



Universiteit  
Leiden  
The Netherlands

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

Broese, J.M.C.; Heij, A.H. de; Janssen, D.J.A.; Skora, J.A.; Kerstjens, H.A.M.; Chavannes, N.H.; ... ; Kleij, R.M.J.J. van der

### **Citation**

Broese, J. M. C., Heij, A. H. de, Janssen, D. J. A., Skora, J. A., Kerstjens, H. A. M., Chavannes, N. H., ... Kleij, R. M. J. J. van der. (2021). Effectiveness and implementation of palliative care interventions for patients with chronic obstructive pulmonary disease: a systematic review. *Palliative Medicine*, 35(3), 486-502. doi:10.1177/0269216320981294

Version: Publisher's Version

License: [Creative Commons CC BY-NC 4.0 license](#)

Downloaded from: <https://hdl.handle.net/1887/3196088>

**Note:** To cite this publication please use the final published version (if applicable).





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

*Palliative Medicine*  
2021, Vol. 35(3) 486–502  
© The Author(s) 2020



Article reuse guidelines:  
sagepub.com/journals-permissions  
DOI: 10.1177/0269216320981294  
journals.sagepub.com/home/pmj



Johanna MC Broese<sup>1,2</sup> , Albert H de Heij<sup>3</sup> ,  
Daisy JA Janssen<sup>4,5</sup> , Julia A Skora<sup>1</sup>,  
Huib AM Kerstjens<sup>6</sup>, Niels H Chavannes<sup>1</sup>,  
Yvonne Engels<sup>7</sup>  and Rianne MJJ van der Kleij<sup>1</sup>

## 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  $\geq 30\%$  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

<sup>1</sup>Public Health & Primary care, Leiden University Medical Centre, Leiden, The Netherlands

<sup>2</sup>Lung Alliance Netherlands, The Netherlands

<sup>3</sup>Centre of Expertise for Palliative Care, University of Groningen and University Medical Centre Groningen, Groningen, The Netherlands

<sup>4</sup>Department of Research & Development, CIRO, Horn, The Netherlands

<sup>5</sup>Department of Health Services Research, Care and Public Health Research Institute, Faculty of Health, Medicine and Life Sciences, Maastricht University, The Netherlands

<sup>6</sup>Department of Respiratory Medicine & Tuberculosis, and Groningen Research Institute for Asthma and COPD (GRIAC), University of Groningen and University Medical Centre Groningen, Groningen, The Netherlands

<sup>7</sup>Anaesthesiology, Pain & Palliative Medicine, Radboud University Medical Centre, Nijmegen, The Netherlands

## Corresponding author:

Johanna MC Broese, Department of Public Health and Primary Care, Leiden University Medical Centre, Post zone V0-P, Postbus 9600, Leiden 2300 RC, The Netherlands.  
Email: j.m.c.broese@lumc.nl

**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.<sup>1</sup> 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.<sup>2</sup> 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.<sup>3</sup> 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.<sup>4</sup> 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.<sup>5</sup> As a consequence, their severe symptoms remain undertreated, and a large proportion of this patient group inadvertently dies in the hospital.<sup>6,7</sup> Moreover, the long disease course with declining functional capacity affects their informal caregivers.<sup>8</sup>

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.<sup>9</sup> 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.<sup>10</sup> 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.<sup>9</sup>

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.<sup>11,12</sup> In previous systematic reviews, the vast majority of the interventions described were designed for patients with cancer<sup>4,13,14</sup> or focused on a single intervention component only.<sup>15–17</sup> Research on the effectiveness of interventions that integrate multiple components of palliative care for patients with COPD is still lacking.<sup>18</sup> 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” (Supplemental 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.<sup>19</sup> 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

