FROM REACTIVE TO PROACTIVE: IMPLEMENTING PALLIATIVE CARE FOR PATIENTS WITH COPD

Johanna M.C. Broese

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Cover and lay-out: Eveline Korving, Schreef Studio
Cover illustration: Eveline Korving, Schreef Studio
Printing: Optima Grafische Communicatie, Rotterdam, The Netherlands

This thesis was funded by a grant of the Netherlands Organization for Health Research and Development (ZonMw), research grant number 844001401.

Financial support for printing of this thesis was kindly provided by the Department of Public Health and Primary Care of the Leiden University Medical Center, the Leiden University Libraries, and Long Alliantie Nederland.

ISBN: 978-94-6361-901-1

From reactive to proactive:

implementing palliative care for patients with COPD

Proefschrift

ter verkrijging van
de graad van doctor aan de Universiteit Leiden,
op gezag van rector magnificus prof. dr. ir. H. Bijl,
volgens besluit van het college voor promoties
te verdedigen op dinsdag 17 oktober 2023
klokke 15.00 uur

door

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geboren te Harlingen
in 1990

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Chapter 1

General introduction

COPD

Chronic Obstructive Pulmonary Disease (COPD) is a progressive disabling lung disease that affects millions of people worldwide.[1] It is mainly caused by tobacco smoking, but also non-smokers can develop COPD due to air pollution, occupational exposure, or genetic factors.[1] Patients with COPD experience many symptoms such as breathlessness and fatigue.[2] The disease course is typically characterized by a gradual decline with episodes of acute worsening of the disease – acute exacerbations – for which up to 20% of patients require at least one hospital admission per year for treatment.[3] The management of COPD is mainly disease-oriented and aims to preserve optimal lung function, decrease symptoms, and prevent recurrent exacerbations.[1] It includes smoking cessation, bronchodilators, pulmonary rehabilitation, and in advanced stages it may include oxygen therapy. In a very small number of patients non-invasive mechanical ventilation, surgery, or bronchoscopic interventions may be beneficial.[1] No curative treatment for COPD is available, except for lung transplantation for which there is an enormous donor shortage, and which is very costly.[4]

COPD and mortality

COPD is a life-threatening disease, with many patients dying prematurely from it. It is one of the top three causes of death worldwide.[5] In the Netherlands, it is the number five cause of death, with yearly more than 6000 people dying from COPD.[6] The mortality risk increases with the frequency of acute exacerbations and is higher than with heart attacks.[7, 8] Therefore the term 'lung attack' has been introduced to illustrate the severe consequences of acute exacerbations of COPD and to put emphasis on the urgent need for action for patients and healthcare providers.[9]

Symptom burden and quality of life

Patients with COPD have a high symptom burden leading to poor quality of life, similar or even higher than patients with incurable lung cancer.[10, 11] Comorbidities are frequently present, often related to the common pathways of smoke-induced diseases, and increase the symptom burden and physical limitations even further.[1] Breathlessness is the most prevalent symptom, but other debilitating symptoms such as fatigue, cough, pain, insomnia, anxiety and depression are often present.[12] Many patients have fear of becoming breathless or suffocating, resulting in avoidance of activities and physical deconditioning.[13] The physical limitations reduce participation in family and social life, resulting in feelings of social isolation[14, 15] and increasingly experiencing being 'a burden to family'.[16, 17] COPD is stigmatized in our society as people view it as a self-inflicted disease due to the patient's smoking history, leaving patients feeling ashamed or guilty, or thinking they do not deserve proper care.[18] Moreover, the prolonged disease course with decreasing functional status negatively affects their informal caregivers. Also, with increasing dependency, their relationship changes, which can be grieving for both patient and informal caregiver.[19] As COPD affects many aspects of quality of life and limits the life-expectancy, patients with advanced COPD may benefit from a palliative care approach.

Palliative care

Palliative care is 'care improving the quality of life of patients and their families, who are facing a life-threatening condition or frailty, through prevention and relief of suffering by means of early identification and careful assessment, and treatment of physical, psychological, social and spiritual problems. Over the course of the illness or frailty, palliative care aims to preserve autonomy, access to information and the opportunity to make choices.'[20] The phrase 'through prevention and relief of suffering' emphasizes the need for a proactive rather than a reactive attitude. Palliative care includes advance care planning (ACP). ACP is a continuous and dynamic process of discussing patient goals and preferences.[21] Doing so, care becomes aligned with the patient's wishes and preferences. It aims to improve the relationship with the patient, enable patients to prepare themselves for the end-of-life, and avoid overtreatment and unwanted hospital admissions, preventing patients from dying in an acute care setting.[22] Emerging evidence indicates that palliative care has a positive impact on enhancing the quality of life and reducing symptom burden for patients with life-limiting illnesses. Also, it has the potential to increase patient and informal caregiver satisfaction with care and reduce healthcare utilization.[23]

The publication of the Quality Framework Palliative Care in 2017 aimed to encourage implementation of palliative care in the Netherlands.[20] The framework describes the essential elements to deliver high-quality palliative care. In the Netherlands, palliative care is considered not a separate specialism, but all healthcare providers should include 'generalist' palliative care when caring for and treating palliative patients. Thus, a palliative care approach should be integrated into routine COPD care, starting early in the disease trajectory.[24, 25] Only in the case of complex needs, specialist palliative care should be involved.

Palliative care provision in COPD

Although guidelines recommend palliative care for patients with COPD,[26, 27] palliative care still is no daily practice for patients with COPD and their informal caregivers. Communication about palliative and end-of-life care topics is unlikely. A systematic review found that the proportion of patients with whom palliative and end-of-life care were discussed, varied between 0 and 56% across 17 studies, of which the majority found a proportion less than 30%.[28] In a study among Dutch pulmonologists and pulmonologists in training, participants reported to have discussed life-sustaining treatment preferences in 20% of their patients with GOLD stadium 3-4, and life expectancy 16%.[29] Also, patients with COPD are less likely to be referred to palliative care services than those with cancer. And when they are referred, it is mostly at the very end of life, with a median of 10 days before death in patients with COPD.[30] In 2011, a national guideline 'Palliative care for people with COPD' was developed by the Lung Alliance Netherlands (LAN).[31] However, a survey among Dutch pulmonologists in 2015 showed that the guideline was used by only half of the pulmonologists.[32]

Palliative care is hampered by several barriers related to the disease course, patients and their family, and healthcare providers. One of the main barriers is the unpredictable disease trajectory of COPD, making it difficult to determine when to start palliative care and discuss ACP.[28] Whereas cancer is directly associated with death ("how long do I still have, doctor?"), and often has a clear moment when life-prolonging treatment is not available anymore, most people are unaware that they could die of COPD.[33] Moreover, symptoms and limitations worsen gradually over the years, making patients to view them as a normal part of aging and struggle with accepting support.[34] Half of the patients with COPD have a low education level and low health literacy, limiting their understanding of their disease and prognosis.[35] Many healthcare providers avoid ACP conversations because of a lack of such communication skills, a fear to take away the patient's hope or increase feelings of anxiety, the assumption that palliative care is restricted to the terminal and dying phase, or time constraints. Furthermore, there is a lack of care continuity and collaboration between healthcare providers.[36]

