Multicomponent services for symptoms in serious respiratory illness: a systematic review and meta-analysis

Anna Spathis [1,2], Charles C. Reilly [3,4], Claudia Bausewein [5], Lynn F. Reinke [6], Lorena Romero [7], Natasha E. Smallwood [8,9], Magnus Ekström [10] and Anne E. Holland [8,9,11,12]

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Edited by Anne E. Holland, Magnus Ekström and Natasha E. Smallwood

[1]Department of Public Health and Primary Care, University of Cambridge, Cambridge, UK. [2]Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK. [3]Department of Physiotherapy, King's College Hospital, London, UK. [4]Cicely Saunders Institute of Palliative Care, Policy and Rehabilitation, King's College London, London, UK. [5]Department of Palliative Medicine, LMU University Hospital Munich, LMU Munich, Munich, Germany. [6]College of Nursing, University of Utah, Salt Lake City, UT, USA. [7]The Ian Potter Library, Alfred Health, Melbourne, Australia. [8]Department of Respiratory Medicine, Alfred Health, Melbourne, Australia. [9]School of Translational Medicine, Monash University, Melbourne, Australia. [10]Respiratory Medicine, Allergology and Palliative Medicine, Department of Clinical Sciences Lund, Lund University, Lund, Sweden. [11]Department of Physiotherapy, Alfred Health, Melbourne, Australia. [12]Institute for Breathing and Sleep, Melbourne, Australia.

Corresponding author: Anna Spathis (aos10@cam.ac.uk)

Shareable abstract (@ERSpublications)
Multicomponent services improve breathlessness mastery and health-related quality of life, with minimal risk. These findings support use of these services for people living with serious respiratory illness, although the certainty of evidence is very low. https://bit.ly/3WFsTUE

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Abstract

Background People living with serious respiratory illness experience a high burden of symptoms. This review aimed to determine whether multicomponent services reduce symptoms in people with serious illness related to respiratory disease.

Methods Electronic databases were searched to identify randomised controlled trials (RCTs) evaluating multicomponent services that enrolled patients due to symptoms, rather than underlying disease, and provided at least one nonpharmacological intervention. The primary outcome was chronic breathlessness and secondary outcomes were health-related quality of life (HRQoL), cough, fatigue and adverse events. At least two authors independently screened studies, assessed risk of bias and extracted data.

Results Five RCTs, involving 439 patients, were included. In comparison to usual care, multicomponent services improved breathlessness mastery (Chronic Respiratory Questionnaire (CRQ) mastery scale, mean difference (MD) 0.43 points, 95% CI 0.20–0.67, three RCTs, 327 participants) and HRQoL (CRQ total score, MD 0.24 points, 95% CI 0.04–0.40, two RCTs, 237 participants). Fatigue did not improve with multicomponent services and no studies evaluated cough. No serious adverse events were reported. The one study evaluating mortality found increased survival in those accessing a multicomponent service. The certainty of evidence was very low, mainly due to detection and reporting bias.

Conclusion Multicomponent services improve breathlessness mastery and HRQoL, with minimal risk. These findings support the use of multicomponent symptom-directed services for people living with serious respiratory illness.

Introduction

People living with serious illness related to respiratory disease experience a high symptom burden. Chronic breathlessness is consistently reported as a common, distressing and disabling symptom [1–3]. Moderate-to-severe daily breathlessness is experienced by half of those with COPD. In pulmonary fibrosis, breathlessness is almost ubiquitous [4] and breathlessness has been identified as a major driver of reduced

quality of life [5, 6]. Breathlessness is frequently ranked by patients as their worst symptom [7] and drives unscheduled healthcare usage [8, 9]. Other symptoms, such as fatigue, anxiety and cough, are also highly prevalent and contribute to poor health-related quality of life (HRQoL).

Respiratory symptoms are often inadequately recognised [10] and undertreated [11, 12]. Over the last two decades, multicomponent services have emerged in response to these challenges, embedded within palliative care services and, increasingly, also within respiratory services. These symptom-directed services are mostly focused on breathlessness management and provide a holistic, multidisciplinary, complex intervention involving mostly nonpharmacological self-management support, such as breathing and relaxation techniques and promotion of activity [13]. They provide care after, or in parallel with, medical optimisation of the underlying long-term condition(s).

One systematic review of multicomponent symptom-directed services has been undertaken to date. Brighton *et al.* [14] evaluated 37 studies representing 18 services and conducted a quantitative synthesis of data from 12 studies relating to seven services. The services mostly managed breathlessness caused by advanced cancer (12 of 18 services) and involved a median of four to six consultations over 4–6 weeks. Distress due to breathlessness (measured by a 0–10 numerical rating scale) and depression scores (Hospital Anxiety and Depression Scale depression domain) improved significantly; statistically nonsignificant increases in breathlessness mastery (Chronic Respiratory Questionnaire mastery scale) were observed.

