From reactive to proactive: implementing palliative care for patients with COPD

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Chapter 3

Effectiveness and implementation of palliative care interventions for patients with chronic obstructive pulmonary disease: A systematic review

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Abstract

Background
Although guidelines recommend palliative care for patients with chronic obstructive pulmonary disease, there is little evidence for the effectiveness of palliative care interventions for this patient group specifically.

Aim
To describe the characteristics of palliative care interventions for patients with COPD and their informal caregivers and review the available evidence on effectiveness and implementation outcomes.

Design
Systematic review and narrative synthesis (PROSPERO CRD42017079962).

Data sources
Seven databases were searched for articles reporting on multi-component palliative care interventions for study populations containing ≥30% patients with COPD. Quantitative as well as qualitative and mixed-method studies were included. Intervention characteristics, effect outcomes, implementation outcomes and barriers and facilitators for successful implementation were extracted and synthesized qualitatively.

Results
Thirty-one articles reporting on twenty unique interventions were included. Only four interventions (20%) were evaluated in an adequately powered controlled trial. Most interventions comprised of longitudinal palliative care, including care coordination and comprehensive needs assessments. Results on effectiveness were mixed and inconclusive. The feasibility level varied and was context-dependent. Acceptability of the interventions was high; having someone to call for support and education about breathlessness were most valued characteristics. Most frequently named barriers were uncertainty about the timing of referral due to the unpredictable disease trajectory (referrers), time availability (providers) and accessibility (patients).

Conclusion
Little high-quality evidence is yet available on the effectiveness and implementation of palliative care interventions for patients with COPD. There is a need for well-conducted effectiveness studies and adequate process evaluations using standardized methodologies to create higher-level evidence and inform successful implementation.

Keywords: Chronic obstructive pulmonary disease, palliative care, breathlessness, quality of life, systematic review

What is already known about the topic?

- Patients with advanced COPD have a high symptom burden and impaired quality of life. Although guidelines recommend palliative care for patients with COPD, implementation remains often challenging and an up-to-date overview of the evidence on its effectiveness is lacking.

What this paper adds?

- This review provides a comprehensive overview of evidence on the effectiveness and implementation of palliative care interventions targeting patients with COPD and their informal caregivers.
- Within different care contexts, short-term palliative care assessments as well as longitudinal palliative care interventions with care coordination have been implemented. Highly valued intervention characteristics are the direct access to a professional for support, an ongoing relationship with a professional and education about breathlessness.
- Few interventions have been evaluated using a controlled study design. Positive effects were found on outcomes related to advance care planning and perceived symptom control and self-management, but not on health outcomes.

Implications for practice, theory or policy

- Research on palliative care in COPD should focus on what is important to patients with end-stage COPD and their informal caregivers. More knowledge is needed on which outcomes best reflect their needs.
- Controlled studies with sufficient power are needed to evaluate the effectiveness of palliative care on patients with COPD and their informal caregivers.

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is the third leading cause of death worldwide.[1] Patients suffering from end-stage COPD experience severe breathlessness and other debilitating symptoms such as fatigue, pain, anxiety and depression, leading to poor quality of life and emphasizing the need for adequate palliative care.[2] Palliative care aims to improve the quality of life of patients with a life-threatening disease and their families by early identification, assessment and treatment of physical, psychological, social and spiritual problems.[3] Growing evidence suggests that palliative care, in general, has positive effects on quality of life and can decrease symptom burden in patients with life-limiting illnesses. Additionally, it can improve patient and informal caregiver satisfaction with care and reduces healthcare utilization.[4] However, for patients with advanced COPD, palliative care is not yet part of standard care, and discussions about goals of (end-of-life) care rarely take place, or only late in the disease course.[5] As a consequence, their severe symptoms remain undertreated, and a large proportion of this patient group inadvertently dies in the hospital. [6, 7] Moreover, the long disease course with declining functional capacity affects their informal caregivers.[8]

Implementing palliative care for patients with COPD is challenging. Due to the unpredictable disease trajectory, healthcare professionals struggle to determine when to refer patients for specialized palliative care.[9] Further, palliative care for patients with COPD needs to be differently organized than for oncological patients because it demands integration of palliative care and disease-oriented care until the end-of-life.[10] The implementation of palliative care in COPD-care is further complicated as professionals must perform actions they are not used to, such as discussing holistic needs and end-of-life topics.[9]

Although guidelines recommend palliative care for patients with COPD, there is little evidence for the effectiveness of palliative care interventions for this patient group specifically.[11, 12] In previous systematic reviews, the vast majority of the interventions described were designed for patients with cancer[4, 13, 14] or focused on a single intervention component only.[15-17] Research on the effectiveness of interventions that integrate multiple components of palliative care for patients with COPD is still lacking.[18] Further, it remains unclear how palliative care can be organized for this patient group and what are requirements for successful implementation. Finally, no reviews have included intervention outcomes at the level of the informal caregiver and professional.

To guide future palliative care provision for patients with COPD and to identify gaps in the current evidence-base, we, therefore, aimed to review multi-component palliative care interventions targeting patients with advanced COPD and their informal caregivers. Specifically, we aimed to:

1. Synthesize the characteristics of multi-component palliative care interventions targeting patients with COPD and their informal caregivers;

2. Review the evidence for the effectiveness of those interventions on patient, informal caregiver and healthcare professional outcomes;
3. Review the evidence on implementation outcomes and barriers and facilitators of implementation.

Methods

The protocol of this systematic review has been registered in the international Prospective Register of Systematic Reviews (PROSPERO) database (ID: CRD42017079962). We used the Cochrane Handbook for Systematic Reviews of Interventions to perform the review, and followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement for reporting.

Literature search

The electronic databases MEDLINE, Embase, Web of Science, COCHRANE Library, PsycINFO, CENTRAL and Emcare were searched for eligible studies. In the search strategy, we combined a broad range of synonyms of the search terms "COPD" and "palliative care" (Supplementary table 1). Articles that were published between 1 January 1990 and 9 June 2020 were screened for inclusion, without language restrictions. We searched for other potentially relevant studies by screening the reference lists and citations of included studies.

Study selection

Articles reporting on primary research data of multi-component palliative care interventions targeting patients with COPD were included. The intervention described in the article needed to be referred to as a palliative care or end-of-life care intervention, program or approach. We defined a multi-component intervention as an intervention comprising multiple components which interact to produce change, following the complex intervention definition of the Medical Research Council.[19] Interventions focusing only on a single component (such as advance care planning or opioids for breathlessness) were excluded. If the study population was mixed, articles were included if at least 30% of the study population suffered from COPD. Case reports and non-primary research data, such as reviews, editorials, conference abstracts and books were excluded. We also included uncontrolled before-and-after studies, qualitative and mixed-method studies, as this 1) reflects the most frequent type of studies performed and provides a comprehensive overview of all available evidence, and 2) because we wanted to gain in-depth insight into mechanisms or elements contributing most to intervention effectiveness and successful implementation. Title and abstract screening and subsequent full-text screening was done by two reviewers independently (J.B., and J.S. or A.H.). In case of any incongruences, the in- or exclusion of an article was discussed until consensus was reached. In case of doubt, a third researcher (R.K.) was consulted.

Data extraction

Data on design, participants, intervention characteristics and all reported outcomes at patient, informal caregiver and healthcare professional level were extracted using a piloted extraction form. If necessary and possible, additional data was derived from published study protocols or supplementary documents, or requested from the authors. Data extraction of the included articles was done by two reviewers independently (J.B. as first reviewer for all articles and A.H., D.J., Y.E. or R.K. as a second reviewer). Any incongruencies were discussed until consensus was reached. Implementation outcomes and barriers and facilitators for implementation were extracted by one reviewer (J.B.) and discussed with a second reviewer who has great expertise in implementation (R.K.).

Quality appraisal

Quality appraisal was performed by two reviewers (J.B. and A.H.) independently, using the Mixed Methods Appraisal Tool.[20] After two screening questions, each study is appraised by rating appraisal criteria for the corresponding category. Any discrepancies in the quality appraisal were resolved by discussion, and if needed, a third reviewer (R.K.) was consulted. To compare study quality, we assigned four stars to a study when 75 to 100% of the criteria were positively rated (high quality), three stars for 50-75% (moderate quality), two stars for 25-50% (low quality) and one star for 0-25% (very low quality).

