of the evidence to recommendation tables in Table S4 (Supplementary Information). After review of the Guidelines by an expert advisory group, minor alterations were made to the text but no major changes were made to the recommendations. The Guidelines were reviewed by the New Zealand Cardiothoracic Physiotherapy Special Interest Group, consumer representatives, the Clinical Care and Resources Sub-Committee, Nursing, COPD, Physiotherapy and OLIV Special Interest Groups of TSANZ. The Australian and New Zealand Pulmonary Rehabilitation Guidelines will be disseminated through key stakeholder groups such as the Lung Foundation Australia (including the Australian Pulmonary Rehabilitation Network), Lung Foundation New Zealand, Thoracic Society of Australia and New Zealand, Australian Physiotherapy Association, Physiotherapy New Zealand, Exercise and Sports Science Association Australia, Sport and Exercise Science New Zealand, Royal Australian College of General Practitioners, Royal New Zealand College of General Practitioners, Australian College of Nursing, New Zealand Nurses Organisation, as well as through clinicians registered to receive the COPD-X

Guidelines, university programmes that provide physiotherapy and exercise physiology programmes. The TSANZ will develop quality standards that will be used to evaluate implementation and impact of the Guidelines. The Australian and New Zealand Pulmonary Rehabilitation Guidelines will be reviewed within 5 years of publication to assess the need for update.

PICO QUESTIONS

Background, Summary of evidence, Recommendation, Justification and implementation

PICO 1: Is PR effective compared with usual care in patients with COPD?

Background: Patients with COPD experience breathlessness, reduced functional capacity, reduced HRQoL and poor psychological well-being. PR, incorporating exercise training and education, is recommended for patients with COPD with a view to improving breathlessness, exercise capacity, HRQoL and psychological well-being.^{12,15} PR is typically commenced when a person with COPD is in a stable phase; however, there is increasing evidence that PR plays an important role following an exacerbation of COPD. In Australia and New Zealand, PR following an exacerbation of COPD is typically commenced in the outpatient setting, whereas in some European centres PR occurs in the inpatient setting. The following recommendations are presented for two categories of patients: stable COPD and following an exacerbation of COPD.

PICO 1a: Stable COPD

Summary of evidence: A Cochrane review that examined the evidence for PR in stable COPD⁸ included 65 RCTs. Outcomes of interest were confined to measures of exercise capacity and HRQoL. For exercise capacity measured by the 6-min walk test (6MWT), PR compared with usual care resulted in a mean difference (MD) of 44 m (95% CI: 33–55) in favour of PR (38 studies, number of participants (n) = 1879). A sensitivity analysis of studies with lower risk of bias yielded a smaller MD in 6MWT for PR compared with usual care (MD: 26 m, 95% CI: 21–32, 20 studies, n = 1188, moderate quality evidence). This MD falls within the range of the minimal important difference (MID) (range: 25–33 m).²⁴ For HRQoL, the effect of PR was larger than the MID for all four domains of the Chronic Respiratory Disease Questionnaire (CRQ) (i.e. Fatigue, Emotional Function, Mastery and Dyspnoea) (MID is 0.5 units per domain)²⁵ and the three components (Symptoms, Impacts and Activity) and Total score of the St George's Respiratory Questionnaire (SGRQ) (MID: –4 points)²⁵ (SGRQ Total score MD: –6.89 units, 95% CI: –9.26 to –4.52, 19 studies, n = 1146, moderate quality evidence). A sensitivity analysis of studies at lower risk of bias yielded a slightly smaller MD for SGRQ Total score, but this still exceeded the MID (MD: –5.15 units, 95% CI: –7.95 to –2.36, seven studies, n = 572, moderate quality evidence due to a high level

of heterogeneity). Importantly, the Cochrane Airways Group has decided to close the Cochrane review of PR, stating that further RCTs comparing PR to conventional care in COPD are no longer warranted as further RCTs will not result in improved quality of evidence or improved precision in the estimate of effect. The Cochrane Airways Group believes that the remaining issues around risk of bias, such as blinding of patients and personnel, cannot be addressed with better study design.²⁶

Recommendation: The Guideline panel recommends that patients with stable COPD should undergo PR (strong recommendation, moderate quality evidence).

Justification and implementation: This recommendation places a high value on moderate quality evidence of short-term (immediately following PR) significant and clinically important effects on valued outcomes of improved exercise capacity and HRQoL.^{27,28}

PICO 1b: Following an exacerbation of COPD

Summary of evidence: A Cochrane review that examined the evidence for PR following exacerbations of COPD⁹ included 17 RCTs examining a range of outcomes related to exercise capacity, HRQoL, subsequent hospitalizations, mortality and adverse events. Of the total 17 trials, five commenced PR within 2 weeks of participants being discharged from hospital for an exacerbation of COPD,^{29–33} similar to COPD management in the Australian and New Zealand healthcare context. Trials that commenced PR during an inpatient stay were excluded. Meta-analyses of these five trials are presented in Figure S1 (Supplementary Information). A large effect on exercise capacity was found with an MD in 6MWT of 56 m (95% CI: 27–85, two studies,^{31,32} $n = 116$, moderate quality evidence), which exceeded the MID.²⁴ A large effect on HRQoL was also found (SGRQ Total score MD: –10.64 units, 95% CI: –15.51 to –5.77, five studies,^{28–32} $n = 248$, moderate quality evidence), which exceeded the MID.²⁵ PR commenced within 2 weeks of hospital discharge tended to reduce repeat hospital admissions (OR: 0.30, 95% CI: 0.07–1.29, four studies,^{28–31} $n = 187$, moderate quality evidence) with no effect on mortality (OR: 0.34, 95% CI: 0.05–2.34, two studies,^{28,31} $n = 101$, low quality evidence). No adverse events were reported in these studies.

Recommendation: The guideline panel recommends that PR is provided after an exacerbation of COPD, within 2 weeks of hospital discharge (weak recommendation, moderate quality evidence).

Justification and implementation: This recommendation places a high value on moderate quality evidence of short-term (immediately following PR) significant and clinically important effects on valued outcomes of improved exercise capacity, HRQoL and reduced hospital readmissions.^{27,28,34}

PICO 2: Does PR affect HCU?