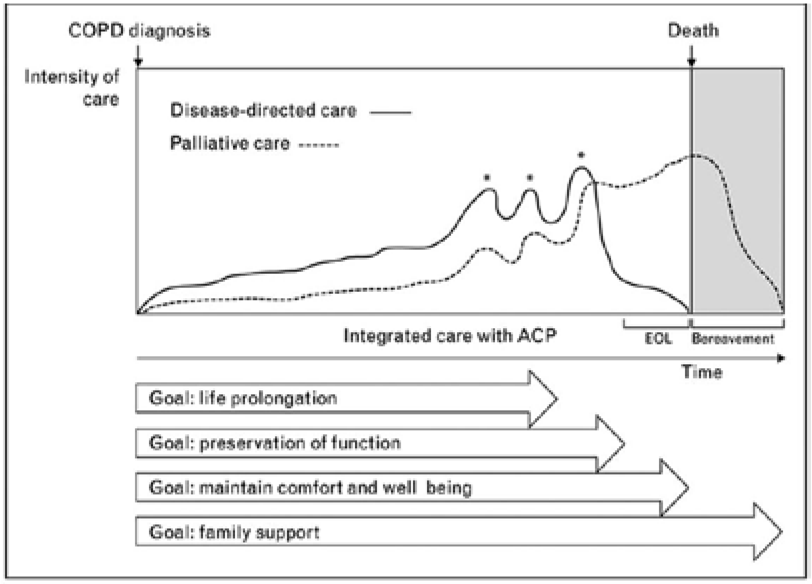


Figure 1. Care model of the integration of disease-oriented and palliative care, as proposed by Harrington et al. (2017)[24]

Although barriers and facilitators to palliative care provision have been studied, insufficient knowledge existed on how to overcome these barriers and successfully implement palliative care for patients with COPD. Researchers and policy makers have gradually become aware of the significant unrealized potential of effective interventions, due to the fact that they are not actively implemented after development.[37] In recent decades, implementation research has been a developing field. It entails the understanding of implementation barriers and facilitators and generates evidence for implementation strategies, how to translate knowledge into practice and improve healthcare.[38] Also, elements of both clinical effectiveness and implementation research can be combined using so-called 'effectiveness-implementation hybrid designs', to achieve more rapid translational gains and more effective implementation strategies.[39]

The COMPASSION project

To improve and implement palliative care provision in COPD, a national 4-year project was initiated by the Lung Alliance Netherlands, the Leiden University Medical Center, and Radboudumc in 2017, with financial support from The Netherlands Organization for Health Research and Development (ZonMw). The project was called COMPASSION, as it is an acronym for COPD Palliative and Supportive care Implementation and should be a central element in providing COPD-care.

In collaboration with representatives of relevant patient, family and professional organizations, we developed an integrated palliative COPD care intervention that integrates existing scientific and practical knowledge. From the immense enthusiasm with which healthcare providers collaborated in this project, it became clear that it was a topic with high potential for improvement. As identifying patients for palliative care was considered the most important aspect for improvement by pulmonologists,[32] an important first step was to determine to whom palliative care should be provided. Earlier research, focused on general practitioners, showed that identification of palliative patients with organ failure in general practice was not succesful.[40] Instead, hospital admission for an acute exacerbation of COPD appeared more feasible, as care is concentrated in this setting, allowing healthcare providers to make it a routine. Also, it is associated with increased mortality and it aligned the successful national transmural care pathway for patients hospitalized with an exacerbation of COPD.[41] The ProPal-COPD tool, combining the Surprise Question ("Would I be surprised if this patient were to die within the next 12 months?") with six clinical indicators was chosen as screening instrument. It had previously been developed by Duenk et al. and appeared a promising tool to identify patients in the palliative phase, with a high sensitivity to predict death within 12 months in an internal validation study.[42]

To enhance the adoption of the intervention by healthcare providers, a multifaceted implementation strategy was developed comprising a training, an online toolbox with information and practical tools, and support with planning and monitoring of implementation. As palliative care is not a standard part of medical training, doctors and nurses lack skills to communicate about palliative and end-of-life topics. Communication training using role play was found successful in previous research of Tilburgs et al,[43] and was also included in the COMPASSION training. Within a cluster randomized controlled trial, the strategy was tested in hospital regions spread over the Netherlands. Alongside the study and after the study had ended, we continued to develop the online toolbox into its current form. The training has been transformed into a blended learning program. Scan the QR-code to view the online toolbox or click the following link: https://palliatievezorgcopd.nl

Aims and outline of this thesis

This thesis aims to study how to improve and implement the provision of palliative care for patients with COPD and their informal caregivers. More specifically, the aim was to broaden the knowledge on the effectiveness and process of integrating palliative care into COPD care. To achieve this goal, several studies using different designs have been conducted. First, we explored current palliative care practice in COPD and available literature by addressing the following two research questions:

1. **To what degree is palliative care for patients with COPD currently implemented and formalized in primary and secondary care in the Netherlands?**

2. **Have palliative care interventions been developed for patients with COPD and what evidence is available on the effectiveness and implementation outcomes?**

Chapter 2 describes a national survey among pulmonologists and general practitioners to explore the current content and organization of palliative care for patients with COPD. **Chapter 3** provides an overview of the literature to date on palliative care interventions for patients with COPD. We assessed the characteristics of such interventions, reviewed the available evidence on effect outcomes, and identified barriers and facilitators to successful implementation.

Next, we performed a cluster randomized controlled trial – the COMPASSION study – in which the clinical effectiveness and implementation process of palliative care in COPD were studied using mixed-methods. The research questions were:

3. **What is the effect of the implementation of integrated palliative care on patient, informal caregiver and healthcare provider outcomes?**

4. **What is the effect of a multifaceted implementation strategy on implementation outcomes and what barriers hamper the implementation of integrated palliative care in routine COPD care?**

Chapter 4 describes the study protocol of the COMPASSION study in detail. In Chapter 5 and 6 the results of the COMPASSION study are presented. **Chapter 5** reports on the effects of the integrated palliative care intervention on quality of life and other patient outcomes. **Chapter 6** describes a comprehensive evaluation of the implementation strategy and process of implementing palliative care into regular COPD care.

Within the COMPASSION study, hospitalized patients were screened for palliative care needs using the ProPal-COPD tool. The trial data were used to address the last research question of this thesis:

5. **What is the accuracy of the ProPal-COPD tool in predicting 1-year mortality, and what are user experiences of healthcare providers?**

In **Chapter 7,** we externally validated the ProPal-COPD tool and we explored user experiences of healthcare providers.

In **Chapter 8**, the main research findings of the studies and their implications are discussed. Finally, recommendations for clinical practice, education, policy and future research are provided.

References

1. GOLD. Pocket Guide to COPD Diagnosis, Management, and Prevention. A Guide for Health Care Professionals 2023.
2. Janssen DJ, Spruit MA, Wouters EF, et al. Daily symptom burden in end-stage chronic organ failure: a systematic review. *Palliat Med* 2008; 22: 938-948. DOI: 0269216308096906 [pii];10.1177/0269216308096906 [doi].
3. Seemungal TA, Hurst JR and Wedzicha JA. Exacerbation rate, health status and mortality in COPD--a review of potential interventions. *Int J Chron Obstruct Pulmon Dis* 2009; 4: 203-223. 20090611. DOI: 10.2147/copd.s3385.
4. Leard LE, Holm AM, Valapour M, et al. Consensus document for the selection of lung transplant candidates: An update from the International Society for Heart and Lung Transplantation. *J Heart Lung Transplant* 2021; 40: 1349-1379. 20210724. DOI: 10.1016/j.healun.2021.07.005.
5. Lozano R, Naghavi M, Foreman K, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012; 380: 2095-2128. 2012/12/19. DOI: 10.1016/s0140-6736(12)61728-0.
6. CBS StatLine. Overledenen; belangrijke doodsoorzaken, https://opendata.cbs.nl/statline/#/CBS/nl/dataset/7052_95 (accessed 11 June 2023).
7. Hoogendoorn M, Hoogenveen RT, Rutten-van Mölken MP, et al. Case fatality of COPD exacerbations: a meta-analysis and statistical modelling approach. *Eur Respir J* 2011; 37: 508-515. 20100701. DOI: 10.1183/09031936.00043710.
8. Wong CM, Hawkins NM, Petrie MC, et al. Heart failure in younger patients: the Meta-analysis Global Group in Chronic Heart Failure (MAGGIC). *Eur Heart J* 2014; 35: 2714-2721. 20140617. DOI: 10.1093/eurheartj/ehu216.
9. Holverda S, Rutgers MR and Kerstjens HAM. Time to rename COPD exacerbations: implementing the term lung attack. *Lancet Respir Med* 2020; 8: e25. DOI: 10.1016/s2213-2600(20)30123-5.
10. Habraken JM, van der Wal WM, Ter Riet G, et al. Health-related quality of life and functional status in end-stage COPD: a longitudinal study. *Eur Respir J* 2011; 37: 280-288. 2010/06/10. DOI: 10.1183/09031936.00149309.
11. Edmonds P, Karlsen S, Khan S, et al. A comparison of the palliative care needs of patients dying from chronic respiratory diseases and lung cancer. *Palliat Med* 2001; 15: 287-295. 2002/06/11. DOI: 10.1191/026921601678320278.
12. 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. 2011/04/23. DOI: 10.1089/jpm.2010.0479.
13. Sigurdardottir KR, Haugen DF, van der Rijt CC, et al. Clinical priorities, barriers and solutions in end-of-life cancer care research across Europe. Report from a workshop. *European*