Data analysis

Data were analysed using narrative synthesis.[21] Study characteristics were summarized in terms of country, design, objective, study participants, inclusion strategy, intervention and organizational characteristics and outcomes. The intervention components were categorized according to twelve palliative care domains based on the Dutch Quality Framework Palliative care,[12] Clinical Practice Guidelines for Quality Palliative Care[22] and Quality standard End of life care for adults.[23] The operationalization of domains is described in Supplementary table 2. Outcomes were classified into three categories: outcomes at patient, informal caregiver, and healthcare professional level. Quantitative results reported in studies in which no statistical testing was performed, were disregarded. The text in articles reporting on qualitative outcomes was coded phrase by phrase after which common themes were identified.[24] We categorized implementation outcomes following the proposed terminology and operationalization of Proctor et al[25] (see Supplementary table 3). According to Proctor et al, implementation outcomes are defined as "the effects of deliberate and purposive actions to implement new treatments, practices, and services" [25] (page 65). Process outcomes reflecting trial feasibility (and not intervention feasibility) were not evaluated. Barriers and facilitators to implementation of palliative care interventions were categorized using the framework of Fleuren et al.[26] This instrument consists of 29 determinants in four categories: determinants associated with the (a) innovation, (b) adopting person, (c) organization and (d) socio-political context. We extracted determinants for three types of users: referrers (professionals who refer patients to the palliative care intervention),

providers (professionals who provide the intervention) and patients (individuals who receive the intervention). If needed, determinants of the Consolidated Framework for Implementation Research[27] or newly defined determinants were added inductively. The codebook used is available in Supplementary table 4.

Results

The database search yielded 5621 unique records. In total, 166 articles were excluded based on publication date. Next, we excluded 5310 articles based on title-abstract screening. The full-text versions of the remaining 145 articles were assessed for eligibility. Twenty-three of them met inclusion criteria. Screening of references and citations of included articles identified eight additional articles. A flow diagram of the study selection is displayed in figure 1. Finally, 31 articles were included that reported on 20 unique palliative care interventions; six interventions were evaluated in more than one article.

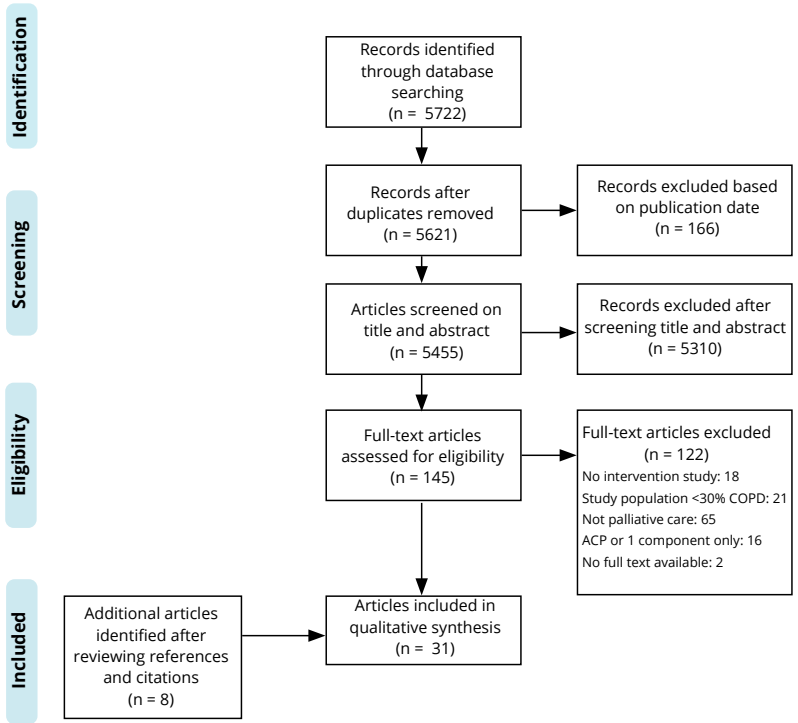

Figure 1. PRISMA flow diagram of the study selection process.

Study characteristics

Characteristics of included studies and interventions are summarized in Table 1. All studies took place in western countries, of which most in the USA (n=5) and the United Kingdom (n=4). Three RCTs[28-30], two non-randomized controlled trials[31-33], seven uncontrolled before-and-after studies[34-41], six qualitative studies[42-47], one non-comparative study[48] and ten pilot/feasibility studies[37, 49-54 55-57] were included. The study design of one article was unclear.[58] Two articles reported on the same study and were collated.[32, 33] Five quantitative studies[30, 33, 35, 41, 48] and six pilot/feasibility studies[37, 50-52, 54, 55] also included qualitative data. Eighteen studies (60%) focused specifically on COPD. Other studies focussed on refractory breathlessness[29, 30, 38, 42, 43, 54] or also included patients with heart failure[28, 34, 44, 58] or heart failure and cancer[33, 45]. Sample sizes in quantitative studies ranged from 13 to 228 patients and in qualitative (sub)studies from 6 to 78 patients. The mean age of study populations ranged between 63 and 76 years.

Intervention characteristics

Half of the interventions were developed based on literature according to the description in the article; two were based on specific guidelines. Thirteen of the twenty interventions comprised of longitudinal care in which there was regular contact of a nurse with patients via home visits[28, 34-36, 39, 44, 55, 57], outpatient visits[31, 33, 47] or a combination of both[38]. Vitacca et al. included telemonitoring.[56] The majority of longitudinal care interventions included symptom management and needs assessments, disease education and self-management, advance care planning and care coordination. Informal caregiver support was incorporated in eight interventions and consisted of caregiver education,[28, 30, 33, 35, 38] nurse assessment of needs[28, 33, 44, 55, 57], invitation to support groups[33] and respite care[38] and was unspecified in Iupati et al.[36] Most were organized by a community care organization, such as a hospice care service or home service. Six other interventions comprised of one comprehensive needs assessment with a short follow up.[29, 30, 37, 52-54] They included one to four home visits and/or outpatient visits and were mostly organized by pulmonary care and palliative care departments. Four interventions specifically focussed on the management of breathlessness[29, 30, 37, 54] and comprised of various pharmacological and non-pharmacological interventions to address breathlessness and how to cope with this symptom. Farquhar et al. also included informal caregiver education. Lastly, one intervention was a 6-week multidisciplinary geriatric rehabilitation program in a specialist nursing facility. Patients in need of palliative care were proactively identified by six interventions, by screening patients during hospitalization for acute exacerbation[31, 40, 52] or by using a computerized screening program based on diagnosis and hospitalizations or measures of disease severity.[33, 34] In most other cases, patients were referred to the service by healthcare professionals.

Table 1. Description of included studies and palliative care interventions.