Background: Exacerbations are common in patients with COPD and increase in prevalence with worsening

airflow limitation.³⁵ Hospitalizations for severe exacerbations have major significance as they lead to disease progression, deterioration in HRQoL and increased mortality.^{36–38} Within Australia and New Zealand, consistent with international data, severe exacerbations leading to hospitalization are the primary driver of all COPD-related medical care costs accounting for 50–75% of the direct COPD-associated healthcare costs.^{6,39–41} During 2013–2014, the hospitalization rate for COPD among patients aged 55 years and over was 1008 per 100 000 population in Australia³⁹ and the average cost of one hospital admission for COPD (2011–2012 data) without complications or comorbidities (average length of stay (LOS): 5.0 days) was \$A5500, equivalent to more than 100 general practice consultations.⁴² A majority of patients with COPD have two or more co-morbidities,⁴³ resulting in an estimated doubling or tripling of the cost of care.⁴⁴

Summary of evidence: The search strategy yielded 2546 citations of which 2505 citations were excluded based on title and abstract. A total of 41 full papers were extracted and reviewed. An additional four papers were sourced from PR statements, systematic reviews and clinical practice guidelines. In total, 45 papers underwent full review of which nine RCTs reported the effect of PR on HCU, defined as the reporting of respiratory-related admissions, LOS (i.e. the mean or median LOS for hospital admissions in the follow-up period) or total bed days (i.e. the absolute numbers of days in hospital in the follow-up period) and satisfied the criteria for data extraction.^{29–32,45–49} In five trials,^{45–49} patients had stable COPD and in the remaining four trials^{29–32} patients commenced PR no later than 3 weeks following an exacerbation of COPD requiring hospitalization. PR was delivered in hospital outpatient departments (six trials),^{29,31,32,45,46,48} within the patient's home (two trials)^{30,47} and in one trial, rehabilitation took place within physiotherapy private practices.⁴⁹ The follow-up period for collection of HCU data ranged from 3 months, including the 8-week intervention period,^{29,31} to at least 12 months.^{32,45,46,48,49} Eight RCTs ($n = 712$) evaluated the effect of PR on respiratory-related admissions,^{29–32,45–47,49} four trials ($n = 358$) assessed LOS^{32,45,47,48} and two trials ($n = 241$) reported the effect of PR on total bed days.^{29,49} Two trials^{31,45} ($n = 260$) demonstrated that PR significantly reduced hospital admissions, both in those with stable COPD⁴⁵ and those who commenced PR within 7 days following discharge from hospital for an exacerbation of COPD.³¹

A meta-analysis of the four trials^{29–32} ($n = 194$) (Fig. S1, Supplementary Information) in which PR commenced within 2 weeks of discharge after an exacerbation of COPD showed a trend towards a reduction in readmissions following rehabilitation (OR: 0.30 (95% CI: 0.07–1.29)). Of the four RCTs that assessed the effect of PR on LOS, two reported a significant reduction in the mean LOS in the group receiving rehabilitation (9.4 (SD: 10.2) days vs 18.1 (19.3) days, $P = 0.021$ ⁴⁵ and 5.9 (0.33) days vs 9.3 (4.11) days, $P = 0.035$)⁴⁷ with no effect on LOS demonstrated in the remaining two trials.^{32,48} The two trials^{29,49} that reported the effect of PR on total bed days, one of which was in patients with less severe COPD,⁴⁹ found no difference between the rehabilitation and control groups; however, neither trial

was powered to detect changes in HCU. Quality of the evidence was rated down for indirectness (high proportion of males in some studies) and imprecision (small number of participants and large CIs around the estimates).

Only one of the nine RCTs was carried out in Australia⁴⁷ and none took place in New Zealand. An additional RCT from Australia⁵⁰ (published as abstract only) showed a significant reduction in hospital admissions and LOS following PR compared with a control group. Owing to the lack of relevant RCTs carried out in the local healthcare context, non-RCT evidence from Australia or New Zealand was considered. Six non-RCTs carried out in Australia that compared HCU in the 12 months before and after PR were identified.^{51–56} All reported a reduction in hospitalizations for exacerbations of COPD following PR. One study was a large sample ($n = 267$) trial that showed a significant reduction in admissions in the year after compared with the year before a PR programme that comprised exercise training alone or in combination with a structured disease-specific education programme.⁵¹ A further five observational studies ($n = 975$) of PR delivered in hospital outpatient departments^{52–55} and in non-healthcare facilities within the community⁵⁶ also reported a reduction in hospitalizations in the 12 months following rehabilitation. Because of their uncontrolled nature, regression to the mean cannot be excluded in these studies. Although there is a paucity of data from RCTs carried out in Australia or New Zealand, given the large body of evidence supporting the benefits of PR it is unlikely that any further RCTs with long-term follow-up, such as are needed for evaluating the effect of PR on HCU, will be undertaken in Australia or New Zealand due to the ethical concerns of denying patients PR where this is available.

Recommendation: The guideline panel recommends that patients with moderate-to-severe COPD (stable or following discharge from hospital for an exacerbation of COPD) should undergo PR to decrease hospitalizations for exacerbations (strong recommendation, moderate-to-low quality evidence).

Justification and implementation: This recommendation places a high value on moderate-to-low quality evidence for outcomes that are important to patients. The recommendation is 'strong' since, from a patient's perspective, avoidance of being hospitalized, housebound or confined to bed as a result of an exacerbation has high importance.³⁴

PICO 3: Is a home- or community-based PR programme as effective as a hospital-based PR programme?

Background: Despite strong evidence for the benefits of PR highlighted in PICO 1, the proportion of patients with COPD who participate in PR is low, estimated at no more than 5–10% of patients with moderate-to-severe COPD.^{10,11} Most PR programmes in Australia and New Zealand have been offered in a hospital outpatient setting and access is limited for patients who do not live close to such centres. A common patient-reported barrier to participating in hospital-based

programmes is difficulty with transport to the facility.⁵⁷ PR programmes conducted in home- or community-based settings could help to overcome these barriers and potentially improve access and uptake.

To examine the evidence relating to the effectiveness of home- and community-based PR programmes, three separate comparisons were made:

- Is home-based PR more effective than usual care for patients with COPD?
- Is home-based PR as effective as hospital-based PR for patients with COPD?
- Is community-based PR more effective than usual care for patients with COPD?

We defined home-based PR as programmes where the intervention took place in the participant's home, and community-based rehabilitation as programmes where the intervention took place in a community-based setting (i.e. not a hospital and not at home). As with all the other questions, the definition of PR intervention in the Cochrane review⁸ was used as the criterion for study inclusion with an additional criterion for question 3 that the exercise therapy delivered must include a lower limb endurance training component (i.e. not just 'general exercises'). This was to improve applicability of the Guideline findings to Australian and New Zealand practice, where prescription of lower limb endurance exercise is a core part of the prescribed exercise therapy in PR.^{58,59}

PICO 3a: Is home-based PR more effective than usual care for patients with COPD?