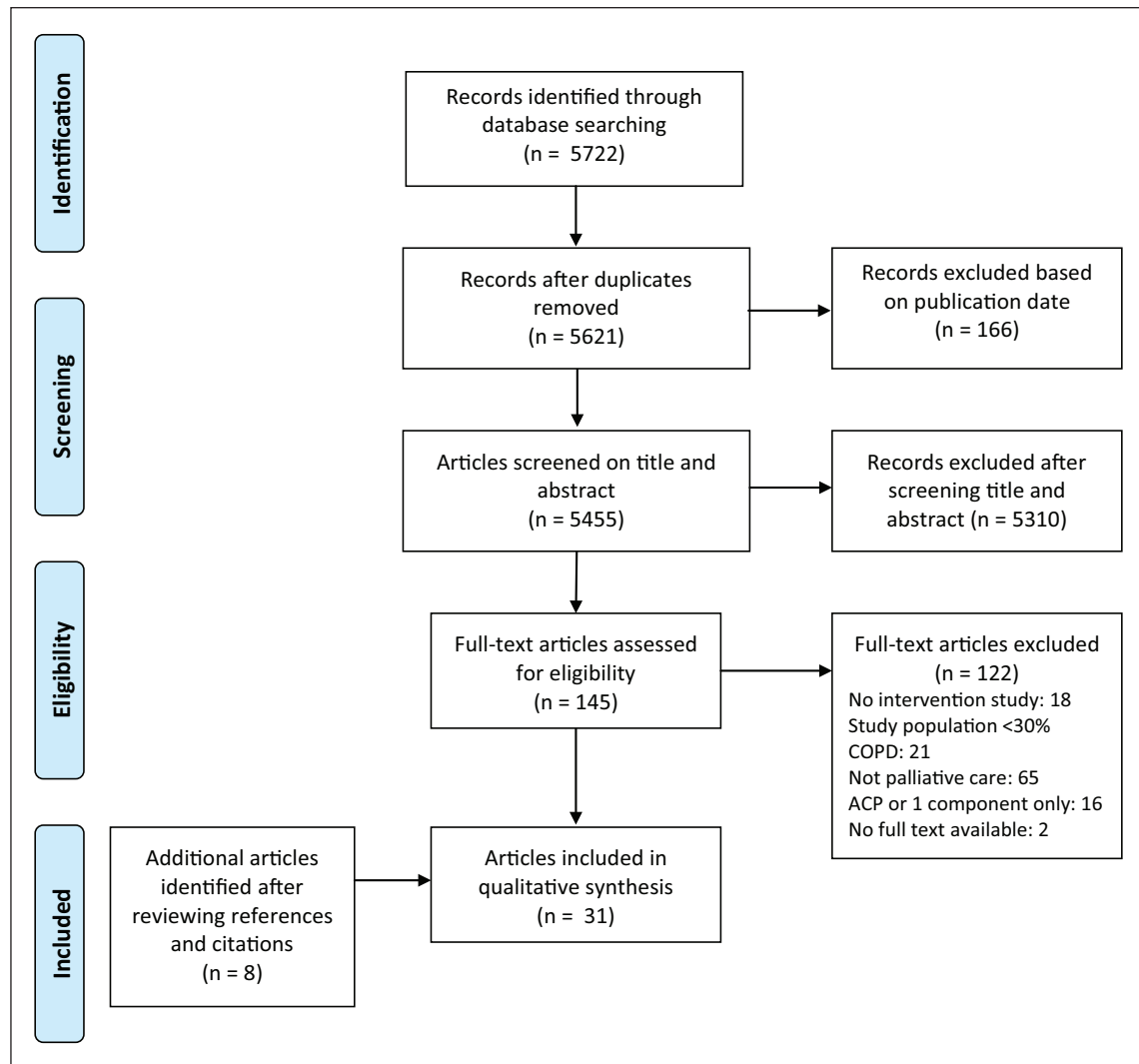
Data on design, participants, intervention characteristics and all reported outcomes at patient, informal caregiver and healthcare professional level were extracted using a piloted extraction form. If necessary and possible, additional data was derived from published study protocols or supplementary 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.<sup>20</sup> 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.<sup>21</sup> 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,<sup>12</sup> Clinical Practice Guidelines for Quality Palliative Care<sup>22</sup> and Quality standard End of life care for adults.<sup>23</sup> The operationalization of domains is described in Supplemental 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.<sup>24</sup> We categorized implementation outcomes following the proposed terminology and operationalization of Proctor et al.<sup>25</sup> (see Supplemental Table 3). According to Proctor et al.,<sup>25</sup> implementation outcomes are defined as “the effects of



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

deliberate and purposive actions to implement new treatments, practices, and services” (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.<sup>26</sup> 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<sup>27</sup> or newly defined determinants were added inductively. The codebook used is available in Supplemental 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.