Included studies			Intervention description							
Author (year)	**Study design**	**Sample size**	**Intervention name; Development**	**Country**	**Coordinating organization**	**Intervention**	**Conditions**	**Healthcare professionals**	**Contacts**	**Duration (months)**
Aiken[28]	RCT	190 patients	Phoenix care program; N.S.	USA	Hospice care service	Home-based case management focused on disease and symptom management, patient and caregiver education, social and psychological support and preparation for end of life through discussing legal documents	COPD, HF	N Other team members: P, SW, SPI	Combined home visits and phone calls	3 – 18, until death or referral to hospice
Lockhart[58]	Unclear	N.S.								
Bove[47]	Q	7 pulmonary nurses, 3 pulmono-logists, 2 municipal nurses	CAPTAIN; Based on literature	Denmark	Hospital (outpatient pulmonology department)	A new outpatient structure in which patients are assigned to a nurse, with ad hoc consultations depending on patient's needs and annual advance care planning discussions	COPD	NR, PM	Outpatient consultations depending on patient's needs and annual advance care planning	Until death
Bove[46]	Q	10 patients								
Buckingham[52]	RCT +Q (pilot/ feasibility)	RCT: 32 patients Q: 8 patients, 3 carers and 28 SWs or HCPs	HELP-COPD program; based on Systematic literature review (step 1 MRC framework)	UK	Hospital (pulmonology department)	Holistic assessment of physical, psychological, social and spiritual needs 4 weeks after an hospital admission for an acute exacerbation	COPD	NR	1 home visit, 3 phone calls for follow up	6
Duenk[31]	CCT	228 patients	PROLONG study; based on national guideline Palliative care in COPD	Netherlands	Hospital (specialized palliative care team)	Proactive palliative care plan and monthly meetings with specialized palliative care team trained in palliative care in COPD	COPD	PCN or PCP Cooperation with PM	In- or outpatient consultation and monthly meetings outpatient or via phone	12, or until death
Edes[34]	BA	43 patients	Home-based Primary care program + non-VA community hospice agency; N.S.	USA	Home care	Home care including symptom management and advance directive discussions, assessing nutrition, nursing needs, spiritual/religious concerns, depression, community support services, financial matters, family communication, functional status, mobility and home safety	COPD, HF	N, OT and SW Other team members: D, GER	1 to 9 home visits per month based on clinical judgement	Median=6
Farquhar[30]	RCT +Q	RCT: 87 patients, 57 carers Q: 78 patients or patient-carer dyads	Breathlessness Intervention Service; Based on literature review (step 1 MRC framework)	UK	Palliative care department in a tertiary referral and cancer centre	Assessment of breathlessness and symptom management including a hand-held fan, education, learning an anxiety-reduction technique and a mindfulness meditation CD, deciding a management plan, designing an exercise program, and assessing the carer's needs.	refractory breathless-ness	PT and PCP	1 home assessment, 3 outpatient visits, phone call for questions	1
Farquhar[49]	RCT +Q (trial feasibility)	RCT and Q: 13 patients, 12 carers								
Farquhar[50]	BA +Q (pilot/ feasibility)	13 patients a								
Booth[42]	Q	10 patients, 9 carers, 4 GPs, nurses								
Higginson[29]	RCT	105 patients	Breathlessness Support Service; based on previous studies on holistic breathlessness services,	UK	University hospital (respiratory medicine and palliative care)	Multi-professional service with holistic assessment and optimization of disease-management with a breathlessness pack including information,	refractory breathless-ness	PM, PCP, PT, OT Other team members: SW	1 home visit and 2 outpatient visits	1

Table 1. *Continued*

Included studies			Intervention description							
Author (year)	**Study design**	**Sample size**	**Intervention name; Development**	**Country**	**Coordinating organization**	**Intervention**	**Conditions**	**Healthcare professionals**	**Contacts**	**Duration (months)**
Higginson[29]	RCT	105 patients	systematic literature review and local stakeholders consultation			management and pacing guidance, a hand-held fan or water spray, and a short mantra to help breathing and relaxation during crises and a crisis plan				
Reilly[43]	Q	25 patients								
Horton[53]	BA (pilot/ feasibility)	30 patients, 18 carers	COPD IMPACT study; based on existing needs assessment and adapted existing education material	Canada	Hospice care service	Education on disease self management and end-of-life issues and comprehensive palliative care consultation and treatment plan	COPD	N, RT Other team members: P	1 home visit, weekly phone contact and follow up visits if needed	4
Iupati[36]	BA	73 patients	GP Led and Hospice Led community program; N.S.	New Zealand	Hospice care service	GP led program: case management and 24-h access to hospice nursing advice and visits. Hospice led program: 24-h access to nursing and medical team advice and consultations	COPD	PCP, PCN, GP	Hospice doctor's visits and nurses' visits. Inpatient hospice care if needed. Phone advice if needed.	Undefined
Janssens[57]	RCT (pilot/ feasibility)	49 patients	Early palliative care; based on literature review	Switzerland	Community ambulatory palliative care team	Monthly home visits for symptom assessment and management, disease education, advance care planning, support of relatives, social and spiritual support, care coordination	COPD	PCN and PCP	Monthly home visits	12
						and alternative approaches such as relaxation, reflexology, massages				
Johnston[44]	Q	6 patients, 6 carers, HCPs, stakeholders	EOLC-LTC service; N.S.	UK	Primary care service	Community service providing palliative care assessment and care planning, information on disease process, treatment, medication, local and national services, advice on symptom control and psychological support for patient/carer	COPD, HF	PCN	Home visits	Undefined
Long[37]	BA +Q (pilot/ feasibility)	BA: 15 patients Q: 13 patients	Advance practice nurse-delivered palliative care intervention; based on existing scientific evidence for intervention elements	USA	Tertiary care pulmonary specialty medical centre	Pharmacologic and non-pharmacologic interventions for dyspnea, anxiety, and depression, including pursed-lip breathing, activity pacing, fan, morphine, relaxation exercises, anxiolytics, psychotherapy referral and antidepressants	COPD	N Other team members: PM	3 outpatients visits, phone call weekly	3
Qian[54]	BA +Q (pilot/ feasibility)	BA: 26 patients Q: 9 patients	Advanced Lung Disease Service – short term; N.S.	Australia	Hospital (respiratory and palliative care)	Integrated respiratory and palliative care service providing individualized breathlessness plan, information leaflets, breathlessness education and hand-held fan	refractory breathless-ness, non malignant	NR, PM	2 outpatient visits in clinic	1.5

Table 1. *Continued*

Included studies			Intervention description							
Author (year)	**Study design**	**Sample size**	**Intervention name; Development**	**Country**	**Coordinating organization**	**Intervention**	**Conditions**	**Healthcare professionals**	**Contacts**	**Duration (months)**
Rabow[33]/ Rabow[32]	CCT +Q	CCT: 90 patients Q: 50 patients	Comprehensive Care Team; N.S	USA	General medicine practice	Outpatient comprehensive palliative care consultation service including assessment of needs and end-of-life orientation, education, and services	COPD, HF, cancer	SW, N, SPI, P, ADV Other team members: PSY, PHA, ART	At start, at 6 and 12 months outpatient visit. Home visits by volunteers each month, phone contact each week.	12
Rabow[45]	Q	50 patients								
Rocker[35]	BA +Q	BA: 257 patients Q: 18 patients	INSPIRED COPD Outreach program; reported to be evidence based not further specified	Canada	Community service	Hospital-to-home COPD care focused on improved care transitions, patient and family education and self-management, action plans for exacerbation psychosocial and spiritual needs assessment and support and advance care planning	COPD	RT, SPI Other team members: SW, P, N	4 home visits, access to phone support	3 - 6
Gillis[51]	BA +Q (pilot/ feasibility)	BA: 15 patients Q: 14 patients								
Rocker[41]	BA +Q	19 healthcare professional teams								
Verma[48]	Non-comparative +Q	19 healthcare professional teams								
Scheerens[55]	RCT +Q (pilot/ feasibility)	RCT: 39 Q: 9 patients, 4 ICGs, 10 GPs, 5 PMs, 4 home PCNs	Early Integrated Palliative Homecare; based on explorative literature review, expert consultations, and focus groups (step 0-1 MRC framework)	Belgium	Home care	Palliative homecare including leaflets on coping mechanisms, protocol on symptom management and support, a care plan and action plan	COPD	PCN	Monthly home visits	6
Smallwood[38]	BA	171 patients	Advanced Lung Disease Service – long term; N.S.	Australia	Hospital (respiratory and palliative care)	Integrated respiratory and palliative care service providing long-term holistic care, individualised symptom management and disease optimisation, self-management education, routine discussion of goals of care and breathlessness management including breathing techniques, activity pacing and handheld fan	refractory breathless-ness, non malignant	NR, PM, PSY, PCP Other team members: EDP, GER, PSY	Clinic or home visits and phone support	Depending on patient's needs (median 15)
Steinel[39]	BA	30 patients	Pulmonary Disease Management Program; N.S.	USA	Home healthcare service	Long-term and continuous home healthcare by pulmonary specialty team, including a palliative care model to manage dyspnoea, loss of functional capacity and emotional suffering	COPD	NR	Home care until death, access to a team member at all times	24, or until death
Van Dam[40]	BA	61 patients	GR-COPD program; based on national and international guidelines on pulmonary rehabilitation and palliative care	Netherlands	Specialized nursing facility	Tailored geriatric rehabilitation programme including inhalation techniques, smoking cessation, control of symptoms, physiotherapy, occupational therapy, nutritional	COPD	GER, N, PT, PSY, OT, SLP, D, SW	6-week inpatient rehabilitation program. 18–22 h of nursing care and 4 h of individual therapy per week	1.5 (median 35 days)

Table 1. *Continued*

Included studies			Intervention description							
Author (year)	**Study design**	**Sample size**	**Intervention name; Development**	**Country**	**Coordinating organization**	**Intervention**	**Conditions**	**Healthcare professionals**	**Contacts**	**Duration (months)**
						status, psychosocial intervention aimed at depression, anxiety or adverse coping strategies, self-management strategies and peer support contact, spiritual needs, advance care planning				
Vitacca[56]	BA (pilot/ feasibility)	10 patients	Tele-assisted palliative homecare; based on previous studies on tele-assisted care	Italy	Hospital (respiratory rehabilitation unit)	An inpatient advance care planning talk and post-discharge pulse oximetry recording and regular telephone monitoring including palliative care assessments	COPD	P, N	1 inpatient talk and weekly telephone monitoring after discharge and monthly palliative assessment	6

[a] Farquhar et al. (2009) and Farquhar et al. (2010) report on the same study population, but each uses a different study design and thus were considered as separate studies.