journal of cancer (Oxford, England : 1990) 2010; 46: 1815-1822. 2010/05/12. DOI: 10.1016/j.ejca.2010.03.012.

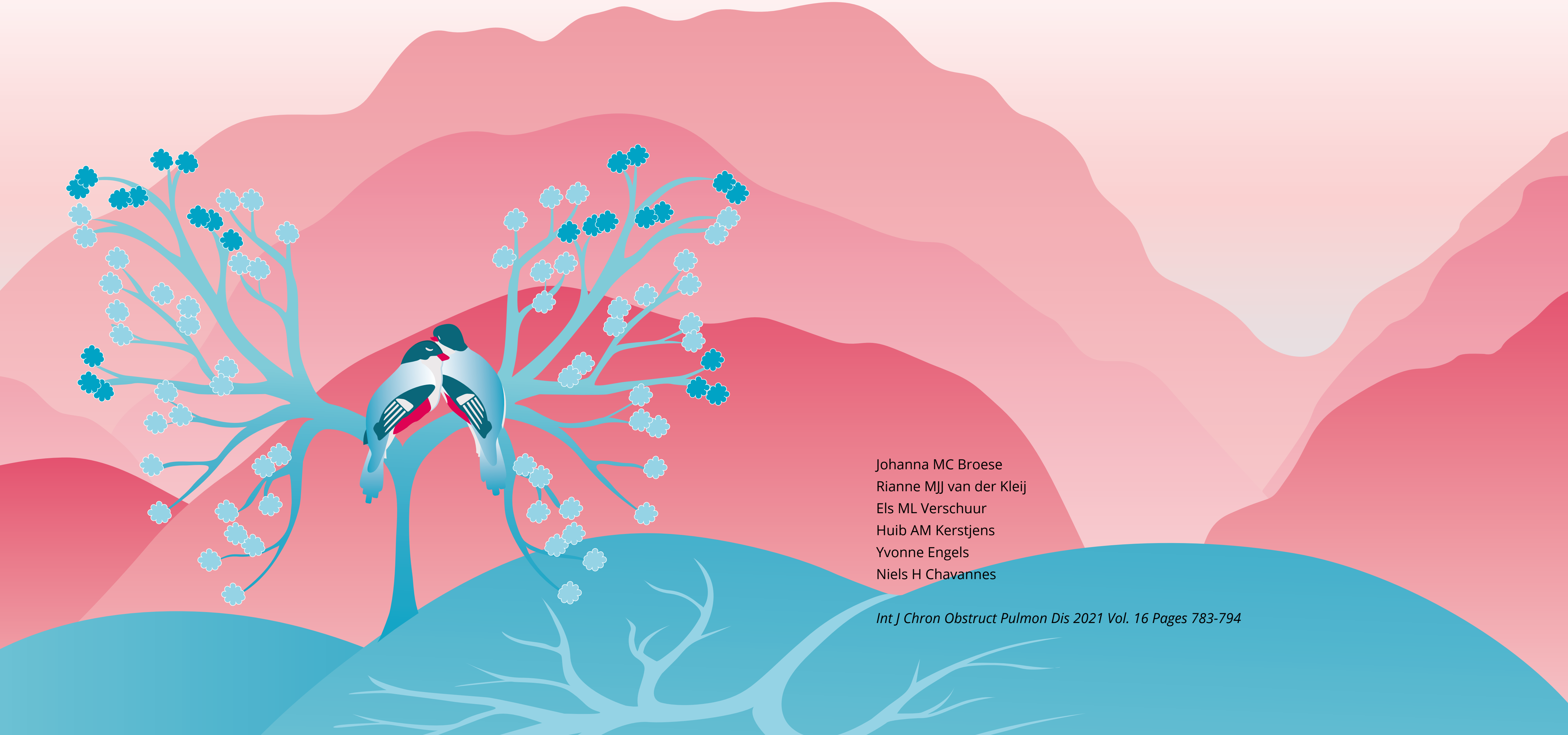
14. Seamark DA, Blake SD, Seamark CJ, et al. Living with severe chronic obstructive pulmonary disease (COPD): perceptions of patients and their carers. An interpretative phenomenological analysis. *Palliat Med* 2004; 18: 619-625. DOI: 10.1191/0269216304pm928oa.
15. Schroedl CJ, Yount SE, Szmuilowicz E, et al. A qualitative study of unmet healthcare needs in chronic obstructive pulmonary disease. A potential role for specialist palliative care? *Annals of the American Thoracic Society* 2014; 11: 1433-1438. DOI: 10.1513/AnnalsATS.201404-155BC.
16. 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. 2015/07/15. DOI: 10.1038/npjpcrm.2015.43.
17. Gysels M and Higginson IJ. Access to services for patients with chronic obstructive pulmonary disease: the invisibility of breathlessness. *J Pain Symptom Manage* 2008; 36: 451-460. 20080520. DOI: 10.1016/j.jpainsymman.2007.11.008.
18. Harrison SL, Robertson N, Apps L, et al. "We are not worthy"--understanding why patients decline pulmonary rehabilitation following an acute exacerbation of COPD. *Disability and rehabilitation* 2015; 37: 750-756. 2014/07/11. DOI: 10.3109/09638288.2014.939770.
19. Nakken N, Janssen DJ, van den Bogaart EH, et al. Informal caregivers of patients with COPD: Home Sweet Home? *European respiratory review : an official journal of the European Respiratory Society* 2015; 24: 498-504. 2015/09/02. DOI: 10.1183/16000617.00010114.
20. IKNL/Palliactief. Netherlands Quality Framework for Palliative Care. 2017.
21. Rietjens JAC, Sudore RL, Connolly M, et al. Definition and recommendations for advance care planning: an international consensus supported by the European Association for Palliative Care. *The Lancet Oncology* 2017; 18: e543-e551. 2017/09/09. DOI: 10.1016/s1470-2045(17)30582-x.
22. Fleuren N, Depla M, Janssen DJA, et al. Underlying goals of advance care planning (ACP): a qualitative analysis of the literature. *BMC Palliat Care* 2020; 19: 27. 2020/03/08. DOI: 10.1186/s12904-020-0535-1.
23. 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. 2016/11/29. DOI: 10.1001/jama.2016.16840.
24. Harrington SE, Rogers E and Davis M. Palliative care and chronic obstructive pulmonary disease: where the lines meet. *Curr Opin Pulm Med* 2017; 23: 154-160. DOI: 10.1097/mcp.0000000000000358.
25. van der Eerden M, Csikos A, Busa C, et al. Experiences of patients, family and professional caregivers with Integrated Palliative Care in Europe: protocol for an international, multicenter, prospective, mixed method study. *BMC Palliat Care* 2014; 13: 52. 2014/12/05. DOI: 10.1186/1472-684x-13-52.
26. IKNL/LAN. *National guideline Palliative care in COPD, version 2.0*. 2021. Utrecht, The Netherlands.