This review is the first to evaluate the impact of multicomponent services for people with chronic breathlessness and other symptoms caused by nonmalignant respiratory disease. It is one of a series of systematic reviews completed by a European Respiratory Society (ERS) taskforce set up to provide guidance on symptom management for adults with serious respiratory illness. The purpose of this review was to determine whether multicomponent services should be recommended to reduce symptoms in people with serious respiratory disease.

Methods

Protocol and registration

The review protocol was developed *a priori* but not registered on the PROSPERO register of systematic reviews, due to the confidentiality requirements of the ERS clinical practice guideline development process. The protocol was prospectively submitted to the editorial office of the *European Respiratory Review* to be held in confidence.

Search strategy

The following databases were searched: Medline (OVID), Embase (OVID), Cochrane Database of Systematic Reviews and CENTRAL (The Cochrane Library) from inception to July 2022. The search was divided into two components. First, a search was conducted to find relevant systematic reviews (from 2017 to July 2022), and any systematic reviews providing evidence for at least one of the outcomes of interest were used as a basis for identification of relevant studies. A second search sought to identify randomised controlled trials (RCTs) that had been published since the search date of the most recent relevant systematic review, if that date was more than 1 year ago. Search results were screened independently by two taskforce members for eligibility.

The search strategy was designed and executed by a medical librarian (see supplementary material), adapted from a search strategy used in a relevant previous systematic review [14]. The search included the following key words: palliative care, advanced disease, nonmalignant disease, chronic obstructive pulmonary disease, interstitial lung disease, multi-professional, multidisciplinary, holistic, complex intervention, nonpharmacological, dyspnoea, breathlessness and short of breath.

Study selection

Only RCTs were eligible for inclusion. Crossover trials were excluded, as any behavioural component to the intervention could have a carryover effect. Studies were eligible if they included adult participants aged 18 years or older and if the participants had serious respiratory illness. Serious respiratory illness was defined as a condition that carries a high risk of mortality, negatively impacts quality of life and daily function, and/or is burdensome in symptoms, treatments or caregiver stress [15]. Where studies involved participants with mixed malignant and nonmalignant disease, authors were asked for data related to the participants with nonmalignant disease only. If separate data could not be obtained, studies were only included when more than 80% of participants had nonmalignant disease.

A multicomponent service was defined as a model of care that offers more than one intervention, including at least one nonpharmacological intervention. Patients needed to be enrolled due to symptoms, not their diagnosis. Pulmonary rehabilitation and disease-specific services were considered outside the scope of this review. Eligible studies had to compare the effects of a multicomponent service with usual care, which could include primary care or secondary care outpatient services.

Screening and selection of studies were reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria (figure 1) [16].

Outcome measures

The primary outcome was chronic breathlessness. Measures of any aspect of breathlessness were included, such as breathlessness intensity, distress due to breathlessness or breathlessness mastery. Other important outcomes were HRQoL, cough and fatigue. Outcomes could be measured with any validated tool. Adverse events were also evaluated. Reporting one of more of these outcomes in a trial was not a prerequisite for inclusion of a study in this review. Due to the small number of included studies and limited data for the pre-specified outcomes, qualitative data from included mixed-methods studies has also been reported to provide additional information about acceptability to participants.

Data management and analysis

Two reviewers undertook and checked data extraction into a custom-designed data collection form and assessed risk of bias for each study using the Cochrane Collaboration's Risk of Bias tool [17]. Certainty of evidence was evaluated using the Grading of Recommendations Assessment, Development and Evaluation