Summary of evidence: Eleven studies were identified that made a direct comparison of home-based PR programmes with usual care control. Three examined home-based programmes that commenced within 4 weeks of a hospital admission for an exacerbation of COPD;^{30,60,61} in the other eight studies the participants were in a stable clinical condition. In five studies, home-based exercise sessions were directly supervised to some degree, ranging from every session³⁰ to once a week^{47,62} or fortnightly.^{63,64} In all 11 studies, participants were assessed in a hospital centre. Compared with usual care, home-based PR in patients with stable COPD resulted in large improvements in HRQoL substantially greater than the MID for all domains of the CRQ and for the SGRQ Impacts and Activity components, with similar improvements in those attending PR following an exacerbation of COPD (reported for CRQ domains of Dyspnoea, Fatigue and Mastery only), based on moderate quality evidence. For example, in stable COPD, the pooled MD between home-based PR and control in CRQ-Dyspnoea was 0.77 units (95% CI: 0.44–1.10, two studies,^{62,65} $n = 77$) and CRQ-Fatigue was 0.86 units (95% CI: 0.40–1.32 units, two studies,^{62,65} $n = 77$). For the 6MWT in stable COPD, the MD in favour of home-based PR was 47 m (95% CI: 24–71, three studies,^{62,63,66} $n = 222$, low quality evidence), exceeding the MID (see Fig. S1 (Supplementary Information) for meta-analyses). Quality of the evidence was downgraded due to risk of bias from lack of assessor blinding, imprecision and indirectness due to high proportions of male participants (>90%).

Recommendation: The guideline panel recommends that home-based PR be offered to patients with COPD as an alternative to usual care (weak recommendation, moderate-to-low quality evidence).

Justification and implementation: This recommendation places high value on moderate-to-low quality evidence of short-term, moderate effects on outcomes of importance to patients such as enhanced HRQoL, reduced breathlessness and improved exercise tolerance. The strength of the recommendation was 'weak' due to the differing models of home-based rehabilitation programmes with lack of evidence regarding the optimal format. As many of the exercise sessions in home-based programmes were unsupervised, it is likely that regular contact with a physiotherapist or accredited exercise physiologist who is experienced in prescribing exercise-based rehabilitation is critical to ensure that patients receive a sufficient exercise dose to obtain programme benefits. Most of the evidence is derived from participants with stable COPD (more than 4 weeks after an exacerbation of COPD) providing greater confidence in recommending implementation of home-based PR in this group.

PICO 3b: Is home-based PR an effective alternative to hospital-based PR for patients with COPD?

Summary of evidence: A search of the literature located 278 citations including three systematic reviews^{8,67,68} of studies examining the effectiveness of home-based PR. One additional RCT from Australia, comparing home-based rehabilitation to a standard hospital-based programme,⁶⁹ was published after the search was conducted and was included because of its direct relevance to this question. Of the included studies, six made a direct comparison of home-based with hospital-based PR.⁶⁹⁻⁷⁴ Two studies were powered for equivalence.^{69,71} In one study, every session of home-based exercise was directly supervised by a physiotherapist;⁷⁴ the other five home-based programmes⁶⁹⁻⁷³ included supervision of the initial session only and/or telephone contact. Three of the studies, including the two largest trials,^{69,71} reported regular weekly contact with participants in the home-based intervention^{69,71,73} but frequency of contact was unreported in the other three studies.^{70,72,74}

Improvements gained post-PR in HRQoL were not statistically different or clinically important between programmes conducted in home and hospital settings (e.g. CRQ-Dyspnoea MD: 0.00 units, 95% CI: -0.22 to 0.23, three studies,⁶⁹⁻⁷¹ $n = 414$ (Fig. S1, Supplementary Information)). However, within-group changes exceeded the MID in both settings.⁶⁹⁻⁷¹ This finding of similar benefits in HRQoL was consistent in all studies for measures using the CRQ and SGRQ. Changes in HRQoL in both settings exceeded the MID for some but not all domains. Changes in exercise tolerance were not clinically or statistically different between home- and hospital-based programmes for the 6MWT (MD: 3.5 m, 95% CI: -12.9 to 19.6, $n = 255$ (Fig. S1, Supplementary Information))^{69,70,72} with similar findings for endurance treadmill test⁷³ and maximal

incremental exercise tests.^{73,74} Quality of the evidence was rated down for risk of bias due to lack of blinding and indirectness due to gender imbalance (60-100% of participants in each study were males).

Recommendation: The guideline panel recommends that home-based PR, including regular contact to facilitate exercise participation and progression, be offered to patients with COPD as an alternative to hospital-based PR (weak recommendation, moderate-to-low quality evidence).

Justification and implementation: This recommendation places high value on moderate quality evidence of no significant differences in short-term outcomes of importance to patients (such as enhanced HRQoL, reduced breathlessness and improved exercise tolerance), whether the PR is a hospital-based or home-based programme. The strength of the recommendation was 'weak' due to the differing models of home-based rehabilitation programmes with lack of evidence regarding the optimal format. As many of the exercise sessions in home-based programmes were unsupervised, it is likely that regular contact with a physiotherapist or accredited exercise physiologist who is experienced in prescribing exercise-based rehabilitation is critical to ensure that patients receive a sufficient exercise dose to obtain programme benefits.

PICO 3c: Is community-based PR more effective than usual care for patients with COPD?