Abbreviations: ADV, volunteer patient advocate; ART, art therapist; BA, before and after study; CCT, non-randomized clinical controlled trial; COPD, chronic obstructive pulmonary disease; D, dietitian; EDP, emergency department physician; GER, geriatric medicine physician; GP, general practitioner; HCP, Healthcare professional; HF, heart failure; N.S., not stated; N, nurse, nurse practitioner, advanced practice nurse; NR, respiratory nurse specialist or nurse trained in respiratory medicine, OT, occupational therapist; P, physician undefined; PCN, palliative care nurse; PCP, palliative care physician; PHA, pharmacist; PM, pulmonologist; PSY, psychologist; PT, physiotherapist; Q, qualitative study; RCT, randomized controlled trial; RT, respiratory therapist; SLP speech and language pathologist; SPI, spiritual care practitioner, chaplain or pastoral counsellor; SW, social worker; UK, United Kingdom; USA, United States of America.

Table 2. Addressed domains by palliative care interventions for patients with COPD.

Intervention (references)	Structure & process						Dimensions				End of life	
	Identification	**Advance Care Planning**	**Individual care plan**	**Informal care giver support**	**Interdisciplinary care**	**Care coordination**	**Physical**	**Psychological**	**Social**	**Spiritual**	**End of life care**	**Bereavement care**
Aiken et al.[28, 58]		✓		✓	✓	✓	✓	✓	✓	✓		
Bove et al.[47]		✓				✓	✓	✓				
Buckingham et al.[52]	✓		✓				✓	✓	✓	✓		
Duenk et al.[31]	✓	✓	✓		✓		✓	✓	✓	✓		
Edes et al.[34]	✓	✓			✓	✓	✓		✓	✓		
Farquhar et al.[30, 42, 49, 50]				✓	✓		✓	✓	✓			
Higginson et al.[29, 43]					✓		✓	✓		✓		
Horton et al.[53]		✓	✓		✓	✓	✓	✓	✓	✓		
Iupati et al.[36]		✓		✓		✓	✓	✓	✓	✓	✓	
Janssens et al.[57]		✓		✓	?	✓	✓	✓	✓	✓		
Johnston et al.[44]		✓		✓		?	✓	✓				
Long et al.[37]							✓	✓				
Qian et al.[54]					✓		✓	✓				
Rabow et al.[32, 33, 45]	✓	✓		✓	✓	✓	✓	✓	✓	✓		
Rocker et al.[35, 41, 48, 51]	✓	✓		✓	✓	✓	✓	✓	✓	✓		
Scheerens et al.[55]		✓	✓	✓		✓	✓	✓	✓	✓		
Smallwood et al.[38]		✓		✓	✓	✓	✓	✓	✓			✓
Steinel et al.[39]						?	✓	✓				
Van Dam et al.[40]	✓	✓	✓		✓		✓	✓	✓	✓		
Vitacca et al.[56]		✓				?	✓	✓	✓	✓		

Quality appraisal

Ratings of the criteria of the Mixed Methods Appraisal Tool per study are provided in Supplementary table 5. Quality of the studies was related to the study design used. All three RCTs were of high quality; non-randomized controlled trials and qualitative studies were of moderate to high quality; study quality of uncontrolled studies ranged from very low to moderate. The quality of pilot/feasibility studies varied from low to high. Two articles were not appraised as they did not pass the screening questions.[35, 58] The following reasons most frequently contributed to a negative rating: lack of information on intervention adherence in controlled trials, insufficient use of quotations that supported interpretations of results in qualitative studies, and absence of adjusting for confounding in uncontrolled studies. In studies with both a quantitative and qualitative component, there often was poor integration of the two components.

Quantitative outcomes

Quantitative results are summarized in Table 3. The most frequently evaluated outcomes were acute healthcare use, health-related quality of life and psychological outcomes. Four out of seven controlled studies reported a primary outcome: mastery of breathlessness[29], distress due to breathlessness[30], health-related quality of life[31] and pain[32]. Janssens et al. had initially planned to measure acute healthcare use as primary outcome.[57] However, they did not reach sufficient power to do so due to severe recruitment issues. One study found a statistically significant positive effect on its primary outcome; Higginson et al. reported a difference in mastery of breathlessness between intervention and control group of 0.58 (0.01 to 1.15).

Outcomes at patient level

Quality of life – Health-related quality of life was assessed in ten studies,[28, 29, 31, 32, 35, 37, 40, 55-57] using seven different measurement instruments. Duenk et al. set health-related quality of life as their primary outcome. Their study and that of Aiken et al. found significant differences between the intervention and control group on specific subscales but not on the total scale.[28, 31] The uncontrolled study of Van Dam et al. reported an improvement on health-related quality of life;[40] all other studies found no differences.[28, 29, 31, 32, 35, 37]

Breathlessness – In two RCTs evaluating holistic breathlessness services,[29, 30] intervention patients showed higher levels of mastery of breathlessness, but only one study found a statistically significant difference.[29] No difference was found on distress due to breathlessness in one RCT.[30] In the study of Rabow et al, intervention patients reported a lower degree of breathlessness interference with daily activities and limitations in daily life compared to control patients.[32] Two other controlled studies did not find an effect on breathlessness intensity.[29, 37]

Anxiety and depression – Rabow et al. reported reduced anxiety in intervention patients, but no change in depression.[32] Eight other studies found no significant differences.[29-31, 35, 37, 55-57]

Other health-related outcomes – Aiken et al. found lower symptom distress in intervention patients at three months, but not at six months.[28] Further, positive effects were reported for the resumption of activities,[28] sleep quality,[32] functional capacity[40] and nutritional status[40].

Spiritual Well-being / Hope – In the study of Rabow et al., intervention patients reported higher overall spiritual well-being than control patients.[32] One study evaluating hope found no difference after the intervention.[35]

Self-management – The study of Aiken et al. revealed an improvement in illness self-management and awareness of resources, at specific time points.[28] Rocker et al. found a positive result on the quality of preparation for self-care[35, 41] and need for information after program participation.[41]

Health care use – Mixed results were found regarding unplanned health care use. Controlled studies showed no effect on the number of emergency department visits or hospitalizations.[28, 31, 32, 55, 57] Uncontrolled studies revealed reduction in the number of emergency department visits and hospitalizations.[35, 38, 39 34-36, 39] One pilot RCT reported more hospitalizations in the intervention group than the usual care group.[55] A comparison of deceased intervention patients with other decedents showed a shorter median length of stay at the Intensive Care Unit.[35]

Advance care planning – Five studies found that, for intervention patients, a personal directive and advance care planning choices were more often documented,[28, 31, 35, 57] and funeral arrangements were more likely to be completed.[32]

Site of death – One controlled study examining site of death found no differences between intervention and control group.[32]

Satisfaction with care – Two controlled studies found no difference between intervention and control group regarding satisfaction with care; [32, 55] the uncontrolled study of Edes et al. reported an improvement.[34]