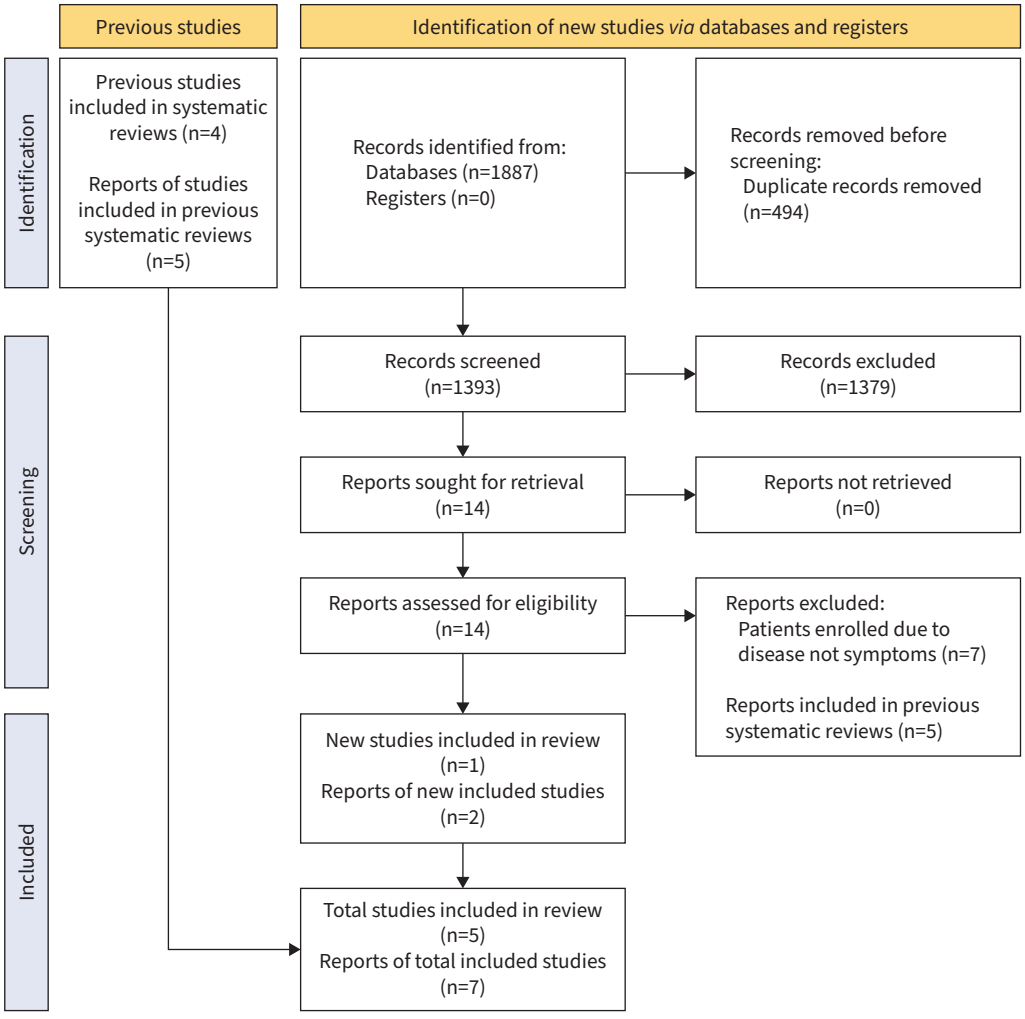

FIGURE 1 Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) flow chart.

(GRADE) approach [18]. Data extraction included the following: participant mean age, diagnoses and numbers, study design, eligibility criteria, primary end-point, outcome measures, and intervention description, along with end-point and/or change scores for each outcome of interest.

Where reported, change from baseline scores were used. Where change from baseline scores were not reported, results adjusted for baseline or end-point scores were used. The I^2 statistic was used to measure heterogeneity among the trials in each analysis. All trials were included in a narrative synthesis. Where data were clinically homogeneous, meta-analyses using a random effects model were conducted using Revman software version 5.4 (Cochrane, http://revman.cochrane.org). No subgroup analyses were planned or conducted. We had planned to perform sensitivity analyses to examine the effects of methodological quality on the pooled estimate by removing studies that were at high or unclear risk of bias for the domains of blinding and incomplete outcome data; however, insufficient numbers of studies were available.

Results

Article selection

The systematic review search identified one relevant systematic review [14], which contained four eligible RCTs. Searching for additional RCTs identified 1393 records, of which 14 were screened in full text, leading to the identification of one additional RCT [19]. This review therefore included five studies (439 participants).

A summary of study characteristics is provided in table 1. The five studies were published between 2006 and 2022 in English. All studies were parallel-arm RCTs, with participant numbers ranging from 13 to 193. The mean participant age was 67–72 years and the percentage of male participants ranged from 49 to 61% in the three studies where age and gender were reported. No included studies reported participant ethnicity. In the three studies that reported baseline characteristics, participants had moderately severe breathlessness (numerical rating scale (NRS) average breathlessness intensity in the last 24 h (score range 0–10) from 4.6 to 5.9) and relatively low breathlessness mastery (Chronic Respiratory Questionnaire (CRQ) mastery (score range 1–7) from 3.4 to 4.1).

Two studies recruited only people with nonmalignant lung disease, mostly COPD [20, 21], and three recruited mixed cohorts with more than 80% of participants having serious respiratory disease [19, 22, 23]. Authors provided specific data for those participants with nonmalignant disease for both of the mixed studies that were included in the meta-analyses. Only data from people with nonmalignant respiratory disease were quantitatively synthesised, with the exception of baseline adjusted data which related to the whole study population.