Six studies that met our definition of community-based PR^{49,75-79} were identified from an existing Cochrane review.⁸ An additional search covering the period not included in the Cochrane review (March 2014 to February 2016) identified one further study.⁸⁰

Summary of evidence: Of the seven included studies, four implemented community-based programmes with exercise sessions of at least moderate intensity supervised twice a week^{49,75,78,80} ($n = 259$), consistent with the provision of PR in Australia and New Zealand. In other studies, the exercise component was of low intensity⁷⁹ or implemented once weekly.^{76,77} Compared with usual care, community-based PR resulted in moderate improvements in overall HRQoL (SGRQ Total score MD: -4.2 units, 95% CI: -6.5 to -1.9, three studies,^{49,78,80} $n = 229$). Exercise frequency and intensity in these three studies were consistent with typical hospital-based programmes in the Australian and New Zealand settings. Pooled data from studies that used the CRQ to measure HRQoL^{76,79} indicated a change in favour of the intervention for the CRQ Dyspnoea domain only (MD: 0.53 units, 95% CI: 0.03-0.80, two studies,^{76,79} $n = 343$) with no differences in other domains (Fig. S1, Supplementary Information). Both of these studies^{76,79} implemented low intensity or frequency of exercise which may help to explain their lack of effect on the other domains of the CRQ. Endurance exercise capacity showed clinically meaningful improvements from community-based PR compared with control (cycle endurance test MD: 221 s, 95% CI: 5-437)⁴⁹ and treadmill (MD: 194 s).⁸⁰ Evidence is limited for effectiveness on 6MWT and incremental shuttle

walk test (ISWT) due to risk of bias (high attrition and lack of blinding),⁷⁵⁻⁷⁹ imprecision (6MWT protocol variation)⁴⁹ and indirectness (low intensity and frequency of exercise).^{76,77,79}

Recommendation: The guideline panel recommends that community-based PR, of equivalent frequency and intensity as hospital-based programmes, be offered to patients with COPD as an alternative to usual care (weak recommendation, moderate quality evidence).

Justification and implementation: This recommendation places high value on moderate quality evidence of short-term, moderate effects on outcomes of importance to patients such as enhanced HRQoL, reduced breathlessness and improved exercise tolerance. None of the studies reported whether participants within 4 weeks after an exacerbation of COPD were included, therefore the recommendation cannot be extended to this group. The optimal model for community-based programmes is not known; however, the exercise training component must be delivered at a similar frequency and intensity as hospital-based programmes in order to achieve clinically meaningful benefits for patients.

Implementation of PR in home- or community-based settings could help overcome common barriers of availability, access and difficulty of travelling to hospital-based programmes expressed by patients with COPD.⁵⁷

PICO 4: In patients with mild disease severity, is PR more effective than usual care?

Background: Patients with COPD present with a range of disease severities, from mild to severe. The Australian COPD-X Guidelines⁷ and an international PR statement¹⁵ recommend referral to PR for all patients, regardless of the degree of disease severity. Spruit *et al.* suggest that patients with mild disease may benefit from preventative strategies and maintenance of physical activity, and PR may be, but is not necessarily included in these strategies.¹⁵ Whilst PR is supported by Level I evidence (PICO 1), the effectiveness in mild disease is not well established. The COPD-X Guidelines define mild COPD as a forced expiratory volume in 1 s (FEV₁) between 60% and 80% predicted, with few symptoms, breathlessness on moderate exertion and little or no effect on daily activities.⁷

Summary of evidence: The search strategy yielded 34 citations and hand searching identified a further 4 citations, 38 in total. Based on evaluation of the abstracts and titles, 30 citations were excluded and a further 4 citations were excluded on review of the full papers, leaving 4 papers for full review and data extraction. Studies defined mild disease in two ways: based on an FEV₁ cut-off⁸¹⁻⁸³ or symptoms.⁸⁴ The studies based on FEV₁ either did not report detailed data for the mild group specifically and did not respond to requests for data,⁸² or were of very low quality.^{81,83} As such, the focus of this question was limited to studies that used symptoms to categorize disease severity.

A systematic review⁸⁴ that examined the effectiveness of PR in COPD patients with a modified Medical

Research Council (mMRC) breathlessness score ≤ 1 included four RCTs^{49,78,79,82} ($n = 489$). Compared with usual care, PR in patients with mild COPD resulted in short-term (up to 6 months) improvements in HRQoL; MD in the SGRQ was -4.2 units (95% CI: -4.5 to -3.9), exceeding the MID⁸⁵ (two studies,^{78,82} $n = 207$, moderate quality). Effects on HRQoL were no longer evident at the longest follow-up period of 24 months. Functional exercise capacity (6MWT) showed a mean improvement of 25.7 m (95% CI: 15.8–35.5 m, four studies,^{49,78,79,82} $n = 313$, moderate quality evidence). This just reached the lower end of the MID.²⁴ Quality of the evidence was rated down for risk of bias, particularly lack of assessor and participant blinding.

Recommendation: The guideline panel recommends that patients with mild COPD (based on symptoms) undergo PR (weak recommendation, moderate-to-low quality evidence).

Justification and implementation: This recommendation places a high value on moderate quality evidence of clinically significant short-term improvement in functional exercise capacity and HRQoL, and low value on cost and uncertainty regarding patient preference. Whilst benefits from PR in patients with symptomatically mild disease are evident, we recognize that patients are heterogeneous in terms of lung function and symptoms. As such, further research is needed to examine the effect of PR in mild disease based on a multidimensional assessment of these variables and an objective assessment of disease severity.

PICO 5: Are programmes of longer duration more effective than the standard 8-week programmes?

Background: The duration of PR programmes reported in the literature varies from 4 weeks to 18 months. PR programmes of 8-week duration are commonly recommended in PR statements¹⁵ and guidelines.¹²⁻¹⁴ While a large number of PR programmes in Australia and New Zealand are conducted over an 8-week duration,^{58,59} it is unclear whether significant benefits may be conferred from programmes of a longer duration.

Summary of evidence: The search strategy to determine whether differences exist between 8-week PR programmes and those of longer duration, in terms of exercise capacity and HRQoL, yielded 6712 citations, of which 6698 citations were excluded based on title and abstract. Fourteen papers were reviewed in full text; however, no RCTs were identified that directly compared PR programmes of 8 weeks to programmes of longer duration.

Recommendation: The panel is unable to make a recommendation due to lack of evidence evaluating whether programmes of longer duration are more effective than the standard 8-week programmes.