### 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

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

Author	Study design	Sample size	Intervention description					Healthcare professionals	Contacts	Duration (months)
			Intervention name; Development	Country	Coordinating organization	Intervention	Conditions			
Aiken <sup>28</sup> Lockhart <sup>58</sup>	RCT Unclear	190 patients N.S.	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	
Bove <sup>67</sup>	Q	Seven pulmonary nurses, three pulmonologists, two 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 <sup>66</sup> Buckingham <sup>52</sup>	Q RCT + Q (pilot/feasibility)	10 patients RCT: 32 patients Q: eight patients, three 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 acute hospital admission for an acute exacerbation	COPD NR	One home visit, three phone calls for follow up	6	
Duenk <sup>31</sup>	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	In- or outpatient consultation and monthly meetings outpatient or via phone	12, or until death	
Edes <sup>34</sup>	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	One to nine home visits per month based on clinical judgement	Median = 6	
Farquhar <sup>20</sup>	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 center	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 breathlessness PT and PCP	one home assessment, three outpatient visits, phone call for questions	1	
Farquhar <sup>49</sup>	RCT + Q (trial feasibility)	RCT and Q: 13 patients, 12 carers								
Farquhar <sup>50</sup>	BA + Q (pilot/feasibility)	13 patients <sup>a</sup>								
Booth <sup>42</sup>	Q	10 patients, 9 carers, 4 GPs, nurses								

(Continued)

**Table 1. (Continued)**

Included studies		Intervention description								
Author	Study design	Sample size	Intervention name; Development	Country	Coordinating organization	Intervention	Conditions	Healthcare professionals	Contacts	Duration (months)
Higginson <sup>29</sup> Reilly <sup>43</sup>	RCT Q	105 patients 25 patients	Breathlessness Support Service; based on previous studies on holistic breathlessness services, systematic literature review and local stakeholders consultation	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, 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	refractory breathlessness	PM, PCP, PT, OT Other team members: SW	One home visit and two outpatient visits	1
Horton <sup>53</sup>	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	One home visit, weekly phone contact and follow up visits if needed	4
Iupati <sup>56</sup>	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 <sup>57</sup>	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 and alternative approaches such as relaxation, reflexology, massages	COPD	PCN and PCP	Monthly home visits	12
Johnston <sup>44</sup>	Q	Six patients, six 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 <sup>57</sup>	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 center	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	Three outpatient visits, phone call weekly	3

(Continued)

Table 1. (Continued)

Included studies		Intervention description								
Author	Study design	Sample size	Intervention name; Development	Country	Coordinating organization	Intervention	Conditions	Healthcare professionals	Contacts	Duration (months)
Qian <sup>54</sup>	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 breathlessness, non malignant	NR, PM	Two outpatient visits in clinic	1.5
Rabow <sup>2,33</sup>	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 <sup>45</sup>	Q	50 patients								
Rocker <sup>25</sup>	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	Four home visits, access to phone support	3–6
Gillis <sup>51</sup>	BA + Q (pilot/feasibility)	BA: 15 patients Q: 14 patients								
Rocker <sup>41</sup>	BA + Q	19 healthcare professional teams								
Verma <sup>48</sup>	Non-comparative +Q	19 healthcare professional teams								
Scheerens <sup>55</sup>	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 <sup>38</sup>	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 breathlessness, 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)

(Continued)



**Table 1.** (Continued)

Included studies		Intervention description								
Author	Study design	Sample size	Intervention name; Development	Country	Coordinating organization	Intervention	Conditions	Healthcare professionals	Contacts	Duration (months)
Steinel <sup>39</sup>	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 <sup>40</sup>	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 status, psychosocial intervention aimed at depression, anxiety or adverse coping strategies, self-management strategies and peer support contact, spiritual needs, advance care planning	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)
Vitacca <sup>56</sup>	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

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.

<sup>a</sup>Farquhar et al. <sup>49,50</sup> report on the same study population, but each uses a different study design and thus were considered as separate studies.