Outcomes at informal caregiver level

Only one study examined outcomes at informal caregiver level and found no differences in caregiver distress due to patient breathlessness, nor on anxiety and depression between the intervention and control group.[30]

Outcomes at healthcare professionals' level

Outcomes at professional level were only assessed in one uncontrolled study. A positive effect on several skills regarding quality improvement and implementation was reported.[48]

Costs

Two controlled studies found no difference in healthcare costs of intervention patients,[30, 32] of which one also evaluated cost-effectiveness and found high costs gained per quality-adjusted life-year.[30] Three uncontrolled studies reported lower healthcare costs per patient in the period after the start of the intervention.[34, 35, 39]

Qualitative outcomes

Qualitative outcomes were derived from interviews in fourteen qualitative (sub)studies.[30, 35, 37, 41-48, 52, 54, 55] In most studies, patients reported improved self-confidence to manage symptoms[30, 35, 37, 41, 43, 44, 46] and positive psychological effects.[30, 35, 37, 43, 45, 52] Besides, in some cases, hospitalization was prevented due to earlier diagnosis and treatment.[44-46] Regarding informal caregivers, increased confidence was reported because they knew how they could help their relatives with breathlessness.[30, 42] Regarding healthcare professionals, nurses providing palliative care got more insight in and understanding of the suffering of patients with COPD and complexities around COPD-care.[47, 48]

Table 3. Summary of quantitative outcomes and results at the level of the patient, informal caregiver and healthcare professional, and costs. The direction of effects and references are shown.

	Study design				
	RCT	**Pilot RCT**	**CCT**	**BA**	**Pilot BA**
Patient					
Quality of life	⭘28 ○29	○57 ○55	○31 ○32	●40 ○35	○37 ○56
Breathlessness intensity	○29		●32		○37
Breathlessness affect	●29 ○30				
Anxiety / Depression	○29 ○30	○57 ○55	⭘32 ○31	○35	○37○56
Other health-related outcomes	⭘28 ○29	○57○55	⭘32	●40	○56
Spiritual Wellbeing/Hope			●32	○35	
Self management	⭘28			●35 ●41	
ED visits	○28	○57	○32	●35 ●38 ●39	
Hospital admissions		○57 ⊘55	○31 ○32	●34 ●35 ●36 ●39 ○38	
Advance care planning	⭘28	●57	●31 ●32	●35	
Site of death			○32		
Satisfaction with care		○55	○32	●34	
Informal caregiver					
Caregiver distress due to patient breathlessness	○30				
Anxiety/Depression	○30				
Healthcare professional					
Team skills acquisition				●41	
Costs	○30		○32	●34 ●35 ●39	

The direction of effects and references are shown.
● = Positive effect—if, after statistical analysis, a significant effect was reported favouring the intervention group (RCT and non-randomized controlled studies), or positive effect between baseline and after intervention (before-and-after studies).
○ = No statistically significant effect—if, after statistical analysis, no significant effect was reported.
⭘ = Mixed effects—if in that specific outcome category, more than one outcome was reported with both positive and no effects.
⊘ = Negative effect—if, after statistical analysis, a significant effect was reported favouring the control group (RCT and non-randomized controlled studies), or a negative effect between baseline and after intervention (before-and-after studies).
BA: before and after study; CCT: non-randomized clinical controlled trial; ED: emergency department; RCT: randomized controlled trial.

Implementation outcomes and barriers and facilitators

Implementation outcomes

In the included studies, acceptability and feasibility were the most frequently assessed implementation outcomes. Supplementary table 3 provides the operationalization of implementation outcomes. Acceptability was mostly assessed by interviewing patients,[42, 44, 45, 52, 54 46, 55] informal caregivers and referring healthcare professionals,[42, 44, 52] but also by using a questionnaire among participants[43] or by collecting patient stories anecdotally.[58] All studies reported that patients, informal caregivers and healthcare professionals valued the palliative care intervention. Components of the interventions that were highly valued included being listened to and direct access to a professional for support,[30, 35, 42, 44, 46, 50, 55], continuity of the relationship[44, 46] and education about breathlessness management.[30, 35, 42, 43, 50, 55] Specifically regarding breathlessness, non-pharmacological interventions such as a hand-held fan and

Table 4. Barriers and facilitators for implementation (determinants) of referrers, providers and patients that were present in ≥3 studies.

User type	Determinant	Category	Direction (references)	Example (reference)Referrer
Referrer				
	Relevance for patient	Innovation	Facilitator[33,42,52]	The innovation was perceived as helpful for patients, which motivated professionals to refer patients.[52]
	Awareness of content of innovation	Adopting person	Barrier[44,51,58]	Referrers were not aware that the service existed, which hampered referral of patients to the innovation.[44]
	Disease-specific characteristics	Adopting person	Barrier[33,41,44]	Due to the unpredictable disease trajectory of COPD, referrers found it challenging to determine whether a patient was at the end of life, and thus eligible for referral to the innovation.[44]
Provider				
	Time available	Organization	Barrier[33,41,44, 48,51,55]	Staff were unable to dedicate adequate time to the improvement efforts.[33]
	Staff capacity	Organization	Facilitator[58] Barrier[33,53]	Consistent staffing by knowledgeable people aware of the program goals contributed to a smooth implementation of the innovation.[58]
	Compatibility	Innovation	Facilitator[48] Barrier[44,52]	The timing of the assessment meant that actions overlapped with existing discharge planning.[52]
	Financial resources	Organization	Barrier[33,48,53]	Lack of continuous resourcing was a barrier to implementation.[48]
Patient				
	Accessibility	Innovation	Barrier[33,37,41,52,53]	Patients experienced difficulty travelling to ambulatory services.[53]

breathing techniques were reported to be most helpful.[30, 42, 43, 54, 55] Four studies reported on intervention feasibility using predefined feasibility criteria (e.g. participation rates and completion of the program).[37, 51, 52, 55]

The feasibility level varied and was mostly related to specific intervention context characteristics. For instance, Buckingham et al. encountered fewer actions during assessments than expected due to overlap of their service with existing discharge services.[52] Two studies reported on the completion of program components (fidelity)[37, 51] and one on usefulness (appropriateness) as one of the feasibility criteria.[37] One study evaluating nationwide dissemination of their approach reported on adoption and sustainability;[41, 48] Fifteen of nineteen teams to which the intervention was disseminated incorporated all core interventions of the program and reported sustained improvements.

Barriers and facilitators for implementation

In ten articles barriers and facilitators for implementation (determinants) of nine different palliative care interventions were reported,[33, 37, 41, 42, 44, 48, 51-53, 55, 58] mostly derived from interviews with referring healthcare professionals and intervention participants. Determinants for referrers, providers and patients that were present in three or more studies are shown in Table 4. All determinants are shown in Supplementary table 6.

Discussion

Main findings

This study reviewed the characteristics of multi-component palliative care interventions for patients with COPD and the available evidence on their effectiveness and implementation, to provide guidance on future palliative care provision and to identify knowledge gaps in the literature. We found that a range of longitudinal and short-term interventions in different care settings has been developed to enhance palliative care provision to patients with COPD. Although the acceptability of the interventions was high among patients, informal caregivers and healthcare professionals, we found only limited evidence on their effectiveness. Quantitative and qualitative data suggest positive effects related to perceived symptom control, self-management and self-confidence. Most frequently named barriers to implementation were uncertainty about the timing of referral due to the unpredictable disease trajectory (referrers), time availability (providers) and accessibility (patients).

Interpretation of findings

The current evidence for multi-component palliative care interventions for patients with COPD is scarce and inconclusive; only four interventions (20%) were evaluated in an adequately powered controlled trial; eight (40%) were evaluated in a pilot or feasibility study only. The assessed outcome measures were heterogenous, and only a few statically significant effects were found.

Six out of seven studies found no positive effect on quality of life. This can be due to several reasons. First, just one study had quality of life set as primary outcome[31] and therefore most studies were not powered for this outcome. Second, it is very likely that interventions affect only certain dimensions of quality of life. As quality of life is often reported as one construct in which physical aspects are prominently present, effects on other dimensions are likely to be missed or underestimated. A positive effect on health status was only seen in an inpatient pulmonary rehabilitation intervention,[40] which may be due to the fact that pulmonary rehabilitation is an intensive intervention and addresses many aspects that are included in health-related quality of life questionnaires. Third, in this patient group with end-stage disease, an improvement in quality of life is possibly hard to achieve because of the progressive nature of the disease. However, in patients with heart failure and cancer, significant effects on quality of life have been found,[4, 59] suggesting that there are perhaps other reasons specifically related to COPD or the conducted research.