All studies evaluated multicomponent services that enrolled patients with a primary presenting symptom of breathlessness. Three studies evaluated similar interventions, with individualised self-management support from a multidisciplinary team at home or as an outpatient, using mostly nonpharmacological approaches such as breathing and relaxation techniques [19, 20, 23]. Another study, published only as an abstract, involved a similar intervention delivered only by nurses in an outpatient setting [21]. One small study (n=13 participants) tested the feasibility of a brief breathlessness intervention delivered by paramedics at emergency call-out for acute-on-chronic breathlessness; this was the only study not included in the meta-analyses [22]. All four studies involved in the quantitative synthesis had a primary end-point between 4 and 8 weeks.

Risk of bias assessment

Certainty of evidence was affected by risk of bias, mainly detection, performance and attrition bias (figure 2). The main sources of bias related to lack of blinding of participants to group allocation and loss to follow-up being high or different between groups. Three studies described baseline differences between groups in key outcomes [19–21]. Where mean differences adjusted for baseline were not available, change data was used in preference to end-point data. The overall certainty of evidence was very low.

Effectiveness

Breathlessness was evaluated using the CRQ and four different breathlessness NRS scores (figure 3). Multicomponent services improved breathlessness mastery (CRQ mastery) compared to usual care (mean difference (MD) 0.43 points, 95% CI 0.20–0.67, three RCTs, 327 participants, I^2=0%) [19, 20, 23]. Although the mean effect did not reach the minimum important difference (MID) of 0.5 points, the upper confidence interval exceeded this value [24].

Multicomponent services improved average breathlessness intensity over the last 24 h measured by 0–10 NRS (MD −0.50 points, 95% CI −1.00–0.00, two RCTs, 238 participants, I^2=0%), although the change

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TABLE 1 Characteristics of included studies

Study, year, country	Study design	Subjects (n)	Diagnoses	Mean±SD age (years)	Key eligibility criteria	Main outcomes	Intervention
Farquhar [20], 2016, UK	Fast-track, single-blind, parallel-arm RCT, with individual randomisation	87	COPD 80%; other nonmalignant 20%	72±11	Included if breathless despite disease optimisation; might benefit from self-management programme Excluded if dementia, confusion or learning difficulties; other vulnerable groups such as head injury, severe trauma, mental illness	Primary: distress due to breathlessness NRS Secondary: NRS worst/average breathlessness over last 24 h, modified Borg at rest and exertion; activity that makes breathlessness worst; CRQ; HADS; carer distress due to patient breathlessness NRS; carer HADS; EQ-5D	Palliative care AHPs and doctor; home based; range of mostly nonpharmacological techniques to support self-management; flexible individualised approach
Higginson [23], 2014, UK	Fast-track, single-blind, parallel-arm RCT, with individual randomisation	105	COPD 54%; cancer 20%; ILD 18%; HF 5%; other conditions 3%	67±10	Included if MRC dyspnoea scale score ⩾2; optimal disease management; advanced disease; willing to engage with short-term home support Excluded if unknown cause of breathlessness; primary diagnosis of chronic hyperventilation syndrome, completely housebound or <2 weeks from treatment of an acute exacerbation	Primary: CRQ mastery Secondary: NRS average, worst breathlessness over last 24 h, spirometry and oxygen saturation, CRQ; POS, HADS; EQ-5D; LCADL, CSRI; hospital attendances, survival	Palliative care and respiratory AHPs and doctors; outpatient and home; range of nonpharmacological techniques and pharmacological approaches to support self-management; flexible individualised approach
Hutchinson [22], 2022, UK	Feasibility cluster RCT	13	COPD (10/13), heart disease (7/13)	Not reported	Paramedics needed to be willing to be trained in the intervention Patients included if receiving a 999 ambulance response at home from a participating paramedic, with self-reported cardiorespiratory disease Patients excluded if needing immediate lifesaving intervention or transfer to ED	Feasibility measures (including recruitment, attrition); adverse events	Paramedic providing a formalised nonpharmacological intervention including positioning, fan and breathing techniques
Pearce [21], 2006, UK	RCT with individual randomisation	51	COPD 100%	Not reported	Disease therapy optimised and breathlessness remains predominant symptom	Primary: CRQ mastery Secondary: CRQ, spirometry, functional status, shuttle walk, Borg, oxygen saturation	Four nurse-led weekly outpatient sessions with breathing control, psychosocial support and relaxation techniques
Schunk [19], 2021, Germany	Fast-track, single-blind, parallel-arm RCT, with individual randomisation	183	COPD 63%; ILD 9%; HF 8%; PHT 5%; cancer 7%; other conditions 8%	71±9	Included if life-limiting, progressive disease causing breathlessness, able to engage in a multifaceted intervention programme Excluded if chronic hyperventilation syndrome, asthma or unknown cause; current treatment for cancer or participating in drug trial for underlying condition; acute exacerbation of the underlying condition	Primary: CRQ mastery Secondary: CRQ, average breathlessness over last 24 h, HADS, SPPB, EQ-5D, lung function tests, pulse oximetry	Palliative care and respiratory AHPs and doctors; outpatient and home; range of nonpharmacological techniques and pharmacological approaches to support self-management; flexible individualised approach