Justification and implementation: There is no direct evidence comparing 8-week programmes to those of longer duration. In order to provide some guidance for programme duration, we extracted data from trials included in the most recent Cochrane review of PR⁸ that were consistent with current

Australian and New Zealand practice of two to three supervised exercise sessions per week. We compared outcomes from RCTs of 8-week PR programmes and RCTs of 12-week PR programmes. For the outcome of 6MWT, there were six RCTs of 8-week programmes compared with usual care ($n = 218$)⁸⁶⁻⁹¹ and four RCTs of 12-week programmes compared with usual care ($n = 225$).^{72,75,92,93} Meta-analyses demonstrated an MD for 6MWT of 77 m (95% CI: 54-100) for the 8-week programmes and 57 m (95% CI: 27-88) for the 12-week programmes. No significant difference in improvement in 6MWT between programmes of different durations was observed ($P = 0.31$). For the outcome of SGRQ, there were five RCTs of 8-week programmes compared with usual care ($n = 182$)^{86-88,91,94} and only one RCT of a 12-week PR programme compared with usual care ($n = 26$),⁹² thus, there were insufficient data to compare SGRQ between programmes of 8- and 12-week duration for HRQoL. For the 8-week programmes versus usual care, the MD for SGRQ Total score was -9.6 units (95% CI: -15 to -4) which is greater than the MID of -4 points.²⁵ The MD for SGRQ Total score for the study of a 12-week PR programme was -5 units (95% CI: -14 to 4) (meta-analyses are presented in Fig. S1 (Supplementary Information)).

PICO 6: Does ongoing supervised exercise at a lower frequency than the initial PR programme maintain exercise capacity and quality of life to 12 months in patients with COPD?

Background: These Guidelines recommend the use of PR programmes for patients with stable COPD and following an exacerbation of COPD (PICO 1a and b). However, functional exercise capacity and HRQoL often decline in the 12 months following PR completion.^{95,96} Consequently, ongoing supervised exercise programmes are offered following PR. In Australia, 72% of PR programmes offer supervised maintenance exercise programmes (Lung Foundation Australia, unpublished data) at a lower frequency than the initial programme (e.g. once a week or once a month). Whether this is the best way to maintain the benefits gained from PR to 12 months and beyond remains unclear.

Summary of evidence: The search strategy yielded 51 citations of which 32 full papers and 8 abstracts were extracted and reviewed. Of these, the recommendations in this Guideline are based on the review of 11 RCTs that reported maintenance exercise programmes consisting of supervised exercise at a lower frequency than the initial PR programmes.^{49,79,95-103} A comparison across the studies was challenging given that three studies reported long-term changes compared with the beginning of the PR programmes (pre-rehabilitation) and eight studies compared outcomes to the end of the PR programmes (post-rehabilitation). Furthermore, studies were heterogeneous in the delivery of interventions (e.g. frequency of supervised exercise) and measurement of outcomes.

When weekly supervised exercise was performed as a maintenance exercise programme, one study ($n = 22$)

reported that at 12 months, functional exercise capacity and HRQoL were not significantly different to pre-rehabilitation and showed no differences compared with a group who was supervised monthly.¹⁰⁰ In contrast, in three studies ($n = 204$) where results at 12 months were compared with post-rehabilitation, weekly supervised exercise maintained functional exercise capacity,^{79,103} peak exercise capacity,¹⁰³ endurance exercise capacity¹⁰³ and HRQoL.^{99,103} However, there was no difference compared with the control groups that consisted of standard care or unsupervised home exercise with regular review.^{79,99,103} In studies where supervised exercise sessions were progressively reduced (weekly supervised exercise followed by second weekly, followed by monthly) during the maintenance period, two studies ($n = 77$) reported that at 12 months, exercise capacity was better than pre-rehabilitation in the intervention groups, and that the control groups (unsupervised home exercise) had declined below pre-rehabilitation levels.^{98,102} However, no between-group differences were reported.^{98,102} Based on the results of the studies described above, there appears to be no added benefit gained from weekly supervised exercise or a reducing frequency of supervised exercise compared with unsupervised home exercise with regular review, as a maintenance exercise programme.

When monthly or three monthly supervised exercise was performed as a maintenance exercise programme in five studies ($n = 512$), there was a significant decline at 12 months in exercise capacity and HRQoL in both the intervention and control groups, compared with both pre-^{49,101} and post-rehabilitations.⁹⁵⁻⁹⁷ Based on the results of these studies, maintenance exercise programmes of monthly or three monthly supervised exercises are insufficient to maintain exercise capacity or quality of life to 12 months.

The overall quality of the evidence from the studies described above was low and rated down for risk of bias (lack of random sequence generation and assessor blinding with unclear allocation) and imprecision (small numbers of studies and participants contributing to meta-analysis with some studies having missing data).

Recommendation: The guideline panel recommends that: (i) more research is needed to determine the optimal model of maintenance exercise programmes ('in-research' recommendation); (ii) supervised maintenance programmes of monthly or less frequently are insufficient to maintain the gains of PR and should not be offered (weak recommendation, low quality evidence).

Justification and implementation: The recommendation places a high value on low quality evidence that monthly supervised ongoing exercise is insufficient to maintain outcomes of importance to patients compared with standard care. While there may be benefits of weekly, supervised maintenance exercise, current low quality evidence suggests that it is no better than standard care of unsupervised exercise with regular review. When participants were surveyed following the completion of a 12-month maintenance exercise programme, positive attitudes towards both the supervised and unsupervised maintenance exercise programmes

were reported, with no between-group differences found for the importance of exercise, the benefits of the programme or the importance of support from the physiotherapist.¹⁰⁴ Further research is required to clarify the benefits, location and the cost benefit of weekly supervised exercise as a maintenance programme. However, some form of regular ongoing exercise should be encouraged once PR has been completed to sustain the benefits gained.

PICO 7: Does a structured education programme enhance the benefits of PR?

Background: In Australia and New Zealand, the majority of PR programmes have reported providing a structured education programme.⁵⁸ Health education in this format is provided by members of a multidisciplinary team to patients as a group audience. Topics are pre-determined and cover the disease (COPD) and aspects of its management, and may be accompanied by written material. Structured education in PR is reported to be valued by patients with COPD.¹⁰⁵

Summary of evidence: The search strategy yielded 278 citations of which 250 were excluded based on title and abstract. A further 24 citations were excluded on review of the full paper, leaving 4 papers for full review and data extraction.