Kingdom ( $n = 4$ ). Three RCTs,<sup>28–30</sup> two non-randomized controlled trials,<sup>31–33</sup> seven uncontrolled before-and-after studies,<sup>34–41</sup> six qualitative studies,<sup>42–47</sup> one non-comparative study,<sup>48</sup> and 10 pilot/feasibility studies<sup>37,49–57</sup> were included. The study design of one article was unclear.<sup>58</sup> Two articles reported on the same study and were collated.<sup>32,33</sup> Five quantitative studies<sup>30,33,35,41,48</sup> and six pilot/feasibility studies<sup>37,50–52,54,55</sup> also included qualitative data. Eighteen studies (60%) focused specifically on COPD. Other studies focussed on refractory breathlessness<sup>29,30,38,42,43,54</sup> or also included patients with heart failure<sup>28,34,44,58</sup> or heart failure and cancer.<sup>33,45</sup> 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,<sup>28,34–36,39,44,55,57</sup> outpatient visits<sup>31,33,47</sup> or a combination of both.<sup>38</sup> Vitacca et al.<sup>56</sup> included telemonitoring. The majority of longitudinal care interventions included symptom management and needs assessments, disease education and self-management, advance care planning and care coordination (Table 2). Informal caregiver support was incorporated in eight interventions and consisted of caregiver education,<sup>28,30,33,35,38</sup> nurse assessment of needs,<sup>28,33,44,55,57</sup> invitation to support groups<sup>33</sup> and respite care<sup>38</sup> and was unspecified in Lupati and Ensor.<sup>36</sup> 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.<sup>29,30,37,52–54</sup> 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<sup>29,30,37,54</sup> 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<sup>31,40,52</sup> or by using a computerized screening program based on diagnosis and hospitalizations or measures of disease severity.<sup>33,34</sup> In most other cases, patients were referred to the service by health-care professionals.

### *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.<sup>35,58</sup> 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,<sup>29</sup> distress due to breathlessness,<sup>30</sup> health-related quality of life<sup>31</sup> and pain.<sup>32</sup> Janssens et al.<sup>57</sup> had initially planned to measure acute healthcare use as primary outcome. 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,<sup>28,29,31,32,35,37,40,55–57</sup> using seven different measurement instruments. Duenk et al.<sup>31</sup> set health-related quality of life as their primary outcome. Their study and that of Aiken et al.<sup>28</sup> found significant differences between the intervention and control group on specific subscales but not on the total scale. The uncontrolled study of Van Dam et al.<sup>40</sup> reported an improvement on health-related quality of life; all other studies found no differences.<sup>28,29,31,32,35,37</sup>

*Breathlessness*—In two RCTs evaluating holistic breathlessness services,<sup>29,30</sup> intervention patients showed higher levels of mastery of breathlessness, but only one study found a statistically significant difference.<sup>29</sup> No difference was found on distress due to breathlessness in one RCT.<sup>30</sup> In the study of Rabow et al.,<sup>32</sup> intervention patients reported a lower degree of

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

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

**Table 3.** Summary of quantitative outcomes and results at the level of the patient, informal caregiver and healthcare professional, and costs.

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

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.

breathlessness interference with daily activities and limitations in daily life compared to control patients. Two other controlled studies did not find an effect on breathlessness intensity.<sup>29,37</sup>

**Anxiety and depression**—Rabow et al.<sup>32</sup> reported reduced anxiety in intervention patients, but no change in depression. Eight other studies found no significant differences.<sup>29–31,35,37,55–57</sup>

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

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

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

**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.<sup>28,31,32,55,57</sup> Uncontrolled studies revealed reduction in the number of emergency department visits and hospitalizations.<sup>34–36,38,39</sup> One pilot RCT reported more hospitalizations in the intervention group than the usual care group.<sup>55</sup> A comparison of deceased intervention patients with other decedents showed a shorter median length of stay at the Intensive Care Unit.<sup>35</sup>

**Advance care planning**—Five studies found that, for intervention patients, a personal directive and advance care planning choices were more often documented,<sup>28,31,35,57</sup> and funeral arrangements were more likely to be completed.<sup>32</sup>

**Site of death**—One controlled study examining site of death found no differences between intervention and control group.<sup>32</sup>

**Satisfaction with care**—Two controlled studies found no difference between intervention and control group regarding satisfaction with care<sup>32,55</sup>; the uncontrolled study of Edes et al.<sup>34</sup> reported an improvement.