AHP: allied health professional; CRQ: Chronic Respiratory Questionnaire; CSRI: Client Service Receipt Inventory; ED: emergency department; EQ-5D: EuroQol Five-Dimensions; HADS: Hospital Anxiety and Depression Scale; HF: heart failure; ILD: interstitial lung disease; LCADL: London Chest Activity of Daily Living Scale; MRC: Medical Research Council; NRS: numerical rating scale; PHT: pulmonary hypertension; POS: Palliative Outcome Scale; RCT: randomised controlled trial; SPPB: Short Physical Performance Battery.

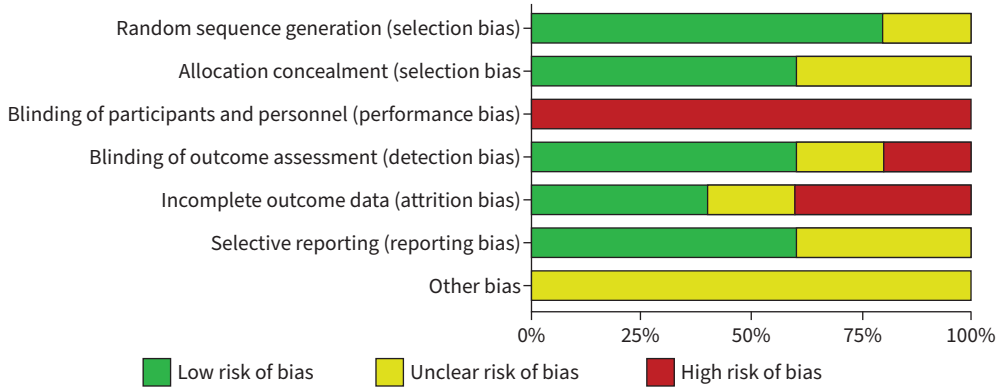


FIGURE 2 Risk of bias graph: judgement on each risk of bias item (percentages across all included studies).

was not significant and less than the MID of 1 point [25]. Three other breathlessness NRS measures were evaluated in one study each. Breathlessness improved with intervention compared to control but no changes were statistically significant (NRS distress from breathlessness MD −0.24 points, 95% CI −1.30–0.82, one RCT, 87 participants [23]; NRS worst breathlessness intensity in last 24 h MD −0.58 points, 95% CI −2.09–0.94, one RCT, 65 participants [23]; NRS intensity of breathlessness on exertion in the last 24 h MD −0.84 points, 95% CI −1.92–0.25, one RCT, 65 participants [23]). For all NRS measures, the lower end of the confidence interval included the MID so clinically relevant effects could not be excluded.

HRQoL improved with multicomponent services compared to usual care (CRQ total score, MD 0.24 points, 95% CI 0.04–0.40, two RCTs, 237 participants, I^2=0%), but neither the MD nor the upper end of the confidence interval included the MID (0.5 points) [19, 23]. Improvements in the CRQ dyspnoea domain (MD 0.13 points, 95% CI −0.10–0.36, three RCTs, 259 participants, I^2=0%) and CRQ fatigue domain were not statistically significant (MD 0.10 points, 95% CI −0.16–0.37, three RCTs, 261 participants, I^2=0%) and the confidence interval did not include the MID of 0.5 points [19, 21, 23]. The EuroQol Five-Dimensions (EQ-5D) visual analogue scale for measuring HRQoL did not show a significant improvement (MD 3.28 points, 95% CI −6.16–12.72, one RCT, 64 participants). The symptom of cough was not evaluated in any study.

Undesirable effects

One study reported adverse events [19]. In the intervention arm, 44/71 participants (62%) experienced 65 events; amongst control participants 48/80 (60%) experienced 79 events. Two events were considered intervention-related: a skin reaction following an allergy test and a side-effect from morphine; neither were serious adverse events.

Withdrawals or loss to follow-up varied across the five studies. One study reported 21% and 23% withdrawals from the trial from the intervention and control arms, respectively [23]; another found that withdrawals clustered around the intervention, at 18% in the intervention group compared to 5% in the control arm (data from whole study cohorts) [19]. Both studies recruited participants with advanced disease in services provided by palliative care and respiratory specialists; attrition rates were consistent with those usually found when recruiting in these contexts.

In the single study that measured mortality, survival from randomisation to 6 months was better in the intervention than the control group (50 of 53 (94%) *versus* 39 of 52 (75%)), with survival differences significant for both COPD and interstitial lung disease [23].