While no consistent effects were found on health outcomes, advance care planning activities were increased in all studies measuring it.[28, 31, 32, 35, 57] Also, positive effects were reported on quantitative outcomes related to perceived control of breathlessness[29] and self-management.[28, 35] This corresponds with the consistent finding from qualitative studies that after the intervention, patients experienced increased perceived control to manage their symptoms and improved self-confidence[30, 35, 37, 41, 43, 44] due to increased knowledge about their symptoms and the reassurance that support was available if necessary. In line with our findings, a recent meta-analysis on holistic breathlessness interventions found positive effects in the affective domain of breathlessness, but not in level of breathlessness nor quality of life.[14]

Qualitative evidence suggests that longitudinal palliative care interventions prevent emergency department and hospital admissions in some cases due to earlier diagnosis and treatment.[44-46] Quantitative outcomes, however, reveal mixed results. Controlled studies showed no differences between intervention and control group, whereas uncontrolled studies showed a reduction in emergency department and hospital admissions. This difference was also present in healthcare costs, as hospitalizations are responsible for the biggest part of healthcare expenditures:[60] controlled studies reported no statistically significant differences between intervention and usual care patients, and uncontrolled trials showed lower healthcare expenses during the intervention than before. Either way, in line with previous reviews, our results suggest that adding palliative care to usual care does not increase healthcare costs.[4, 59]

Palliative care interventions targeting patients with COPD

Two main intervention types could be identified: short-term palliative care assessments and longitudinal palliative care interventions with care coordination. Both types were regarded as acceptable and helpful to patients with COPD, and were appreciated by referring healthcare professionals since they meet the unaddressed needs of this patient group. Although the high heterogeneity of interventions and outcome measures prevents quantifying which components are most beneficial, qualitative data revealed some characteristics that were consistently

valued and perceived as helpful by patients. This implies that patient and family education on breathlessness management, direct access to a professional for support and an ongoing relationship are essential components to include in future interventions. As these components are rather COPD-specific than palliative care characteristics, it seems that, with sufficient training to healthcare professionals and different care organization, these components could be integrated into regular COPD-care. This would meet the current recommendations of guidelines that integrated palliative care should be provided by generalist or respiratory care professionals, and palliative care specialists become involved only when care needs become complex.[11, 12]

Implementing palliative care interventions

We identified several factors related to the implementation of palliative care interventions for patients with COPD. First, identifying eligible patients appeared challenging, as is also reflected by the variability in the inclusion criteria and strategies used across studies. The emergency department appeared not to be a feasible recruitment setting for a home-based program,[51] but barriers were also encountered in the ambulatory setting[53] and during computerized screening.[33] Using a natural transition point to identify patients with palliative care needs proactively, such as hospitalization for an acute exacerbation,[31, 35, 40, 52] has been recommended in previous research[61] and could possibly facilitate identification of patients. Further, palliative care can best be integrated within existing services to prevent duplication of assessments[52] and to guarantee continuity of care. To facilitate healthcare professionals to provide palliative care, a model that can be adapted to regional needs and providing access to tools showed to be practical.[41] For this vulnerable patient group with high disease burden and low socio-economic status, care needs to be easily accessible, as well in terms of physical distance as financially. This might be resolved by performing assessments during home visits and monitoring patient's needs by phone. Lastly, general organizational conditions such as sufficient time, financial resources and personnel are required for successful implementation.

Study quality and characteristics

The heterogeneity in methodology and used measurement instruments made quantitative pooling of results impossible. Among included studies, study quality was dependent on study design used: most controlled studies were better conducted than studies with a before-and-after design. As most studies did not report a primary outcome and power calculation, the studies may have been underpowered, causing the effects to be underestimated. On the contrary, four studies evaluated many outcomes without controlling for multiple testing,[28, 32, 35, 41] leading to an increased risk of unjustified positive results. Moreover, a clear difference was found in the direction of effects between controlled and uncontrolled studies, specifically with regard to acute healthcare use and costs. In uncontrolled studies, a positive effect can falsely be attributed to the intervention, leading to an overestimation of effect, whilst in fact, it is the reflection of the normal disease course or other influences.

Furthermore, the included studies provided little information on the actual delivery of the intervention. As a consequence, it remains unclear whether or not the inconsistency of effects found is due to implementation errors.

Recommendations for future research

For future evaluations, outcomes should be chosen related to the goal of the intervention. Quality of life, although the ultimate goal of palliative care, might be a rather distal outcome measure and difficult to modify in this patient group. Qualitative research can identify which outcomes are most important to patients with end-stage COPD and can increase our understanding of the underlying working mechanisms and what works for whom and under what circumstances. Eventually, consensus on the outcome sets to be used is needed in order to compare different interventions and to be able to conduct meta-analyses. Our review revealed a striking difference between the results of quantitative and qualitative studies included. This may be due to the different focus of these two methods. Qualitative research mainly aims to examine the experiences of individuals, and not health effects. In general, additional care or attention from a professional will result in a more positive patient evaluation. That being said, the added value of palliative care interventions in COPD may just be to improve those subjective experiences of individuals in their final stage of the disease. Therefore, we argue that the discrepancy found between the quantitative and qualitative results advocates for a reconsideration of research outcome choices. Hence, we should consider what can most significantly impact the patients' well-being and experience, and not solely focus on health effect parameters. Additionally, we were surprised to find so few outcomes at informal caregiver and professional level. We recommend to include outcomes such as informal caregiver burden and professional's self-efficacy, to acquire knowledge on how informal caregivers can be supported and how professionals can be equipped with the necessary skills. Next, we recommend that future research includes comprehensive process evaluations to unravel requirements for successful implementation and to explore implementation strategies that enhance adoption of new care practices. Various validated tools can be used for this purpose, such as the TIDieR checklist for reporting of intervention characteristics and monitoring intervention fidelity.[62] Also, the Measurement Instrument for Determinants of Innovations framework and Context and Implementation of Complex Interventions framework have been previously used in the palliative care research field and can be used in future studies to measure implementation determinants and contextual factors.[63, 64]

Strengths and limitations

To our knowledge, this is the first study reviewing all evidence on the effectiveness and implementation of palliative care interventions in COPD. Since we did not exclude studies based on design or quality, we were able to use all available information in literature in order to give a broad overview. We used a comprehensive and broad search strategy across multiple databases. Study selection, quality assessment and data extraction were conducted by two

authors independently. Implementation outcomes and barriers and facilitators to implementation were categorized using well-established operationalizations.

This systematic review also has some limitations. Although we used a broad search strategy across databases, we included articles only if the authors referred to the intervention as “palliative”. This allowed us to use a clear and objective criterion, as there are no fixed criteria which characteristics an intervention must have in order to be labelled as palliative care, nor which patients with COPD should be labelled as “palliative patients”. As a consequence, we disregarded interventions targeting patients with severe COPD, but were not referred to as palliative. This may have resulted in the exclusion of relevant interventions with similar intervention characteristics. Due to poor reporting and inconsistent terminology used across studies, categorization of characteristics, implementation outcomes and barriers and facilitators was sometimes difficult. Since all study designs were included, there was high methodological variation between studies and variation in risk of bias. Also, there was heterogeneity in used measurement instruments. For these reasons, the results of the synthesized evidence have to be interpreted with caution.

Conclusions

Although the relevance of palliative care interventions for patients with COPD and their informal caregivers has been widely acknowledged, this study found that little high-quality evidence is available on the effectiveness and implementation of palliative care interventions in COPD-care. There is a need for well-conducted controlled effectiveness studies of sufficient power to reach definite conclusions, and that also explore which characteristics of palliative care complex interventions in COPD are especially effective and for whom. Finally, with clearer results, its implementation should be facilitated and documented with adequate process evaluations using standardized methodologies.