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

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

### *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.<sup>30</sup>

### *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.<sup>48</sup>

### *Costs*

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

### *Qualitative outcomes*

Qualitative outcomes were derived from interviews in fourteen qualitative (sub)studies.<sup>30,35,37,41–48,52,54,55</sup> In most

studies, patients reported improved self-confidence to manage symptoms<sup>30,35,37,41,43,44,46</sup> and positive psychological effects.<sup>30,35,37,43,45,52</sup> Besides, in some cases, hospitalization was prevented due to earlier diagnosis and treatment.<sup>44–46</sup> Regarding informal caregivers, increased confidence was reported because they knew how they could help their relatives with breathlessness.<sup>30,42</sup> 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.<sup>47,48</sup>

### *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,<sup>42,44,45,46,52,54,55</sup> informal caregivers and referring healthcare professionals,<sup>42,44,52</sup> but also by using a questionnaire among participants<sup>43</sup> or by collecting patient stories anecdotally.<sup>58</sup> 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,<sup>30,35,42,44,46,50,55</sup> continuity of

the relationship<sup>44,46</sup> and education about breathlessness management.<sup>30,35,42,43,50,55</sup> Specifically regarding breathlessness, non-pharmacological interventions such as a hand-held fan and breathing techniques were reported to be most helpful.<sup>30,42,43,54,55</sup> Four studies reported on intervention feasibility using predefined feasibility criteria (e.g. participation rates and completion of the program).<sup>37,51,52,55</sup> The feasibility level varied and was mostly related to specific intervention context characteristics. For instance, Buckingham et al.<sup>52</sup> encountered fewer actions during assessments than expected due to overlap of their service with existing discharge services. Two studies reported on the completion of program components (fidelity)<sup>37,51</sup> and one on usefulness (appropriateness) as one of the feasibility criteria.<sup>37</sup> One study evaluating nationwide dissemination of their approach reported on adoption and sustainability<sup>41,48</sup>; 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,<sup>33,37,41,42,44,48,51–53,55,58</sup> 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<sup>31</sup> 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,<sup>40</sup> 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,<sup>4,59</sup> 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.<sup>28,31,32,35,57</sup> Also, positive effects were reported on quantitative outcomes related to perceived control of breathlessness<sup>29</sup> and self-management.<sup>28,35</sup> 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<sup>30,35,37,41,43,44</sup> 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.<sup>14</sup>

Qualitative evidence suggests that longitudinal palliative care interventions prevent emergency department and hospital admissions in some cases due to earlier diagnosis and treatment.<sup>44–46</sup> 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<sup>60</sup>: 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.<sup>4,59</sup>

### *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.<sup>11,12</sup>

### *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,<sup>51</sup> but barriers were also encountered in the ambulatory setting<sup>53</sup> and during computerized screening.<sup>33</sup> Using a natural transition point to identify patients with palliative care needs proactively, such as hospitalization for an acute exacerbation,<sup>31,35,40,52</sup> has been recommended in previous research<sup>61</sup> and could possibly facilitate identification of patients. Further, palliative care can best be integrated within existing services to prevent duplication of assessments<sup>52</sup> 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.<sup>41</sup> 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,<sup>28,32,35,41</sup> 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.<sup>62</sup> 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.<sup>63,64</sup>

### 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.

### Conclusion

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.

### Acknowledgements

The authors would like to thank Jan W. Schoones, information specialist at the Walaeus Library of the Leiden University Medical Centre, for assisting in developing and conducting the search strategy for this systematic review.

### 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.

This work was financed by The Netherlands Organization for Health Research and Development (ZonMw).

### Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

### Funding

The author(s) received no financial support for the research, authorship and/or publication of this article.

### ORCID iDs

Johanna MC Broese  <https://orcid.org/0000-0003-4815-2305>

Albert H de Heij  <https://orcid.org/0000-0002-8085-3358>

Daisy JA Janssen  <https://orcid.org/0000-0002-1827-9869>

Yvonne Engels  <https://orcid.org/0000-0002-7669-1018>

### Data management and sharing

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



## Supplemental material

Supplemental material for this article is available online.