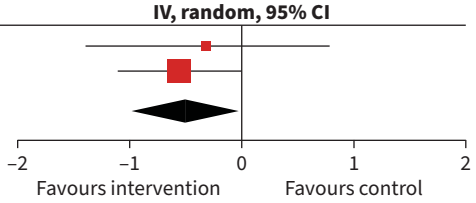
Qualitative findings

Four of the five included studies were of mixed-methods design, with one reporting the qualitative data in two separate reports [26, 27]. Across all studies, qualitative data demonstrated high intervention acceptability to patients and informal carers, along with evidence of a qualitatively positive impact. Participants consistently felt more confident in their ability to cope with breathlessness and reduction of fear was another theme. People valued the positive and personalised approaches of these services, with reinforcement of existing effective coping strategies and advice on practical strategies that delivered meaningful improvements in daily life.

a)

Study or subgroup	Mean difference	SE	Weight (%)	Mean difference IV, random, 95% CI
Study 2, Higginson *et al*. [23]	−0.31	0.5536	21.0	−0.31 (−1.40–0.78)
Study 5, Schunk *et al*. [19]	−0.55	0.2857	79.0	−0.55 (−1.11–0.01)
Total (95% CI)			**100.0**	**−0.50 (−1.00– −0.00)**

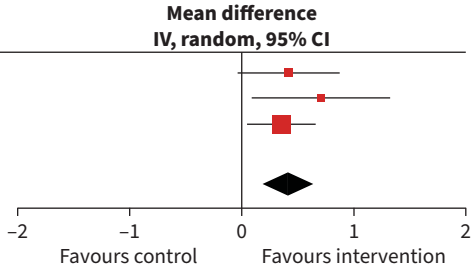
Heterogeneity: Tau²=0.00; Chi²=0.15, df=1 (p=0.70); I²=0%
Test for overall effect: z=1.97 (p=0.05)



b)

Study or subgroup	Mean difference	SE	Weight (%)	Mean difference IV, random, 95% CI
Study 1, Farquhar *et al*. [20]	0.43	0.2296	26.5	0.43 (−0.02–0.88)
Study 2, Higginson *et al*. [23]	0.72	0.3163	14.0	0.72 (0.10–1.34)
Study 5, Schunk *et al*. [19]	0.37	0.1531	59.6	0.37 (0.07–0.67)
Total (95% CI)			**100.0**	**0.43 (0.20–0.67)**

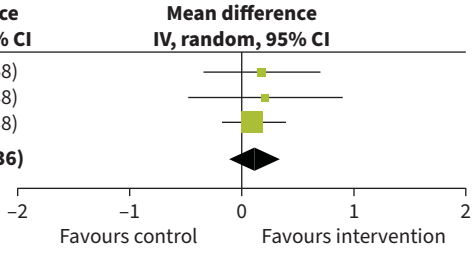
Heterogeneity: Tau²=0.00; Chi²=0.99, df=2 (p=0.61); I²=0%
Test for overall effect: z=3.68 (p=0.0002)



c)

Study or subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight (%)	Mean difference IV, random, 95% CI
Study 2, Higginson *et al*. [23]	2.63	1.19	33	2.46	0.86	31	20.6	0.17 (−0.34–0.68)
Study 4, Pearce *et al*. [21]	0.88	1.24	22	0.68	1.04	22	11.6	0.20 (−0.48–0.88)
Study 5, Schunk *et al*. [19]	0.43	0.85	71	0.33	0.9	80	67.8	0.10 (−0.18–0.38)
Total (95% CI)			**126**			**133**	**100.0**	**0.13 (−0.10–0.36)**

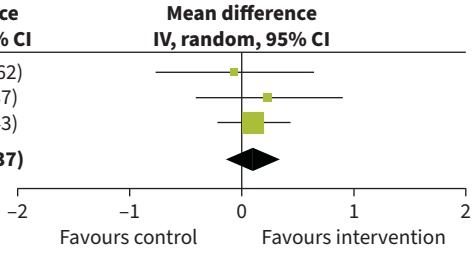
Heterogeneity: Tau²=0.00; Chi²=0.11, df=2 (p=0.95); I²=0%
Test for overall effect: z=1.07 (p=0.28)



d)

Study or subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight (%)	Mean difference IV, random, 95% CI
Study 2, Higginson *et al*. [23]	3.12	1.22	35	3.19	1.59	31	14.4	−0.07 (−0.76–0.62)
Study 4, Pearce *et al*. [21]	0.49	1.16	22	0.26	0.99	22	16.9	0.23 (−0.41–0.87)
Study 5, Schunk *et al*. [19]	0.31	0.91	71	0.2	1.07	80	68.7	0.11 (−0.21–0.43)
Total (95% CI)			**128**			**133**	**100.0**	**0.10 (−0.16–0.37)**