Two RCTs compared a twice weekly outpatient PR programme that included supervised exercise training and a structured education programme to supervised exercise training alone.^{51,106} One of these RCTs was a large Australian trial ($n = 267$).⁵¹ Patients in both models demonstrated significant improvements in key outcomes; however, there were no additional benefits attributable to the education programme in exercise capacity (6MWT), HRQoL (CRQ), dyspnoea (Medical Research Council (MRC) dyspnoea score), self-efficacy or health behaviour in the short term or long term (12 months). In the Australian trial, the findings were limited by a low completion rate in the intervention group (60%) and a large loss to follow-up (26%) that was greater in the exercise-only group.⁵¹ However, in the secondary outcome of HCU, for which data were available for all participants, there remained no enhanced benefit of the education programme in terms of hospitalizations in the 12 months following PR. The smaller trial ($n = 22$) found that the lecture series negatively affected emotional function compared with exercise training alone ($P = 0.03$), despite the additional attention participants received from healthcare professionals.¹⁰⁶ This trial was not adequately powered to detect differences between groups in most outcomes and lacked blinding. Similarly, an observational study of Italian patients who elected to attend a structured education programme ($n = 226$) or not ($n = 59$) in conjunction with supervised exercise training demonstrated no differences between groups in exercise capacity (6MWT), breathlessness (MRC), HRQoL (SGRQ) or responses to a knowledge and learning impact questionnaire.¹⁰⁷ An evaluation of a new structured education programme for COPD in PR delivered in 11 hospitals and community-based programmes in Northern Ireland demonstrated high patient satisfaction and a significant improvement in knowledge,

understanding and self-efficacy.¹⁰⁸ The results from these observational studies are at high risk of bias due to study design, selection bias and lack of blinding.^{107,108}

Recommendation: The guideline panel recommends that PR be offered to all patients with COPD, irrespective of the availability of a structured multidisciplinary group education programme (weak recommendation, moderate-to-low quality evidence).

Justification and implementation: This recommendation places a high value on moderate-to-low quality evidence from a small number of studies. The role of education within PR is highly valued by patients and clinicians. The provision of knowledge in an appropriate format is an essential component of effective patient self-management. It is possible that behaviour change in PR may be further promoted with the addition of self-management interventions.^{15,109} The Guideline panel only reviewed structured group education and did not review individualized models of education or self-management interventions for patients with COPD and therefore cannot make a recommendation regarding these strategies within the context of PR.

PICO 8: Do patients who experience oxygen desaturation during exercise have greater improvements if oxygen supplementation is provided during training?

Background: Exercise-induced oxygen desaturation (EID) is common among patients with COPD, with an Australian study indicating that 47% of those referred to a PR programme demonstrated a decrease in oxygen saturation to <90% during a 6MWT.¹¹⁰ It is plausible that the intensity of exercise training achieved in a PR programme by patients with COPD who experience EID may be compromised, particularly if clinicians attempt to minimize EID by decreasing training intensity or imposing mandatory rests. A reduction in training intensity may have repercussions for the magnitude of training effect achieved. Consequently, oxygen supplementation may be provided in PR programmes for patients with COPD who experience EID. It has been known for over 50 years that oxygen supplementation can improve exercise capacity in COPD¹¹¹ but the effect of oxygen supplementation during exercise training for patients with COPD who experience EID is unclear.

Summary of evidence: The search strategy yielded 2052 citations of which 2042 were excluded based on title and abstract. A total of 10 full papers were extracted and reviewed. Of these, four RCTs were identified¹¹²⁻¹¹⁵ addressing the question. The level of evidence of these RCTs was low due to imprecision and high risk of bias from lack of assessor blinding and drop-out.

The results from the RCTs examining whether oxygen supplementation should be provided during exercise training for patients with COPD who experience EID were inconsistent. Most of the RCTs¹¹²⁻¹¹⁴ indicated that there was no difference using supplemental oxygen versus no supplemental oxygen (i.e. compressed air or room air) on exercise capacity, breathlessness and levels of anxiety/depression following exercise

training in patients with EID. In contrast, one study demonstrated greater improvement in endurance walking capacity using supplemental oxygen during training compared with no supplemental oxygen (i.e. room air).¹¹⁵ However, the exercise testing protocol in this study at baseline and follow-up was not consistent as the end tests were performed on the gas to which each participant was randomized, and compared with baseline assessment which was performed on room air. This protocol eliminated the ability to conclude whether improvements were due to the acute effects of the supplemental oxygen or due to a training effect. No RCTs examined mortality or HCU.

Recommendation: The guideline panel recommends that further research of oxygen supplementation during training is required in patients with COPD who have exercise-induced desaturation to reduce the uncertainty around its lack of effect to date ('in-research' recommendation).

Justification and implementation: There is insufficient evidence to confirm the benefits of oxygen supplementation during exercise training compared with no oxygen supplementation in patients with COPD who have EID. Currently, supplemental oxygen is used in most Australian PR programmes to ensure safety and relieve symptoms for patients with COPD experiencing EID. The provision of supplemental oxygen during PR increases programme costs and restricts the venues where training can be delivered. More research is needed to provide clarity as to whether supplemental oxygen during exercise training should be used in patients with COPD who experience EID.

PICO 9: Is PR effective in chronic respiratory diseases other than COPD?

PICO 9a: Is PR effective in patients with bronchiectasis?

Background: Bronchiectasis is characterized by bronchial dilatation secondary to inflammation, infection and reduced mucociliary clearance. Patients with bronchiectasis experience persistent cough with sputum production, reduced exercise tolerance, breathlessness, fatigue and poor HRQoL. Exacerbations of bronchiectasis are common and are an indicator of poor prognosis.¹¹⁶ Treatment for bronchiectasis aims to improve control of symptoms, reduce exacerbation frequency, maintain lung function and optimize HRQoL. Such treatment includes careful antibiotic selection and may include airway clearance techniques.¹¹⁷

Summary of evidence: To inform this Guideline, a systematic review was used.¹⁸ The search strategy for this review yielded 82 citations and of these, 3 RCTs with a total of 135 participants with stable bronchiectasis were included.^{118–120} HRQoL improved in the PR group compared with control (SGRQ Total score MD: -4.6 points, 95% CI: -6.5 to -2.6, two studies, $n = 103$, moderate quality evidence). The ISWT improved by 64.5 m compared with control (exceeding the MID;²⁴ 95% CI: 49.4–79.6 m, three studies,^{118–120} $n = 122$, moderate quality evidence). Quality was rated down for risk of bias (lack of assessor blinding in some studies). A single study ($n = 76$) reported no difference between

groups for anxiety or depression, although the number of participants with mood disturbance at baseline was low.¹¹⁸ No studies reported HCU, although one trial reported a lower frequency of exacerbations in the PR group, with a longer time to first exacerbation (8 months vs 6 months, $P = 0.047$).¹¹⁸ Longer term follow-up in one study showed that benefits of PR were not sustained at 6 or 12 months.¹¹⁸

Recommendation: The guideline panel recommends that patients with bronchiectasis undergo PR (weak recommendation, moderate quality evidence).