## References

- WHO. Fact Sheet Top 10 global causes of deaths, <http://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death> (2016, accessed 4 September 2018).
- Habraken JM, ter Riet G, Gore JM, et al. Health-related quality of life in end-stage COPD and lung cancer patients. *J Pain Symptom Manage* 2009; 37: 973–981.
- WHO. Definition Palliative care, <http://www.who.int/cancer/palliative/definition/en/> (2002, accessed 4 September 2018).
- Kavalieratos D, Corbelli J, Zhang D, et al. Association between palliative care and patient and caregiver outcomes: a systematic review and meta-analysis. *JAMA* 2016; 316: 2104–2114.
- Carlucci A, Guerrieri A and Nava S. Palliative care in COPD patients: is it only an end-of-life issue? *Eur Respir Rev* 2012; 21: 347–354.
- Janssen DJ, Spruit MA, Uszko-Lencer NH, et al. Symptoms, comorbidities, and health care in advanced chronic obstructive pulmonary disease or chronic heart failure. *J Palliat Med* 2011; 14: 735–743.
- Cohen J, Beernaert K, Van den Block L, et al. Differences in place of death between lung cancer and COPD patients: a 14-country study using death certificate data. *NPJ Prim Care Respir Med* 2017; 27: 14.
- Fried TR, Bradley EH, O’Leary JR, et al. Unmet desire for caregiver-patient communication and increased caregiver burden. *J Am Geriatr Soc* 2005; 53: 59–65.
- Tavares N, Jarrett N, Hunt K, et al. Palliative and end-of-life care conversations in COPD: a systematic literature review. *ERJ Open Res* 2017; 3: 00068-2016.
- Maddocks M, Lovell N, Booth S, et al. Palliative care and management of troublesome symptoms for people with chronic obstructive pulmonary disease. *Lancet* 2017; 390: 988–1002.
- Lanken PN, Terry PB, Delisser HM, et al. An official American Thoracic Society clinical policy statement: palliative care for patients with respiratory diseases and critical illnesses. *Am J Respir Crit Care Med* 2008; 177: 912–927.
- Boddaert M, Douma J, Dijkhoorn F, et al. Netherlands Quality Framework for Palliative Care. IKNL/Palliactief, 2017.
- Phongtankuel V, Meador L, Adelman RD, et al. Multicomponent palliative care interventions in advanced chronic diseases: a systematic review. *Am J Hosp Palliat Care* 2018; 35: 173–183.
- Brighton LJ, Miller S, Farquhar M, et al. Holistic services for people with advanced disease and chronic breathlessness: a systematic review and meta-analysis. *Thorax* 2019; 74: 270–281.
- Bausewein C, Booth S, Gysels M, et al. Non-pharmacological interventions for breathlessness in advanced stages of malignant and non-malignant diseases. *Cochrane Database Syst Rev* 2008; 2: CD005623.
- Jabbarian LJ, Zwakman M, van der Heide A, et al. Advance care planning for patients with chronic respiratory diseases: a systematic review of preferences and practices. *Thorax* 2018; 73: 222–230.
- Ekström M, Nilsson F, Abernethy AA, et al. Effects of opioids on breathlessness and exercise capacity in chronic obstructive pulmonary disease. A systematic review. *Ann Am Thorac Soc* 2015; 12: 1079–1092.
- Disler RT, Currow DC, Phillips JL, et al. Interventions to support a palliative care approach in patients with chronic obstructive pulmonary disease: an integrative review. *Int J Nurs Stud* 2012; 49: 1443–1458.
- Craig P, Dieppe P, Macintyre S, et al. Developing and evaluating complex interventions: the new Medical Research Council guidance. *BMJ (Clinical research ed)* 2008; 337: a1655.
- Hong QN, Pluye P, Fàbregues S, et al. Mixed Methods Appraisal Tool (MMAT), version 2018. *Registration of Copyright (#1148552), Canadian Intellectual Property Office, Industry Canada* 2018.
- Reeves BC, Deeks J, Higgins JPT, et al. Chapter 24: Including non-randomized studies on intervention effects. In: Higgins JPT, Thomas J, Chandler J, et al. (eds) *Cochrane handbook for systematic reviews of interventions version 6.0 (updated July 2019) Cochrane*. 2019, [www.training.cochrane.org/handbook](http://www.training.cochrane.org/handbook)
- Clinical Practice Guidelines for Quality Palliative Care*. 3rd ed. Pittsburgh, PA: National Consensus Project for Quality Palliative Care, 2013.
- Quality standard for end of life care for adults*. National Institute for Health and Care Excellence, 2013.
- Pope C, Ziebland S and Mays N. Qualitative research in health care. Analysing qualitative data. *BMJ (Clinical research ed)* 2000; 320: 114–116.
- Proctor E, Silmere H, Raghavan R, et al. Outcomes for implementation research: conceptual distinctions, measurement challenges, and research agenda. *Adm Policy Ment Health* 2011; 38: 65–76.
- Fleuren MA, Paulussen TG, Van Dommelen P, et al. Towards a measurement instrument for determinants of innovations. *Int J Qual Health Care* 2014; 26: 501–510.
- Damschroder LJ, Aron DC, Keith RE, et al. Fostering implementation of health services research findings into practice: a consolidated framework for advancing implementation science. *Implement Sci* 2009; 4: 50.
- Aiken LS, Butner J, Lockhart CA, et al. Outcome evaluation of a randomized trial of the PhoenixCare intervention: program of case management and coordinated care for the seriously chronically ill. *J Palliat Med* 2006; 9: 111–126.
- Higginson IJ, Bausewein C, Reilly CC, et al. An integrated palliative and respiratory care service for patients with advanced disease and refractory breathlessness: a randomised controlled trial. *Lancet Respir Med* 2014; 2: 979–987.
- Farquhar MC, Prevost AT, McCrone P, et al. The clinical and cost effectiveness of a Breathlessness Intervention Service for patients with advanced non-malignant disease and their informal carers: mixed findings of a mixed method randomised controlled trial. *Trials* 2016; 17: 185.
- Duenk RG, Verhagen C, Bronkhorst EM, et al. Proactive palliative care for patients with COPD (PROLONG): a pragmatic cluster controlled trial. *Int J Chron Obstruct Pulmon Dis* 2017; 12: 2795–2806.
- Rabow MW, Dibble SL, Pantilat SZ, et al. The comprehensive care team: a controlled trial of outpatient palliative medicine consultation. *Arch Intern Med* 2004; 164: 83–91.
- Rabow MW, Petersen J, Schanche K, et al. The comprehensive care team: a description of a controlled trial of care at the beginning of the end of life. *J Palliat Med* 2003; 6: 489–499.