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Author contributions

J.B. and R.K. designed the protocol; J.B., J.S. and A.H. performed the study selection; J.B., A.H., R.K., D.J. and Y.E. extracted data; J.B. and A.H. appraised study quality; J.B., R.K. and A.H. performed data analysis and interpretation; J.B. wrote the first draft; All authors contributed to critical revision and agreed with the final manuscript.

Data management and sharing

All relevant data are within the manuscript. Any other data are available upon request from the corresponding author.

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Supplementary material

Table S1. Example search strategy for PubMed

(“advanced COPD”[tiab] OR “end-stage COPD”[tiab] OR advanced chronic obstructive*[tiab] OR end-stage chronic obstructive*[tiab]
OR
((“Pulmonary Disease, Chronic Obstructive”[Mesh] OR “chronic obstructive pulmonary disease”[tw] OR “COPD”[tw] OR COPD*[tw] OR “COAD”[tw] OR “Chronic Obstructive Airway Disease”[tw] OR “Chronic Obstructive Lung Disease”[tw] OR “Chronic Airflow Obstructions”[tw] OR “Chronic Airflow Obstruction”[tw] OR “chronic bronchitis”[tw] OR “pulmonary emphysema”[tw] OR “Pulmonary Emphysemas”[tw] OR “Focal Emphysema”[tw] OR “Panacinar Emphysema”[tw] OR “Panlobular Emphysema”[tw] OR “Centriacinar Emphysema”[tw] OR “Centrilobular Emphysema”[tw])
AND
(“Palliative Care”[Mesh] OR “palliative care”[tw] OR “palliative care interventions”[tw] OR “palliative care intervention”[tw] OR “Palliative Therapy”[tw] OR “Palliative Treatment”[tw] OR “Palliative Treatments”[tw] OR “Palliative Surgery”[tw] OR “Palliative therapy”[tw] OR “palliative phase”[tw] OR “palliative phases”[tw] OR “palliation”[tw] OR “palliative”[tw] OR palliat*[tw] OR “Palliative Medicine”[mesh] OR “Terminal Care”[Mesh:noexp] OR “Hospice Care”[Mesh] OR “Resuscitation Orders”[mesh] OR “Terminal Care”[tw] OR “Hospice Care”[tw] OR “Hospice Programs”[tw] OR “Hospice Program”[tw] OR “Bereavement Care”[tw] OR “End-of-Life Care”[tw] OR “Life Care End”[tw] OR “supportive care”[tw] OR “terminally ill”[tiab] OR “Terminally Ill”[Mesh] OR “advanced illness”[tiab] OR “advanced disease”[tiab] OR “Death”[mesh:noexp] OR “dying loved one”[tiab] OR “dying patient”[tiab] OR “dying patients”[tiab] OR “dying people”[tiab] OR “dying person”[tiab] OR “dying”[tiab] OR “last year of life”[tiab] OR “end of life”[tiab] OR “end-of-life”[tiab] OR “terminal illness”[tiab] OR “terminal illnesses”[tiab] OR “death and dying”[tiab] OR “limited life expectancies”[tiab] OR “limited life expectancy”[tiab] OR “limited life span”[tiab] OR “limited lifespan”[tiab] OR “limited life spans”[tiab] OR “critical illness”[tiab] OR “Critical Illness”[Mesh] OR “frail elderly”[tiab] OR “Frail Elderly”[Mesh])))

Table S2. Operationalizations of palliative care domains

Identification	Early and proactive identification of the palliative care phase.
Advance care planning	A continuous and dynamic process of discussions on life goals and choices, and on which care is an appropriate fit, now and in the future.
Individual care plan	A document which is kept with the patient in which the agreements focusing on physical, psychological, social and spiritual well-being are recorded.
Informal caregiver support	Support to a family member who plays an important role in caring for the patient and is actively involved in this.
Interdisciplinary care	Involvement of several disciplines working together in an interdisciplinary team.
Coordination	People approaching the end of life receive consistent care that is coordinated effectively across all relevant settings and services at any time of day or night, and delivered by practitioners who are aware of the person’s current medical condition, care plan and preferences.
Physical dimension	Assessment and management of physical needs.
Psychological dimension	Assessment and management of psychological needs.
Social dimension	Assessment and management of social needs.
Spiritual dimension	Assessment and management of spiritual, religious and existential needs.
End-of-life care	Patients at the end of life are identified at an early stage. The individual care plan is updated accordingly, or the End-of-life care pathway is started.
Bereavement support	People closely affected by a death are offered bereavement support.

Table S3. Operationalizations of implementation outcomes

Acceptability	The perception among implementation stakeholders that a given treatment, service, practice, or innovation is agreeable, palatable, or satisfactory.
Adoption	The intention, initial decision, or action to try or employ an innovation.
Appropriateness	The perceived fit, relevance, or compatibility of the innovation for a given practice setting, provider, or consumer.
Costs	Implementation costs.
Feasibility	The extent to which a new treatment, or an innovation, can be successfully used or carried out within a given agency or setting.
Fidelity	The degree to which an intervention was implemented as it was prescribed in the original protocol or as it was intended by the program developers.
Penetration	Integration of practice within a setting.
Sustainability	The extent to which a newly implemented treatment is maintained or institutionalized.

Table S4. Codebook for extraction of determinants of implementation
Codes from the Measurement Instrument for Determinants of Innovations (MIDI)(1). Inductively added codes based on the Consolidated Framework for Implementation Research (CFIR)(2) in blue and other inductively added codes in pink.

Determinants associated with the innovation	
1. Procedural clarity	Description: Extent to which the innovation is described in clear steps / procedures.
2. Correctness	Description: Degree to which the innovation is based on factually correct knowledge.
3. Completeness	Description: Degree to which the activities described in the innovation are complete.
4. Complexity	Description: Degree to which implementation of the innovation is complex.
5. Compatibility	Description: Degree to which the innovation is compatible with the values and working method in place.
6. Observability	Description: Visibility of the outcomes for the user, for example whether the outcomes of a particular treatment are clear to the user.
7. Relevance for patient	Description: Degree to which the user believes the innovation is relevant for his/her patient.
8. Accessibility	Description: Degree to which the innovation is accessible for the patient.
Determinants associated with the adopting person (user)	
9. Personal benefits/drawbacks	Description: Degree to which using the innovation has advantages or disadvantages for the users themselves.
10. Outcome expectations	Description: Perceived probability and importance of achieving the patient objectives as intended by the innovation.
11. Professional obligation	Description: Degree to which the innovation fits in with the tasks for which the user feels responsible when doing his/her work.
12. Patient satisfaction	Description: Degree to which the user expects patients to be satisfied with the innovation.
13. Patient cooperation	Description: Degree to which the user expects patients to cooperate with the innovation.
14. Social support	Description: Support experienced or expected by the user from important social referents relating to the use of the innovation (for example from colleagues, other professionals they work with, heads of department or management).
15. Descriptive norm	Description: Colleagues' observed behaviour; degree to which colleagues use the innovation.
16. Subjective norm	Description: The influence of important others on the use of the innovation.
17. Self-efficacy	Description: Degree to which the user believes he or she is able to implement the activities involved in the innovation.
18. Knowledge	Description: Degree to which the user has the knowledge needed to use the innovation.
19. Awareness of content of innovation	Description: Degree to which the user has learnt about the content of the innovation.
20. Previous experience with similar innovation	Description: Degree to which the experience of a user with a similar innovation in the past has influence on implementation of the current innovation.
21. Publicity	Description: Degree to which publicity and marketing activities have led to implementation and use of innovation.
22. Tension for change	Description: Degree to which stakeholders perceive the current situation as intolerable or needing change.
23. Disease specific characteristics	Description: Degree to which disease specific characteristics hampers implementation. For example, the unpredictable disease trajectory which makes predicting the palliative phase difficult.
Determinants associated with the organisation	
24. Formal ratification by management	Description: Formal ratification of the innovation by management, for example by including the use of the innovation in policy documents.
25. Replacement when staff leave	Description: Replacement of staff leaving the organization.
26. Staff capacity	Description: Adequate staffing in the department or in the organisation where the innovation is being used.
27. Financial resources	Description: Availability of financial resources needed to use the innovation.
28. Time available	Description: Amount of time available to use the innovation.
29. Material resources and facilities	Description: Presence of materials and other resources or facilities necessary for the use of the innovation as intended (such as equipment, materials or space).
30. Coordinator	Description: The presence of one or more persons responsible for coordinating the implementation of the innovation in the organisation.
31. Unsettled organisation	Description: Degree to which there are other changes in progress (organisational or otherwise) that represent obstacles to the process of implementing the innovation, such as re-organisations, mergers, cuts, staffing changes or the simultaneous implementation of different innovations.
32. Information accessible about use of innovation	Description: Accessibility of information about the use of the innovation.
33. Performance feedback	Description: Feedback to the user about progress with the innovation process.
34. Leadership engagement	Description: Commitment, involvement, and accountability of leaders and managers with the implementation of the innovation.
35. External policy & Incentives	Description: A broad construct that includes external strategies to spread innovations including policy and regulations (governmental or other central entity), external mandates, recommendations and guidelines, pay-for-performance, collaboratives, and public or benchmark reporting.
Determinants associated with the socio-political context	
36. Legislation and regulations	Description: Degree to which the innovation fits in with existing legislation and regulations established by the competent authorities (examples being financial structures, or substantive legislation and supervision from the Dutch Health Care Inspectorate or the Dutch Care Authority).