Heterogeneity: Tau²=0.00; Chi²=0.40, df=2 (p=0.82); I²=0%
Test for overall effect: z=0.78 (p=0.43)



e)

Study or subgroup	Mean difference	SE	Weight (%)	Mean difference IV, random, 95% CI
Study 2, Higginson *et al*. [23]	0.3	0.2449	17.3	0.30 (−0.18–0.78)
Study 5, Schunk *et al*. [19]	0.23	0.1122	82.7	0.23 (−0.01–0.45)
Total (95% CI)			**100.0**	**0.24 (0.04–0.44)**

Heterogeneity: Tau²=0.00; Chi²=0.07, df=1 (p=0.79); I²=0%
Test for overall effect: z=2.37 (p=0.02)

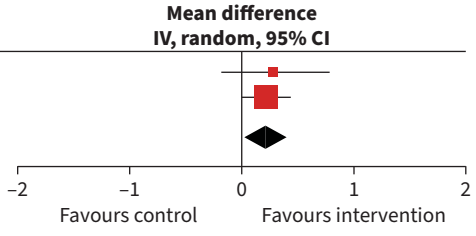


FIGURE 3 Forest plots. a) Average breathlessness intensity over last 24 hours by numerical rating scale 0–10. b) Chronic Respiratory Questionnaire mastery domain. c) Chronic Respiratory Questionnaire dyspnoea domain. d) Chronic Respiratory Questionnaire fatigue domain. e) Chronic Respiratory Questionnaire total score. df: degree of freedom; IV: inverse variance.

Discussion

This systematic review provides evidence that multicomponent services can improve breathlessness mastery and HRQoL in people living with serious respiratory illness. These services were highly valued by patients and their carers, with consistent qualitative evidence for benefit. They were associated with minimal, if any, risk and the one study evaluating mortality found an increase in survival.

The clinical significance of the changes in breathlessness mastery and HRQoL have not been determined. The mean improvements were statistically significant but did not reach the MID. However, the upper

confidence intervals, for the changes in breathlessness mastery and four breathlessness NRS scales, did include the MID, meaning that clinically important differences have not been excluded. Given that the accepted MIDs for these measures have not been generated from people living with serious respiratory illness and the CRQ MID is known to vary with the method used to calculate it, it is possible that smaller improvements may be clinically important [24, 28].

These findings build on those of the main previous systematic review on this topic. Brighton *et al.* [14] evaluated the impact of holistic multicomponent services for people experiencing chronic breathlessness from any advanced disease. Nine of 12 studies included in the meta-analyses only enrolled people with cancer. Distress due to breathlessness (NRS) and depression (Hospital Anxiety and Depression Scale) both improved significantly. Breathlessness mastery (CRQ) also increased but the change was not statistically significant (MD 0.23, 95% CI −0.10–0.55).

Our systematic review included the three studies from the previous review that recruited people with nonmalignant disease, along with one recent large trial which used breathlessness mastery as a primary outcome [19]. Our findings of a significant increase in breathlessness mastery, but not distress due to breathlessness, suggests that breathlessness mastery may be a more relevant outcome measure for people with nonmalignant respiratory conditions. The concept of mastery is consistent with the approach of multicomponent services of empowering and building self-efficacy in symptom self-management [29]. Farquhar *et al.* [20] previously suggested that distress due to breathlessness may be a construct of greater relevance to people with malignant, than nonmalignant, disease, potentially due to distress being less amenable to change in the context of the longer trajectory of nonmalignant disease.

The high value placed on multicomponent services was a strong and consistent finding across all studies collecting qualitative data from patient and carer perspectives. Even in a study without statistically significant quantitative improvements, the qualitative benefits described by participants were considerable [20]. These positive qualitative findings are congruent with several qualitative evaluations of multicomponent breathlessness support services not included in this review [30, 31].

The safety of these services is consistent with their predominantly nonpharmacological approach. Although only one study evaluated mortality, the suggestion of increased survival is of interest [23]. While little can be concluded from a secondary outcome in a single study, this finding is consistent with an emerging body of evidence that survival for people with incurable cancer may improve with early palliative care [32, 33]. The mechanisms for increased survival are not yet known. In lung cancer, quality of life independently predicts survival and longitudinal changes in depression symptoms are associated with differences in mortality [34, 35].

Strengths and limitations

A methodologist ensured that ERS systematic review and meta-analysis methodological requirements were met. The approach avoided risking overestimating the true effect. For example, when both end-point and change data were available, the data type was chosen that would lead to a smaller effect size. If, in each case, the other data type had been chosen, the improvements in breathlessness measures included in the meta-analyses (NRS of average breathlessness in 24 h, CRQ mastery and CRQ dyspnoea) would have all been statistically significant.