27. 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. 2008/04/09. DOI: 10.1164/rccm.200605-587ST.
28. 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 2017/05/04. DOI: 10.1183/23120541.00068-2016.
29. Janssen DJ, Curtis JR, Au DH, et al. Patient-clinician communication about end-of-life care for Dutch and US patients with COPD. *Eur Respir J* 2011; 38: 268-276. 2011/01/15. DOI: 10.1183/09031936.00157710.
30. Beernaert K, Cohen J, Deliens L, et al. Referral to palliative care in COPD and other chronic diseases: a population-based study. *Respir Med* 2013; 107: 1731-1739. 2013/07/03. DOI: 10.1016/j.rmed.2013.06.003.
31. *[Guideline palliative care for people with COPD]. Richtlijn Palliatieve Zorg voor mensen met COPD.* 2011. Amersfoort, the Netherlands: Lung Alliance Netherlands.
32. Duenk RG, Verhagen C, Dekhuijzen P, et al. The view of pulmonologists on palliative care for patients with COPD: a survey study. *Int J Chron Obstruct Pulmon Dis* 2017; 12: 299-311. 2017/02/09. DOI: 10.2147/copd.s121294.
33. Gardiner C, Gott M, Small N, et al. Living with advanced chronic obstructive pulmonary disease: patients concerns regarding death and dying. *Palliat Med* 2009; 23: 691-697. 20091013. DOI: 10.1177/0269216309107003.
34. Pinnock H, Kendall M, Murray SA, et al. Living and dying with severe chronic obstructive pulmonary disease: multi-perspective longitudinal qualitative study. *BMJ (Clinical research ed)* 2011; 342: d142. 2011/01/26. DOI: 10.1136/bmj.d142.
35. Heijmans M, Brabers A and Rademakers J. *Hoe gezondheidsvaardig is Nederland? Factsheet Gezondheidsvaardigheden–Cijfers 2019*. 2019. Utrecht: Nivel.
36. Oishi A and Murtagh FE. The challenges of uncertainty and interprofessional collaboration in palliative care for non-cancer patients in the community: a systematic review of views from patients, carers and health-care professionals. *Palliat Med* 2014; 28: 1081-1098. DOI: 0269216314531999 [pii];10.1177/0269216314531999 [doi].
37. Bauer MS and Kirchner J. Implementation science: What is it and why should I care? *Psychiatry Research* 2020; 283: 112376. DOI: https://doi.org/10.1016/j.psychres.2019.04.025.
38. Eccles MP and Mittman BS. Welcome to Implementation Science. *Implementation Science* 2006; 1: 1. DOI: 10.1186/1748-5908-1-1.
39. Curran GM, Bauer M, Mittman B, et al. Effectiveness-implementation hybrid designs: combining elements of clinical effectiveness and implementation research to enhance public health impact. *Med Care* 2012; 50: 217-226. 2012/02/09. DOI: 10.1097/MLR.0b013e3182408812.
40. Thoonsen B, Vissers K, Verhagen S, et al. Training general practitioners in early identification and anticipatory palliative care planning: a randomized controlled trial. *BMC Fam Pract* 2015; 16: 126. DOI: 10.1186/s12875-015-0342-6 [doi];10.1186/s12875-015-0342-6 [pii].

41. Westbroek LF, Klijnsma M, Salomé P, et al. Reducing the Number of Hospitalization Days for COPD: Setting up a Transmural-Care Pathway. *Int J Chron Obstruct Pulmon Dis* 2020; 15: 2367-2377. 20200930. DOI: 10.2147/copd.S242914.
42. Duenk RG, Verhagen C, Bronkhorst EM, et al. Development of the ProPal-COPD tool to identify patients with COPD for proactive palliative care. *Int J Chron Obstruct Pulmon Dis* 2017; 12: 2121-2128. DOI: 10.2147/COPD.S140037 [doi];copd-12-2121 [pii].
43. Tilburgs B, Koopmans R, Vernooij-Dassen M, et al. Educating Dutch General Practitioners in Dementia Advance Care Planning: A Cluster Randomized Controlled Trial. *J Am Med Dir Assoc* 2020; 21: 837-842.e834. 2019/11/25. DOI: 10.1016/j.jamda.2019.09.010.

Chapter 2

Provision of palliative care in patients with COPD: a survey among pulmonologists and general practitioners



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Int J Chron Obstruct Pulmon Dis 2021 Vol. 16 Pages 783-794

Abstract

Introduction
Patients with advanced chronic obstructive pulmonary disease (COPD) experience significant symptom burden, leading to poor quality of life. Although guidelines recommend palliative care for these patients, this is not widely implemented and prevents them from receiving optimal care.

Objective
A national survey was performed to map the current content and organization of palliative care provision for patients with COPD by pulmonologists and general practitioners (GPs) in the Netherlands.

Methods
We developed a survey based on previous studies, guidelines and expert opinion. Dutch pulmonologists and GPs were invited to complete the survey between April and August 2019.

Results
130 pulmonologists (15.3%; covering 76% of pulmonology departments) and 305 GPs (28.6%) responded. Median numbers of patients with COPD in the palliative phase treated were respectively 20 and 1.5 per year. 43% of pulmonologists and 9% of GPs reported some formalized agreements regarding palliative care provision. Physicians most often determined the start of palliative care based on clinical expertise or the Surprise Question. 31% of pulmonologists stated that they often or always referred palliative patients with COPD to a specialist palliative care team; a quarter rarely referred. 79% of the respondents mentioned to often or always administer opioids to treat dyspnea. The topics least discussed were non-invasive ventilation and the patient's spiritual needs. The most critical barrier to starting a palliative care discussion was difficulty in predicting the disease course.

Conclusion
Although pulmonologists and GPs indicated to regularly address palliative care aspects, palliative care for patients with COPD remains unstructured and little formalized. However, our data revealed a high willingness to improve this care. Clear guidance and standardization of practice are needed to help providers decide when and how to initiate discussions, when to involve specialist palliative care and how to optimize information exchange between care settings.

Keywords
COPD, palliative care, advance care planning, surprise question, organization.

Introduction

Chronic obstructive pulmonary disease (COPD) is the third leading cause of death worldwide.[1] In advanced stages, COPD is associated with a significant symptom burden and poor quality of life.[2] However, palliative care is often not provided to patients with COPD; discussions on palliative and end-of-life care rarely occur,[3] and access to specialist palliative care is limited and late.[44] This lack of palliative care is often attributed to the unpredictable disease course of COPD, making it hard to determine when to start palliative care.[5]

Consequently, physicians and policymakers increasingly acknowledge the need for better and timely palliative care provision for patients with COPD.[6-8] In the Netherlands, various efforts have been deployed to improve quality and timing of palliative care for patients with life-limiting diseases, including COPD. A national multidisciplinary guideline on this topic was published in 2011.[9] Furthermore, the Quality Framework Palliative Care was published in 2017, to incentivize implementation of palliative care in the Netherlands.[10] The framework describes the essential elements needed to deliver high-quality palliative care. In this framework, no distinction is made between oncologic and non-oncologic diseases, following the WHO definition of palliative care.[11]

Previous studies have highlighted that the provision of palliative care to patients with COPD is unstructured and often limited to terminal care only.[3,12] However, no study has yet examined the formalization and implementation of palliative care for patients with COPD in the Netherlands. Therefore, we developed a national survey to explore the current content and organization of palliative care for patients with COPD in primary and secondary care in the Netherlands.

Material and Methods

Design

A national survey study was performed among pulmonologists and general practitioners (GPs) in the Netherlands, to examine both the primary and secondary palliative care provision to patients with COPD.