Table S5. Quality assessment of included studies.

Reference	Study design	Screening questions		1. Qualitative					2. Quantitative randomized controlled trials					3. Quantitative non-randomized					4. Quantitative descriptive					5. Mixed methods					Score
		S1	S2	1.1	1.2	1.3	1.4	1.5	2.1	2.2	2.3	2.4	2.5	3.1	3.2	3.3	3.4	3.5	4.1	4.2	4.3	4.4	4.5	5.1	5.2	5.3	5.4	5.5	
Aiken (2006)	RCT	Y	Y						Y	Y	N	Y	Y																★★★★
Lockhart (2003)	Unclear	N	N																										★
Bove (2018)	Q	Y	Y	Y	Y	Y	Y	Y																					★★★★
Bove (2019)	Q	Y	Y	Y	Y	Y	Y	Y																					★★★★
Buckingham (2015)	RCT +Q (pilot/feasibility)	Y	Y	Y	Y	Y	Y	Y	Y	N	N	N	Y											Y	Y	Y	Y	N	★★★
Duenk (2017)	CCT	Y	Y											Y	Y	Y	Y	U											★★★★
Edes (2006)	BA	Y	Y											N	Y	Y	N	U											★★
Farquhar (2016)	RCT +Q	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	U											Y	Y	Y	Y	Y	★★★★
Farquhar (2009)	RCT +Q (pilot/feasibility)	Y	Y	Y	Y	U	N	U	Y	U	Y	Y	U											Y	N	N	N	N	★★
Farquhar (2010)	BA +Q (pilot/feasibility)	Y	Y	Y	Y	U	Y	U						Y	Y	Y	N	U						Y	Y	Y	Y	Y	★★★
Booth (2006)	Q	Y	Y	Y	Y	Y	Y	Y																					★★★★
Higginson (2014)	RCT	Y	Y						Y	Y	Y	Y	U																★★★★
Reilly (2016)	Q	Y	Y	N	N	Y	Y	Y																					★★★
Horton (2013)	BA (pilot/feasibility)	Y	Y											Y	Y	N	N	Y											★★★
Janssens (2019)	RCT (pilot/feasibility)	Y	Y						Y	Y	Y	U	U																★★★
Iupati (2016)	BA	Y	Y											Y	Y	Y	N	U											★★★
Johnston (2016)	Q	Y	Y	Y	Y	Y	Y	Y																					★★★★
Long (2014)	BA +Q (pilot/feasibility)	Y	Y	Y	Y	Y	N	Y						N	Y	Y	N	Y						Y	Y	Y	N	Y	★★★
Qian (2018)	BA +Q (pilot/feasibility)	Y	Y	Y	Y	Y	Y	Y						Y	Y	Y	N	U						Y	N	N	Y	Y	★★★
Rabow (2003a) / Rabow (2004)	CCT +Q	Y	Y	Y	U	Y	Y	N						Y	Y	Y	Y	N						Y	N	Y	Y	N	★★★
Rabow (2003b)	Q	Y	Y	Y	U	Y	Y	N																					★★★
Rocker (2014)	BA +Q	N	U																										★
Gillis (2017)	BA +Q (pilot/feasibility)	Y	Y	Y	U	U	N	N						Y	Y	Y	N	Y						Y	N	N	U	N	★★
Rocker (2017)	BA +Q	Y	Y	N	N	U	N	U						U	U	U	U	U						Y	N	U	N	N	★
Verma (2017)	Non-comparative +Q	Y	Y	Y	Y	Y	N	Y											Y	U	N	N	N	Y	N	N	N	N	★★
Scheerens (2018)	RCT +Q (pilot/feasibility)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y											Y	Y	Y	U	Y	★★★★
Smallwood (2018)	BA	Y	Y											Y	Y	Y	N	Y											★★★★
Steinel (2003)	BA	Y	Y											N	Y	U	N	U											★
Van Dam (2014)	BA	Y	N+Y											Y	N+Y	Y	N	U											★★
Vitacca (2019)	BA +Q (pilot/feasibility)	Y	Y											Y	Y	Y	N	Y											★★★★

Abbreviations: RCT = Randomized controlled trial; BA = Before-and-after study;
CCT = Non-randomized clinical controlled trial, Q = Qualitative study design,
+Q = Qualitative data additional to quantitative study design,
Y = Yes, N = No, N+Y = for first part of research question answer No,
for second part answer Yes, U = Can't tell.

Table S6. Barriers and facilitators for implementation (determinants) for referrers, providers and patients.

User type	Determinant	References
Referrer		
	Relevance for patient	Booth (2006)
		Buckingham (2015)
		Rabow (2003a)
	Awareness of content of innovation	Lockhart (2003)
		Gillis (2017)
		Johnston (2016)
	Disease characteristics	Rocker (2017)
		Johnston (2016)
		Rabow (2003a)
	Publicity	Lockhart (2003)
	Professional obligation	Lockhart (2003)
	Patient satisfaction	Booth (2006)
	Correctness	Booth (2006)
	Personal benefits/drawbacks	Booth (2006)
		Rabow (2003a)
	Compatibility	Booth (2006)
		Gillis (2017)
	Tension for change	Booth (2006)
		Buckingham (2015)
	Time available	Gillis (2017)
	Complexity	Gillis (2017)
	Completeness	Johnston (2016)
	Procedural clarity	Johnston (2016)
	Financial resources	Rabow (2003a)
Provider		
	Time available	Gillis (2017)
		Rocker (2017)
		Verma (2017)
		Johnston (2016)
		Rabow (2003a)
		Scheerens (2019)
	Staff capacity	Lockhart (2003)
		Horton (2013)
		Rabow (2003a)
	Compatibility	Buckingham (2015)
		Verma (2017)
		Johnston (2016)
	Financial resources	Verma (2017)
		Horton (2013)
		Rabow (2003a)

User type	Determinant	References
	Material resources and facilities	Rabow (2003a)
		Scheerens (2019)
	Knowledge	Lockhart (2003)
		Rocker (2017)
	Correctness	Buckingham (2015)
		Scheerens (2019)
	Information accessible about use of innovation	Buckingham (2015)
		Verma (2017)
	Leadership engagement	Rocker (2017)
		Verma (2017)
	External policy & Incentives	Verma (2017)
	Completeness	Verma (2017)
	Performance feedback	Verma (2017)
	Complexity	Verma (2017)
	Formal ratification by management	Verma (2017)
	Tension for change	Horton (2013)
	Unsettled organization	Rabow (2003a)
	Publicity	Rabow (2003a)
Patient		
	Accessibility	Buckingham (2015)
		Rocker (2017)
		Horton (2013)
		Long (2014)
		Rabow (2003a)
	Relevance for patients	Buckingham (2015)
	Personal benefits/drawbacks	Buckingham (2015)
	Previous experience with similar innovation	Buckingham (2015)
	Compatibility	Buckingham (2015)
	Financial resources	Long (2014)
	Unsettled organization	Rabow (2003a)