34. Edes TE, Lindbloom EJ, Deal JL, et al. Improving care at lower cost for end-stage heart and lung disease: integrating end of life planning with home care. *Mo Med* 2006; 103: 146–151.
35. Rocker GM and Verma JY. 'INSPIRED' COPD outreach program: doing the right things right. *Clin Invest Med* 2014; 37: E311–E319.
36. Lupati SP and Ensor BR. Do community hospice programmes reduce hospitalisation rate in patients with advanced chronic obstructive pulmonary disease? *Intern Med J* 2016; 46: 295–300.
37. Long MB, Bekelman DB and Make B. Improving Quality of Life in Chronic Obstructive Pulmonary Disease by Integrating Palliative Approaches to Dyspnea, Anxiety, and Depression. *J Hosp Palliat Nurs* 2014; 16: 514–520.
38. Smallwood N, Thompson M, Warrender-Sparkes M, et al. Integrated respiratory and palliative care may improve outcomes in advanced lung disease. *ERJ Open Res* 2018; 4.
39. Steinel JA and Madigan EA. Resource utilization in home health chronic obstructive pulmonary disease management. *Outcomes Manag* 2003; 7: 23–27.
40. van Dam van Isselt EF, Spruit M, Groenewegen-Sipkema KH, et al. Geriatric rehabilitation for patients with advanced chronic obstructive pulmonary disease: a naturalistic prospective cohort study on feasibility and course of health status. *Chron Respir Dis* 2014; 11: 111–119.
41. Rocker GM, Amar C, Laframboise WL, et al. Spreading improvements for advanced COPD care through a Canadian Collaborative. *Int J Chron Obstruct Pulmon Dis* 2017; 12: 2157–2164.
42. Booth S, Farquhar M, Gysels M, et al. The impact of a breathlessness intervention service (BIS) on the lives of patients with intractable dyspnea: a qualitative phase 1 study. *Palliat Support Care* 2006; 4: 287–293.
43. Reilly CC, Bausewein C, Pannell C, et al. Patients' experiences of a new integrated breathlessness support service for patients with refractory breathlessness: results of a postal survey. *Palliat Med* 2016; 30: 313–322.
44. Johnston B, Coole C and Jay NM. An end-of-life care nurse service for people with COPD and heart failure: stakeholders' experiences. *Int J Palliat Nurs* 2016; 22: 549–559.
45. Rabow MW, Schanche K, Petersen J, et al. Patient perceptions of an outpatient palliative care intervention: "It had been on my mind before, but I did not know how to start talking about death. . .". *J Pain Symptom Manage* 2003; 26: 1010–1015.
46. Bove DG, Jellington MO, Lavesen M, et al. Assigned nurses and a professional relationship: a qualitative study of COPD patients' perspective on a new palliative outpatient structure named CAPTAIN. *BMC Palliat Care* 2019; 18: 24.
47. Bove DG, Lavesen M, Jellington MO, et al. First year experiences with a palliative out-patients structure for patients with COPD: a qualitative study of health professionals' expectations and experiences. *BMC Palliat Care* 2018; 17.
48. Verma JY, Amar C, Sibbald S, et al. Improving care for advanced COPD through practice change: experiences of participation in a Canadian spread collaborative. *Chron Respir Dis* 2018; 15: 5–18.