Procedure

Pulmonologists (n=668) and pulmonologists in training (i.t.) (n=184) registered by the Netherlands Association of Physicians for Lung Diseases and Tuberculosis (NVALT) were recruited via various and subsequent strategies between April and August 2019, to maximize participation (see Figure 1). Both a digital link to the online survey and a paper version was used. A link to the survey was disseminated via two subsequent digital newsletters of the NVALT, a digital newsletter of the Lung Alliance Netherlands (LAN) and via e-mails to each pulmonology department (n=80) in the Netherlands. Also, pulmonologists visiting the annual Dutch pulmonologist conference were asked to complete a paper version of the survey. Subsequently, paper versions of the survey were sent to pulmonologists of departments of which no pulmonologist had responded yet.

GPs were recruited in two ways. First, postal surveys were sent to a random sample of 900 general practices in the Netherlands, obtained via the Netherlands Institute for Health Services Research (NIVEL). A reminder was sent to non-responding general practices after five weeks. Second, a digital link to the online survey was sent to 165 GPs via two GP expert advice networks on COPD/asthma care (CAHAG) and palliative care (PalHag).

All responses received before August 21, 2019 were included in the analysis. The online data management system Castor edc was used for data collection. Consent to participate was implied by responding to the survey. This study was approved by the Medical Ethics Committee of the Radboud University Medical Center (number 2019-5021).

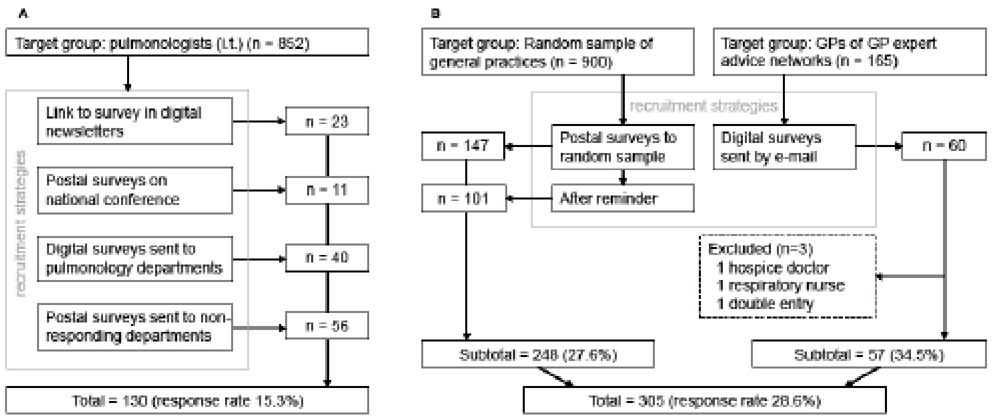


Figure 1 Flowchart of recruitment strategies and numbers of responding pulmonologists (**A**) and general practitioners (**B**). *Abbreviations:* GP, general practitioner; i.t., in training.

Survey

The survey was developed based on previous studies[7,13,14] and national guidelines.[9,10] In several cycles, we presented drafts of the survey to care providers and experts for adaptations and improvements. The survey started with an introductory text explaining the definition of palliative care and the palliative phase in COPD according to the national guideline[9] (Supplementary table S1). Then, questions were presented regarding the presence and plans for future development of any formalized agreements (i.e. a protocol or specific agreements) in their department or practice, and methods used to identify the palliative phase in patients with COPD. This was followed by a question on the level of experience with palliative care provision in COPD and a question on the estimated number of palliative patients with COPD the participant treated on

average per year. Participants who had treated at least one such patient in the last year, were further inquired on the frequency of palliative care aspects provided and topics discussed in the previous year, and collaboration with and referral to other care providers. Answer options ranged from never to always on a 5-point Likert scale. Also, satisfaction with collaboration between pulmonologists and GPs was inquired. The next question of the survey was presented to all respondents and related to perceived barriers towards palliative care discussions; multiple answer entries were allowed on fourteen statements. Lastly, the following characteristics were questioned: age, gender, position, workplace, work experience and education.

Statistical analysis

All data were analyzed using descriptive statistics. For each item, all available data were used. Therefore, the total number of respondents varied per item. Noncontinuous variables were reported as frequencies. Answers in free text boxes were inductively coded and categorized using Atlas.ti. Differences between 1) pulmonologists and GPs and 2) physicians with and without any form of palliative care training were tested using the Mann-Whitney U test for categorical variables (using 5 answer categories) and the Chi-square test for dichotomous variables. Differences were considered significant if $p < .05$. Statistical analyses were performed with IBM SPSS Statistics, version 25.

Results

Study participants

In total, 130 pulmonologists (response rate of 15.3%), including four pulmonologists in training, and 305 GPs (response rate of 28.6%) responded to the survey between April and August 2019 (Figure 1). The responding pulmonologists were employed in 61 of 80 pulmonology departments (76%) in the Netherlands. The median number of COPD patients treated in the palliative phase was on average 20 per year for pulmonologists and 1.5 per year for GPs (Table 1). In the last year, three pulmonologists and sixty-five GPs had not treated any palliative patient with COPD. Non-response per item was on average 12.9% in returned surveys of pulmonologists and 6.0% in those of GPs (Supplementary table S1).

Structure of palliative care

Fifty-six pulmonologists (45.9%) reported that there were no formalized agreements on the palliative care provision to patients with COPD at their department and thirteen (10.7%) indicated did not know. Fifty-two pulmonologists (43.4%) reported that there were formalized agreements; most detailed the possibility to involve a specialist palliative care team (n=22; 18.0%). Sixteen pulmonologists (13.2%) indicated a hospital-specific care pathway was present, five of these were palliative sedation protocols or dying care pathways. Other agreements covered advance care planning discussions (n=9; 7.4%) and agreements on e.g. scoring symptoms or starting morphine (6; 5.0%). Half of the pulmonologists (n=60; 50.4%) indicated that their department had plans to establish formalized agreements in the future; fourteen (11.9%) referred to the development of a new protocol and eight (6.8%) to the adaptation of an existing protocol or care pathway.

The majority of GPs (n=269; 89.4%) reported that there were no formalized agreements. Twenty-six GPs (8.6%) reported that there were; most of them covered patient support by the GP, a practice nurse or palliative care nurse (n=11; 3.7%), and participation in a PaTz (palliative homecare) group (n=8; 2.7%). No protocols were reported. Thirty-five GPs (11.7%) indicated to have plans to formalize palliative care in COPD in the future, of which eight indicated they planned to establish a protocol.

Table 1 Characteristics of participating pulmonologists and general practitioners

	Pulmonologists (n=130) n (%)	**GPs (n=305) n (%)**
Age (years), mean (SD)	46.0 (8.9)	49.4 (9.6)
Gender, male	67 (59.3)	124 (43.5)
Work experience (years), mean (SD)	13.0 (8.8)	17.8 (9.7)
Workplace		
General hospital	54 (47.8)	
Top clinical hospital	48 (42.5)	N/A
University hospital	8 (7.1)	
Other	3 (2.7)	
Experience with palliative care provision in COPD*	97 (78.0)	105 (34.8)
Median number of palliative patients with COPD treated yearly	20 (range 0-1020)	1.5 (range 0-30)
Treated ≥1 palliative patient with COPD last year	127 (97.7)	240 (78.7)
Education		
Palliative care training, any	36 (35.7)	93 (34.6)
Specialized training in palliative care	2 (1.7)	22 (7.4)
Specialized training in asthma/COPD	N/A	25 (8.9)

*Respondents with answers ‘a reasonable amount’ and ‘a lot’.

Identification of the palliative phase in patients with COPD

As reported by our respondents, the palliative phase in patients with COPD was most often determined based on clinical expertise or by using the Surprise Question (SQ) (Figure 2). The SQ reads *‘Would I be surprised if this patient were to die in the next twelve months*?’ More pulmonologists indicated to use the SQ than GPs (76.9% vs. 56.7%, *p*<.001). Many GPs also determined the palliative phase based on information transfer or transfer of care from the pulmonologist to the GP. Thirteen participants (3.1%) indicated not to discern a palliative phase.