Justification and implementation: This recommendation places a high value on moderate-to-low quality evidence of clinically significant improvements in exercise capacity and overall HRQoL, and a low value on uncertainty regarding magnitude and duration of benefit. All trials of PR for bronchiectasis have included airway clearance techniques, which may not be a standard component of PR in some settings. As a result, some providers may require extra training in order to deliver PR for patients with bronchiectasis.

PICO 9b: Is PR effective in patients with ILD?

Background: The ILDs are a diverse group of over 200 chronic lung conditions including idiopathic pulmonary fibrosis (IPF), connective tissue-related ILD, dust-related ILD, granulomatous ILD (e.g. sarcoidosis) and rarer ILDs such as lymphangiomyomatosis. They are characterized by varying degrees of interstitial inflammation and fibrosis, a restrictive ventilatory pattern and marked exercise-induced hypoxaemia. Patients with ILD experience distressing breathlessness on exertion, significant fatigue, reduced HRQoL, as well as high levels of anxiety and depression. There are limited treatment options for many ILDs. For instance in IPF, the most common and most lethal ILD, new pharmacotherapies can slow disease progression but do not provide cure.²³ In this setting, interventions that improve functional capacity and well-being may have an important role.

Summary of evidence: A Cochrane review that examined the evidence for PR in ILD¹⁹ included nine RCTs, of which five were published as abstracts. Compared with usual care, PR resulted in moderate improvements in overall HRQoL (standardized MD (SMD): 0.59, 95% CI: 0.2–0.98, three studies, $n = 106$, low quality evidence). Similar improvements were seen for breathlessness and fatigue domains of HRQoL instruments. Compared with usual care, the 6MWT improved by 44 m (95% CI: 26–63, five studies, $n = 162$, moderate quality evidence), exceeding the MID.²⁴ Effects on HRQoL, symptoms and exercise capacity were no longer evident at 6 months following programme completion.¹⁹ Quality of the evidence was rated down for risk of bias, particularly lack of assessor blinding, and for imprecision. Improvements of similar magnitude were reported in a Cochrane review of exercise training in dust-related respiratory disease, which included a small number of participants with dust-related ILD.¹²¹ No RCTs have examined the impact of PR on anxiety or depression in this setting. Single studies have reported effects of PR on 6-month mortality¹²² and HCU,¹²³ with no differences between groups.

Recommendation: The guideline panel recommends that patients with ILD undergo PR (weak recommendation, low quality evidence).

Justification and implementation: This recommendation places a high value on moderate-to-low quality evidence of short-term, moderate size effects on outcomes of importance to patients such as reduced breathlessness and enhanced HRQoL. However, the choice to undertake PR may be influenced by the relatively short duration of benefit. There is currently no evidence to suggest that the recommendation should vary according to the type of ILD, or that the exercise prescription should vary from that provided to patients with COPD. Because many patients with ILD use supplemental oxygen and/or experience profound exercise-induced desaturation, consideration should be given to providing PR in a setting where supplemental oxygen can be provided during training.

PICO 9c: Is PR effective in patients with PH?

Background: PH is defined as an increase in the resting mean pulmonary arterial pressure to at least 25 mm Hg on right heart catheterization.¹²⁴ Many patients with PH experience breathlessness on exertion; however, a range of other important symptoms may be present, including fatigue, dizziness, chest discomfort, chest pain, palpitations, cough, pre-syncope, syncope, lower limb oedema and abdominal distension. For patients from Group 1 PH (pulmonary arterial hypertension, PAH), specific pharmacotherapies are available and have markedly improved prognosis. However, many patients who are stable on medical therapy report significant exercise limitation and impaired HRQoL.^{125,126}

Summary of evidence: A Cochrane review comparing exercise training to control in PH²⁰ included six RCTs ($n = 206$) with varying classifications of PH. All participants were stable on medical therapy. Three of the RCTs were from the same group in Germany ($n = 137$) and used a 3-week inpatient rehabilitation programme,^{125,127,128} a model that is not available in Australia or New Zealand. HRQoL outcomes showed that, compared with usual care, exercise training improved the physical function score of the 36-Item Short Form Health Survey version 2 (SF-36v2) (MD: 6.3 points, 95% CI: 0.8–13.3, four studies,^{125,126,129,130} $n = 118$, low quality evidence) and the mental health score of the SF-36v2 (MD: 7.4 points, 95% CI: 2.6–12.2, three studies,^{128–130} $n = 87$, very low quality evidence). Compared with usual care, the 6MWT improved by 60 m (95% CI: 30–90, five studies,^{125,127–130} $n = 165$, low quality evidence), which exceeded the MID by a large amount.²⁴ The studies which relied totally on outpatient-based exercise programmes,^{129,130} consistent with the PR model in Australia and New Zealand, reported a smaller MD in 6MWT favouring the exercise group of 34 m (95% CI: 1–67) ($n = 36$), which still exceeded the MID.²⁴ No RCTs evaluated anxiety, depression or HCU. Quality of the evidence was rated down for risk of bias (lack of random sequence generation or assessor blinding), indirectness (may represent a selected subgroup of patients with PH) and imprecision (small numbers of studies and participants contributing to meta-analysis).

None of the studies reported significant adverse events during exercise training such as progression of symptoms, progression of PH, right heart failure or death. One study reported that 3 of the 15 exercise group participants had symptoms during training which comprised dizziness without fainting immediately following cycle ergometer training ($n = 2$) and desaturation from 88% to 74% despite oxygen therapy ($n = 1$).¹²⁵ In a cohort study, the same investigators reported that 25 of the 183 patients (14%) experienced adverse events during a 3-week inpatient rehabilitation programme including syncope, pre-syncope, acute respiratory infection, supra-ventricular tachycardia and haemoptysis.¹³¹

Recommendation: The guideline panel recommends that patients with PH undergo PR (weak recommendation, low quality evidence).