These findings are limited by the very low certainty of evidence. The risk of bias was mostly caused by lack of participant blinding to group allocation, loss to follow-up being high or different between arms, and imprecision caused by relatively low participant numbers. Of the five studies, one was a small feasibility study and another published as an abstract only, further increasing the risk of bias. A decision was made to include these because of the low number of eligible studies. The feasibility study did not contribute data to the meta-analyses and the abstract-only study did not significantly influence the findings in the two analyses where it was included.

Although studies evaluating the impact of multicomponent services on any symptom were eligible, breathlessness was the critical symptom in this review and the only symptom included in the search strategy. The search may therefore have missed studies of multicomponent services for symptoms that did not include breathlessness.

Implications for clinical practice

The findings from this review suggest that multicomponent services can be used to reduce symptoms in people living with serious respiratory illness, given their positive impact on breathlessness mastery and

HRQoL, with minimal risk. All studies evaluated services embedded in palliative care and/or respiratory services, suggesting that implementation out of a trial context is likely to be feasible in these settings. The potential to implement this type of approach within primary care is unknown and research programmes in the UK and Australia are attempting to evaluate this.

The cost of these services is low, with a predominantly nonpharmacological intervention and the main resource being staff time. Two of the studies included in this review reported average costs. For one, the average direct costs of five to six health professional contacts over up to 8 weeks were EUR 357 (SD EUR 132) per patient [19]. Another reported an average cost of GBP 156 (SD GBP 80) per patient, intervention involving two to three in-person visits and an average of three telephone contacts over 4 weeks [20]. Given increasing remote healthcare consultations, offering virtual or hybrid multicomponent services could increase their reach at potentially lower cost [36, 37].

A barrier to clinical implementation of symptom-directed services is the lack of recognition that symptoms can be improved by anything other than management of the underlying disease. Chronic breathlessness is often overlooked and considered an inevitable consequence of serious respiratory illness. Training is needed to encourage health professionals to elicit symptoms proactively and to ensure that a symptom-directed approach is taken in parallel with medical optimisation of the underlying condition.

Most studies evaluating multicomponent services recruited participants with cancer-related breathlessness. People with cancer diagnoses can more easily access symptom-directed support through palliative care services than people with nonmalignant disease. Increasing access to multicomponent services for people with nonmalignant disease has potential to reduce this health inequity.

Implications for research

Further research is needed to determine which patients are most likely to benefit from multicomponent services, to facilitate efficient resource use and delivery of personalised healthcare. Future trials should have extended follow-up periods to examine the long-term impact of services. Studies need to recruit participants from diverse backgrounds, including a range of ethnicities, and work is needed to determine how such services can promote health equity.

Future studies should evaluate how best to integrate multicomponent services alongside existing programmes and services, such as pulmonary rehabilitation. Assessment of the acceptability and effectiveness of virtual or hybrid multicomponent services is also needed. Given the high prevalence and morbidity of cough and fatigue in serious respiratory illness, studies are needed to examine the effectiveness of multicomponent services on a range of symptoms, not only breathlessness.

Conclusion

Symptom-directed multicomponent services improve breathlessness mastery and HRQoL. Given their safety, acceptability and potential impact on survival, our findings support the use of multicomponent services for people experiencing symptoms as a result of serious respiratory illness.

Points for clinical practice

- Multicomponent services may be helpful for reducing symptoms in people with serious respiratory illness.
- These services can be implemented within palliative care or respiratory services.
- Health professionals need to recognise chronic breathlessness and understand that the symptom, as well as the disease, can be a therapeutic target.

Questions for future research

- What are the predictors of benefit from multicomponent services in people with serious respiratory illness?
- How long does the benefit from multicomponent services last?
- How can multicomponent services best be integrated with rehabilitation services?
- What is the effectiveness and acceptability of virtual or hybrid multicomponent services for people with serious respiratory illness?
- What is the impact of multicomponent services on the symptoms of fatigue and cough in people with serious respiratory illness?

Provenance: Commissioned article, peer reviewed.

Previous articles in this series: No. 1: Smallwood NE, Pascoe A, Wijsenbeek M, *et al.* Opioids for the palliation of symptoms in people with serious respiratory illness: a systematic review and meta-analysis. *Eur Respir Rev* 2024; 33: 230265. No. 2: Burge AT, Gadowski AM, Romero L, *et al.* The effect of graded exercise therapy on fatigue in people with serious respiratory illness: a systematic review. *Eur Respir Rev* 2024; 33: 240027. No. 3: Burge AT, Gadowski AM, Jones A, *et al*. Breathing techniques to reduce symptoms in people with serious respiratory illness: a systematic review. *Eur Respir Rev* 2024; 33: 240012.

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