49. Farquhar MC, Higginson IJ, Fagan P, et al. The feasibility of a single-blinded fast-track pragmatic randomised controlled trial of a complex intervention for breathlessness in advanced disease. *BMC Palliat Care* 2009; 8: 9.
50. Farquhar M, Higginson IJ, Fagan P, et al. Results of a pilot investigation into a complex intervention for breathlessness in advanced chronic obstructive pulmonary disease (COPD): brief report. *Palliat Support Care* 2010; 8: 143–149.
51. Gillis D, Demmons J and Rocker G. Expanding the INSPIRED COPD Outreach Program to the emergency department: a feasibility assessment. *Int J Chron Obstruct Pulmon Dis* 2017; 12: 1597–1604.
52. Buckingham S, Kendall M, Ferguson S, et al. HELPing older people with very severe chronic obstructive pulmonary disease (HELP-COPD): mixed-method feasibility pilot randomised controlled trial of a novel intervention. *NPJ Prim Care Respir Med* 2015; 25: 15020.
53. Horton R, Rocker G, Dale A, et al. Implementing a palliative care trial in advanced COPD: a feasibility assessment (the COPD IMPACT study). *J Palliat Med* 2013; 16: 67–73.
54. Qian MYY, Politis J, Thompson M, et al. Individualized breathlessness interventions may improve outcomes in patients with advanced COPD. *Respirology* 2018; 23: 1146–1151.
55. Scheerens C, Pype P, Van Cauwenberg J, et al. Early integrated palliative home care and standard care for end-stage COPD (EPIC): a Phase II Pilot RCT testing feasibility, acceptability, and effectiveness. *J Pain Symptom Manage* 2020; 59: 206–224.e207.
56. Vitacca M, Comini L, Tabaglio E, et al. Tele-assisted palliative homecare for advanced chronic obstructive pulmonary disease: a feasibility study. *J Palliat Med* 2019; 22: 173–178.
57. Janssens JP, Weber C, Herrmann FR, et al. Can early introduction of palliative care limit intensive care, emergency and hospital admissions in patients with severe chronic obstructive pulmonary disease? A Pilot Randomized Study. *Respiration* 2019; 97: 406–415.
58. Lockhart CA, Volk-Craft BE, Hamilton G, et al. The PhoenixCare Program. *J Palliat Med* 2003; 6: 1001–1012.
59. Datla S, Verberkt CA, Hoye A, et al. Multi-disciplinary palliative care is effective in people with symptomatic heart failure: a systematic review and narrative synthesis. *Palliat Med* 2019; 33: 1003–1016.
60. Mannino DM and Buist AS. Global burden of COPD: risk factors, prevalence, and future trends. *Lancet* 2007; 370: 765–773.
61. Landers A, Wiseman R, Pitama S, et al. Patient perceptions of severe COPD and transitions towards death: a qualitative study identifying milestones and developing key opportunities. *NPJ Prim Care Respir Med* 2015; 25: 15043.
62. Hoffmann TC, Glasziou PP, Boutron I, et al. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. *BMJ (Clinical research ed)* 2014; 348: g1687.
63. Verberne LM, Kars MC, Schepers SA, et al. Barriers and facilitators to the implementation of a paediatric palliative care team. *BMC Palliat Care* 2018; 17: 23.
64. Pfadenhauer LM, Gerhardus A, Mozygemba K, et al. Making sense of complexity in context and implementation: the Context and Implementation of Complex Interventions (CICI) framework. *Implement Sci* 2017; 12: 21.