Justification and implementation: This recommendation places a high value on low quality evidence of moderate effects on outcomes of importance to patients (quality of life and exercise capacity). Most evidence relates to inpatient exercise training (68% of participants who have undergone exercise training in RCTs), which may allow closer monitoring and supervision than in outpatient programmes and is not available in Australia or New Zealand. However, no important adverse events have been reported in trials of outpatient exercise training, so there is currently no evidence to suggest that the recommendation should vary according to programme setting. Patients should be stable on pharmacotherapy prior to undertaking an exercise training programme. There is no evidence to suggest that the recommendation should vary according to class of PH. International guidelines for PH management currently recommend that exercise training should be undertaken ‘...by centres experienced in both PH patient care and rehabilitation of compromised patients’.¹²⁴

DISCUSSION

These PR Guidelines address questions considered by a representative multidisciplinary panel of experts in the field and the COPD consumer group to be important in the context of Australian and New Zealand health services. The PICO questions were limited to <10 and we recognize that these do not encompass all the important questions pertaining to PR. Each question was addressed and recommendations formulated using an evidence-based, systematic process.²¹ Strong recommendations were able to be made regarding the effectiveness of PR in improving exercise capacity, HRQoL and reducing hospital admissions for patients with COPD. While there are resources required to provide PR, the cost per quality-adjusted life year (QALY) ratios are within the bounds considered to be cost-effective and likely to result in financial benefits to health services.¹³² Given the compelling evidence of the benefits of PR, policymakers should ensure appropriate strategies are in place to enable equitable access to PR for patients with COPD. Increased availability of PR programmes and referral to these programmes are vital to ensure improved patient access and increased

patient participation in this effective evidence-based intervention.

There were gaps in the available evidence to answer some of the questions. In particular, there was no direct evidence to determine whether PR programmes of longer than 8-week duration were more effective than the standard 8-week programmes that are common in Australia and New Zealand.^{58,59} Some evidence from meta-analyses of programmes of 8-week duration (in which exercise was supervised two to three times per week) provides confidence that this programme duration improves exercise capacity and HRQoL. Limited evidence was available to guide practice for the use of supplemental oxygen during exercise training in patients with COPD who experience EID but who are not prescribed long-term oxygen therapy. As approximately 47% of patients referred to PR in Australia experience EID,¹³³ further high quality research is needed in this area to determine if there are benefits of providing supplemental oxygen during training and whether these benefits are greater than those that can be achieved with training on room air in this patient group. Such research will help to determine whether patients who experience EID need to attend a PR programme where supplemental oxygen is available. Currently, a large Australian RCT is underway examining oxygen supplementation during exercise training in patients COPD who have EID.¹³⁴ Optimal interventions for the long-term maintenance of improvements after completion of a PR programme could not be determined, other than the evidence suggesting that monthly maintenance programmes are not worthwhile. Maintenance of the benefits of PR is an important area of future research and may link with behaviour change and self-management interventions,¹⁰⁹ although these were not addressed in the Guidelines.

While most evidence for PR comes from hospital-based programmes, the Guideline review has demonstrated growing evidence for the effectiveness of PR in other venues such as community or home settings. Such settings may improve access to programmes by eliminating some of the known barriers to programme attendance,⁵⁷ as well as providing patients with choices around venues such as community-based programmes, home-based programmes or programmes provided in primary care by private practitioners. Availability of PR programmes in a variety of settings may improve programme access and adherence. Appropriate funding is a driver for provision of PR. Currently in Australia, PR is funded through hospital funding models based on the Independent Hospital Pricing Authority, Tier 2 (non-admitted hospital services) classifications¹³⁵ and related pricing.¹³⁶ While such funding enables some rehabilitation programmes to be provided via the hospital system, major changes in funding models are required to enable the wider provision of PR in primary care.

In terms of patient education, the Guideline only reviewed patient education delivered in a structured group format, as this is how education has traditionally been delivered in Australian and New Zealand PR programmes.^{58,59} The limited number of RCTs showed no additional benefit of structured education to a PR

programme compared with PR alone. A structured educational format may not be suitable for all patients whose learning styles, needs and cognitive abilities may vary. It was beyond the scope of the Guidelines to further explore this area, in particular self-management education was not addressed. Our findings do not diminish the importance of education for patients undertaking PR; rather this reinforces the need to establish the most effective methods to assist individuals with COPD to gain the skills and knowledge they require to optimally manage their disease.

The review of PR for patients with mild COPD (based on symptoms) found clinically meaningful benefits in HRQoL and exercise capacity. Traditionally, PR programmes in Australia and New Zealand have mainly included patients with moderate-to-severe disease, consistent with the initial studies underpinning the efficacy of PR.⁸ Many patients with mild COPD in Australia and New Zealand are managed by their general practitioner in primary care and are not often referred to PR. However, our review findings demonstrate beneficial outcomes from PR across the spectrum of disease. While the most cost-effective model for providing PR for patients with mild disease is unknown, it is possible that less costly community health and fitness programmes linked with high quality COPD-specific education programmes, which are becoming more available online,¹³⁷ are worth evaluating.

There is growing evidence of the effectiveness of PR for chronic lung diseases other than COPD. The Guidelines have provided reviews of the benefits of PR for patients with bronchiectasis, ILD and PH. The recommendations in favour of PR for patients with these diagnoses suggest that inclusion criteria should facilitate the participation of such patients in PR programmes in Australia and New Zealand. Practitioners providing PR for patients with bronchiectasis, ILD and PH should have adequate skills and knowledge to treat these patient groups and, for some patients, PR may need to be provided in centres with disease-specific expertise.

Given the higher incidence of COPD in Indigenous Australian⁴ and New Zealand communities,⁵ it is important that Indigenous patients with COPD have access to PR. One barrier to attendance at PR may be the lack of attention to cultural needs within mainstream programmes.¹³⁸ Currently in Australia, no PR programmes are specifically designed to accommodate the cultural needs of Aboriginal and Torres Strait Islander Peoples and there is little empirical data on what these needs are. In New Zealand, PR programmes provided for Māori individuals by Māori organizations have identified that attendance is enhanced by the opportunity to make culturally meaningful connections with other patients and staff within the programme, having culturally appropriate information available and communicating in a common Māori language.¹³⁸ It is imperative that greater efforts are made to ensure safe cultural environments for the delivery of PR, either by Indigenous health professionals providing the PR programmes or by mainstream programmes providing a culturally appropriate environment to encourage and maintain attendance.

These PR Guidelines have evaluated the evidence related to the questions posed and provide general

recommendations. For information on the practical aspects of providing PR and individualizing interventions for patients, clinicians should access the Pulmonary Rehabilitation Toolkit¹³⁹ which provides extensive information on establishing a PR programme, patient assessment, exercise training, patient education and patient reassessment.

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Supplementary Information

Additional supplementary information can be accessed via the *html* version of this article at the publisher's website.

Figure S1 Meta-analyses.

Table S1 Search strategies.

Table S2 Papers reviewed.

Table S3 GRADE evidence profile tables.

Table S4 Evidence to recommendation table.