Symptom management

Most respondents (n=283; 79.3%) reported to often or always administer opioids to treat dyspnea (Table 2). No significant differences in frequency were observed between pulmonologists and GPs nor between those with and without palliative care training. GPs prescribed pharmacological treatment for anxiety and depression more often than pulmonologists (*p*=.046). Physicians with palliative care training more frequently provided non-pharmacological treatment for anxiety and depression (*p*=.030 for pulmonologists and *p*=.011 for GPs) than those without (Supplementary table S2).

Doctor-patient-family communication

Almost all respondents indicated to often or always discuss palliative treatment options for dyspnea (n=307; 92.1%) (Table 3). Approximately a third of respondents rarely or never discussed non-invasive ventilation (n=112; 33.4%) or spiritual needs (n=92; 27.8%). GPs discussed seven topics more frequently than pulmonologists. Pulmonologists discussed non-invasive ventilation more often than GPs. Pulmonologists with palliative care training discussed six topics more often than pulmonologists without training (Supplementary table S3): fear of choking (*p*=.015), fear of death/dying (*p*=.025), preferred place of death (*p*=.005), spiritual needs (*p*=.007), caregiver burden (*p*=.003) and goals of care (*p*=.020). Within GPs, no differences were found between those with and without palliative care training.

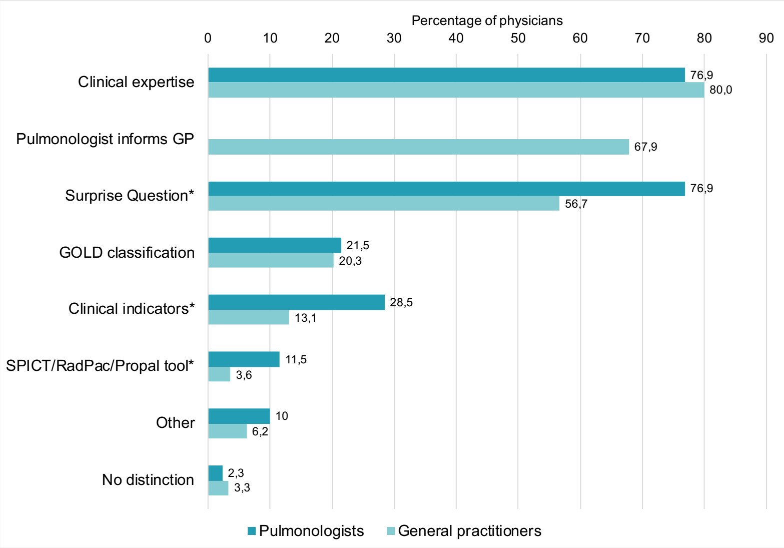


Figure 2 Methods used by pulmonologists and general practitioners to identify the palliative phase in patients with COPD.
*Significant difference (p < .05 using Chi-square test).

Table 2 Symptom management in patients with COPD in the palliative phase that respondents had treated in the previous year, and comparison of pulmonologists and general practitioners.

		All respondents	Pulmonologists	GPs	P-value[a]
Dyspnea using opioids	Never	6 (1.7)	0 (0.0)	6 (2.5)	.077
	Rarely	8 (2.2)	4 (3.3)	4 (1.7)	
	Sometimes	60 (16.8)	18 (15.0)	42 (17.7)	
	Often	202 (56.6)	84 (70.0)	118 (49.8)	
	Always	81 (22.7)	14 (11.7)	67 (28.3)	
Dyspnea using non-pharmacological treatment	Never	12 (3.5)	1 (0.9)	11 (4.8)	.142
	Rarely	35 (10.1)	9 (7.8)	26 (11.4)	
	Sometimes	112 (32.5)	37 (31.9)	75 (32.8)	
	Often	149 (43.2)	58 (50.0)	91 (39.7)	
	Always	37 (10.7)	11 (9.5)	26 (11.4)	
Pain using opioids	Never	24 (6.8)	6 (5.1)	18 (7.7)	.625
	Rarely	84 (23.9)	26 (22.2)	58 (24.8)	
	Sometimes	146 (41.6)	54 (46.2)	92 (39.3)	
	Often	82 (23.4)	26 (22.2)	56 (23.9)	
	Always	15 (4.3)	5 (4.3)	10 (4.3)	
Anxiety/depression using pharmacological treatment	Never	23 (6.6)	9 (7.8)	14 (6.0)	.046
	Rarely	50 (14.4)	22 (19.1)	28 (12.1)	
	Sometimes	155 (44.7)	51 (44.3)	104 (44.8)	
	Often	111 (32.0)	31 (27.0)	80 (34.5)	
	Always	8 (2.3)	2 (1.7)	6 (2.6)	
Anxiety/depression using non-pharmacological treatment	Never	20 (5.9)	5 (4.4)	15 (6.6)	.665
	Rarely	63 (18.5)	25 (21.9)	38 (16.7)	
	Sometimes	149 (43.7)	48 (42.1)	101 (44.5)	
	Often	96 (28.2)	34 (29.8)	62 (27.3)	
	Always	13 (3.8)	2 (1.8)	11 (4.8)	

Data are expressed as absolute values and percentages.
[a]P-values based on Mann-Whitney U test.

Table 3 Frequency of topics discussed by respondents in the previous year, and comparison of pulmonologists and general practitioners.

		All respondents	Pulmonologists	GPs	P-value[a]
Disease course and incurability	Never	2 (0.6)	0 (0.0)	2 (0.9)	.014
	Rarely	4 (1.2)	2 (1.8)	2 (0.9)	
	Sometimes	39 (11.4)	13 (11.4)	26 (11.4)	
	Often	162 (47.4)	67 (58.8)	95 (41.7)	
	Always	135 (39.5)	32 (28.1)	103 (45.2)	
Life expectancy	Never	9 (2.7)	0 (0.0)	9 (4.0)	.050
	Rarely	30 (8.9)	14 (12.5)	16 (7.1)	
	Sometimes	98 (29.0)	41 (36.6)	57 (25.2)	
	Often	133 (39.3)	39 (34.8)	94 (41.6)	
	Always	68 (20.1)	18 (16.1)	50 (22.1)	
Fear of choking	Never	1 (0.3)	0 (0.0)	1 (0.4)	.065
	Rarely	10 (3.0)	3 (2.7)	7 (3.1)	
	Sometimes	53 (15.7)	18 (16.1)	35 (15.5)	
	Often	169 (50.0)	67 (59.8)	102 (45.1)	
	Always	105 (31.1)	24 (21.4)	81 (35.8)	
Fear of death/dying	Never	3 (0.9)	1 (0.9)	2 (0.9)	<.001
	Rarely	13 (3.9)	7 (6.3)	6 (2.7)	
	Sometimes	64 (19.3)	37 (33.0)	27 (12.3)	
	Often	149 (44.9)	46 (41.1)	103 (46.8)	
	Always	103 (31.0)	21 (18.8)	82 (37.3)	
Advantages and disadvantages of life sustaining treatments	Never	0 (0.0)	0 (0.0)	0 (0.0)	.456
	Rarely	7 (2.1)	1 (0.9)	9 (8.0)	
	Sometimes	30 (9.0)	6 (2.7)	21 (9.5)	
	Often	149 (44.7)	58 (51.8)	91 (41.2)	
	Always	147 (44.1)	44 (39.3)	103 (46.6)	
Advantages and disadvantages of non-invasive ventilation	Never	56 (16.7)	0 (0.0)	56 (25.2)	<.001
	Rarely	56 (16.7)	5 (4.4)	51 (23.0)	
	Sometimes	88 (26.3)	28 (24.8)	60 (27.0)	
	Often	93 (27.8)	60 (53.1)	33 (14.9)	
	Always	42 (12.5)	20 (17.7)	22 (9.9)	
Desirability of hospitalization for acute exacerbation	Never	4 (1.2)	1 (0.9)	3 (1.3)	<.001
	Rarely	14 (4.2)	11 (9.8)	3 (1.3)	
	Sometimes	64 (19.0)	39 (34.8)	25 (11.2)	
	Often	158 (47.0)	52 (46.4)	106 (47.3)	
	Always	96 (28.6)	9 (8.0)	87 (38.8)	

Table 3 *Continued*

Palliative treatment options for dyspnea (e.g. morphine)	Never	0 (0.0)	0 (0)	0 (0)	<.001
	Rarely	1 (0.3)	0 (0)	1 (0.4)	
	Sometimes	25 (7.5)	10 (9.1)	15 (6.7)	
	Often	161 (48.3)	73 (66.4)	88 (39.5)	
	Always	146 (43.8)	27 (24.5)	119 (53.4)	
Preferred place of death	Never	6 (1.8)	5 (4.6)	1 (0.4)	<.001
	Rarely	28 (8.4)	21 (19.3)	7 (3.1)	
	Sometimes	61 (18.3)	36 (33.0)	25 (11.2)	
	Often	114 (34.2)	34 (31.2)	80 (35.7)	
	Always	124 (37.2)	13 (11.9)	111 (49.6)	
Spiritual and existential needs	Never	25 (7.6)	15 (13.8)	10 (4.5)	<.001
	Rarely	67 (20.2)	40 (36.7)	27 (12.2)	
	Sometimes	119 (36.0)	36 (33.0)	83 (37.4)	
	Often	85 (25.7)	14 (12.8)	71 (32.0)	
	Always	35 (10.6)	4 (3.7)	31 (14.0)	
Caregiver burden	Never	3 (0.9)	1 (0.9)	1 (0.9)	<.001
	Rarely	25 (7.6)	20 (18.5)	5 (2.2)	
	Sometimes	97 (29.3)	51 (47.2)	46 (20.6)	
	Often	147 (44.4)	32 (29.6)	115 (51.6)	
	Always	59 (17.8)	4 (3.7)	55 (24.7)	
Goals of care	Never	21 (6.4)	1 (0.9)	20 (9.0)	.702
	Rarely	35 (10.7)	12 (11.2)	23 (10.4)	
	Sometimes	131 (39.9)	49 (45.8)	82 (37.1)	
	Often	102 (31.1)	35 (32.7)	67 (30.3)	
	Always	39 (11.9)	10 (9.3)	29 (13.1)	

Data are expressed as absolute values and percentages.
[a]P-values based on Mann-Whitney U test.

Most GPs (n=200; 91.7%) mentioned that, in the past year, they had often or always discussed treatment preferences at home; a minority (n=46; 21.6%) discussed them at the practice. More than half (n=116; 53.5%) often or always discussed these preferences shortly after a hospitalization for an acute exacerbation. Of the pulmonologists, 41.3% (n=43) stated to have often or always discussed preferences when patients visited the emergency department, 66.3% (n=69) during hospitalization and 52.4% (n=54) at the outpatient clinic. More GPs (n=105; 48.4%) than pulmonologists (n=23; 21.9%) mentioned that they often or always planned an appointment specifically for these discussions; 24.4% of the GPs (n=53) and 48.6% of pulmonologists (n=51) never or rarely did so. The majority of pulmonologists (n=92; 86.8%) and GPs (n=159; 72.3%) reported that they never or rarely discussed preferences with a family member without the patient being present. Bereavement support to relatives after the patient deceased was provided more frequently by GPs (n=175; 84.5%) than pulmonologists (n=20; 20.4%).

Collaboration between healthcare providers

When caring for palliative patients with COPD in the past year, pulmonologists indicated they most often collaborate with a specialized COPD-nurse in the hospital (n=82 answered often or always; 77.4%) and GPs most often with a district nurse (n=168 answered often or always; 78.9%) (Figure 3). According to the respondents, patients were most frequently referred to a physical therapist or dietician (Figure 4). Involvement of specialized palliative care providers varied. Almost one-third of pulmonologists (n=33; 31.4%) reported that they often or always refer their palliative patients with COPD to a palliative care consultant; a quarter (n=26; 24.8%) of them referred hardly any. A quarter of GPs (n=55; 25.6%) mentioned to collaborate often or always with a palliative care nurse and more than half never or rarely (n=117; 54.4%).

More than half of the pulmonologists (n=59; 52.7%) and GPs (n=141; 61.8%) were satisfied with the collaboration between pulmonologists and GPs. Satisfaction about the information exchange between the hospital and primary care differed; more GPs were satisfied (n=130; 57.0%) than pulmonologists (n=34; 29.8%).

Barriers to palliative care discussions

The most frequently reported barrier to discuss palliative and end-of-life care topics with patients with COPD was the difficulty in predicting the disease course (Figure 5). The second reported barrier by pulmonologists was lack of time (n=72; 63.7%), whereas only 14.8% (n=43) of the GPs mentioned this barrier. Lack of a clear definition of the palliative phase in COPD was more often indicated as a barrier by GPs than by pulmonologists (n=158; 54.3% vs n=44; 38.9%, *p*=.008). Further, patients' difficulties to specify what future care they want in case of disease deterioration was named as a barrier by both groups (n=88; 30.2% of GPs and n=47; 41.6% of pulmonologists).

Discussion

This is the first study giving a comprehensive overview of the palliative care provision for patients with COPD in primary and secondary care in the Netherlands. In contrast with previous studies conducted in other countries,[3,14,15,16] we found that the majority of physicians regularly discuss palliative care topics with their patients with COPD. In a 2009 study, Dutch pulmonologists reported discussing life-sustaining treatments with 20% of their patients and life expectancy with 16%; the rates found in our study are higher.[17] Interestingly, we found that pulmonologists who had received a training in palliative care were more likely to discuss some important topics, such as spiritual needs, caregiver burden and end-of-life related topics than those without training. These findings may underscore the usefulness of palliative care education. Additionally, almost

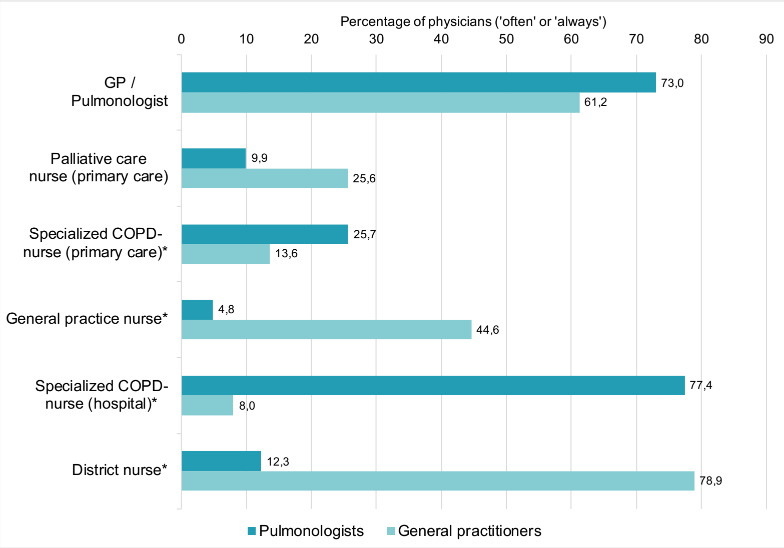


Figure 3 Collaboration with healthcare providers by pulmonologists and general practitioners. Percentages of physicians with answer often or always.
GP, general practitioner; PC, palliative care.
*Significant difference (p < .05 using Mann-Whitney U test).

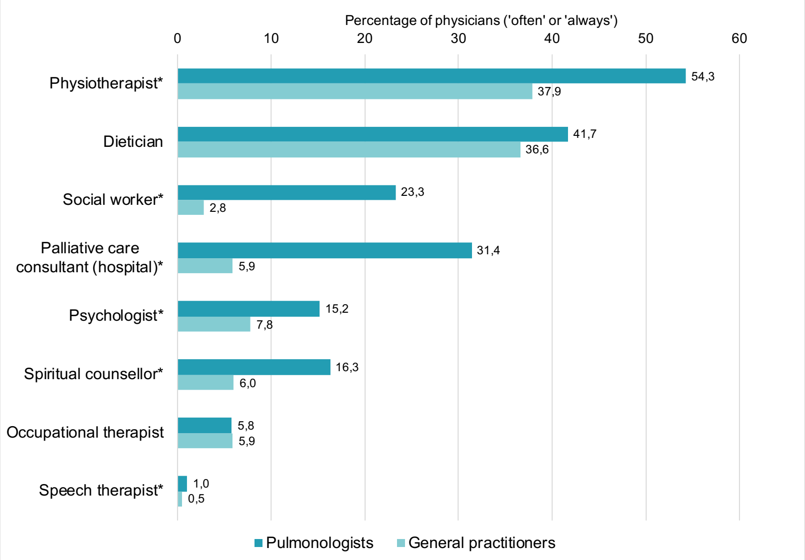


Figure 4 Referral to healthcare providers by pulmonologists and general practitioners. Percentages of physicians with answer often or always.
PC, palliative care.
*Significant difference (p < .05 using Mann-Whitney U test).

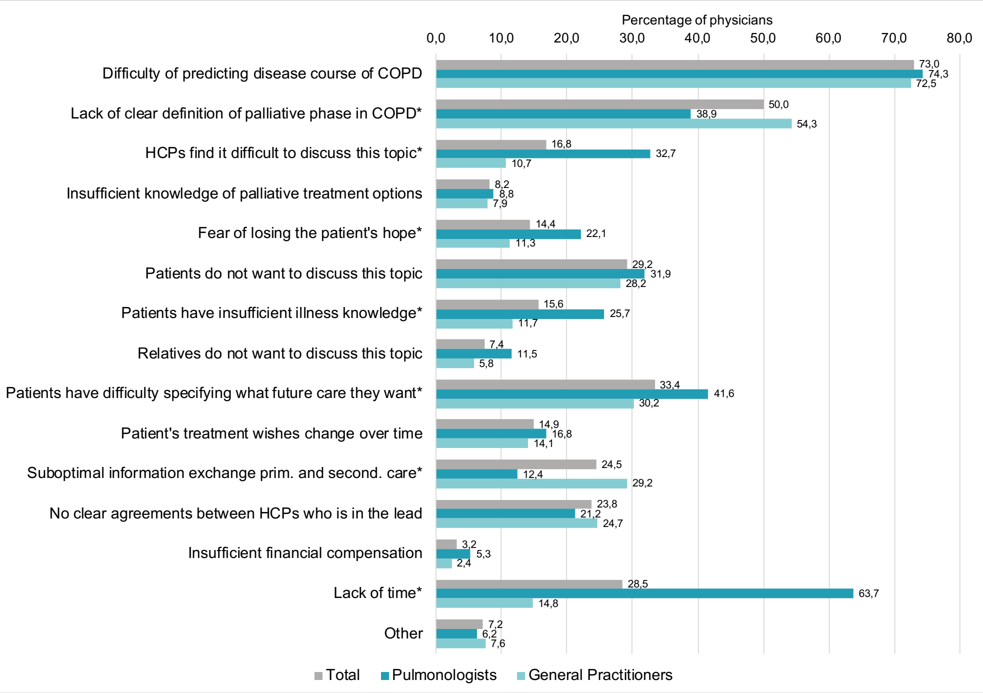


Figure 5. Barriers of palliative care discussions with patients with COPD, as indicated by pulmonologists, general practitioners and all respondents.
HCP, healthcare provider.
*Significant difference between pulmonolgists and GPs (p < .05 using Chi-square test).

all participants, following guideline recommendations, reported to frequently prescribe opioids to treat dyspnea. In comparison, in a survey among Dutch pulmonologists in 2012, half of the participants hardly ever prescribed opioids in COPD patients with refractory dyspnea.[18]

It is plausible that the publication of the Dutch guideline in 2011,[9] and to a lesser extent the Quality Framework in 2017,[10] may have had a positive impact on these care practices. Similarly, an increase in palliative care support was seen in the UK following the introduction of the End of Life Care strategy.[19] Furthermore, a Dutch survey study in 2015 revealed that almost half of the pulmonologists reported no involvement of a specialist palliative care team to treat their COPD patients.[7] Our study showed that this percentage had dropped considerably: only a quarter of pulmonologists hardly ever referred patients to a specialist palliative care team. This may be explained by the requirement for Dutch hospitals to have installed a specialist palliative care team since 2017.[20] Although this requirement concerns oncological palliative care, these teams can also be consulted for non-oncological patients. Involvement of such teams in the care of patients with COPD was found to have a positive effect on advance care planning documentation.[21]

Despite these positive changes, palliative care for patients with COPD remains largely unstructured. The minority of respondents reported scheduling appointments specifically to discuss advance care planning. Furthermore, half of the responding pulmonologists and most GPs reported that their department or practice did not have any form of protocol nor specific agreements. This is comparable to findings from studies performed in the UK, Spain and Sweden.[13,14,22] Moreover, some responding pulmonologists mentioned protocols related to palliative sedation and the dying phase, suggesting that in those cases palliative care is focused on terminal care only. Nevertheless, half of the pulmonologists and one-tenth of GPs said to have the intention to establish a protocol or agreements in the future, acknowledging the need to formalize palliative care in COPD. Though these intentions are promising, the explanations of their plans were nonspecific. As was highlighted earlier, guidelines provide insufficient clear guidance on when and how this care can be best provided.[6] Therefore, more practical knowledge is needed. Examples may be a fixed time in the week scheduled for palliative care consultations, appointment of a care coordinator, clear criteria for (timely) involvement of specialist palliative care, and regular multidisciplinary meetings to discuss palliative patients with COPD.

GPs less frequently encountered a patient with COPD in the palliative phase than pulmonologists, but when they did, they discussed palliative care topics and scheduled these discussions more often than pulmonologists. These findings are not surprising, as advance care planning is considered by GPs a typical GP task.[23] Further, the setting enables them to have these conversations at the patient's home. However, the risk is that patients with COPD with palliative care needs may not be timely recognized by GPs, since they have only one or two per year in their practice at most. GPs find advance care planning more challenging in patients with COPD and heart failure.[23] Many GPs reported that they use the moment a pulmonologist informs the GP about the dire situation of the patient as a starting point. Together with the fact that in the Netherlands most patients with advanced COPD are under treatment of the pulmonologist, it may be more appropriate to consider the identification of patients with palliative care needs primarily the responsibility of a pulmonologist.

To identify those patients, the SQ was, next to clinical expertise, most often used by our participants. Noppe et al. showed that using the SQ in recently hospitalized patients for an acute exacerbation of COPD is a useful and quick method.[24] However, not all patients with palliative care needs were identified with this method. The structural use of symptom assessment tools such as the Edmonton Symptom Assessment Scale[25] might have added value and could facilitate palliative care discussions with patients. Our results emphasize yet again that determining the most appropriate timing to start palliative care is difficult and perceived as an important barrier by most care providers. There is no consensus on when palliative care topics should be discussed and when specialist palliative care should be involved.[6] We found that responding pulmonologists frequently held advance care planning discussions on the emergency department and during hospitalization. In an acute setting, these discussions may be limited to preferences regarding cardiopulmonary resuscitation and mechanical ventilation, while this is only one aspect of advance care planning.[26] Additionally, it means that patients are confronted with these questions by a physician unfamiliar to them. During a planned visit to their regular physician in a non-acute setting, there is more opportunity to discuss the patient's wishes, values and preferences for future care with the patient and his/her family.

Since primary, as well as secondary care, are involved in COPD-care, a well-established collaboration between these settings is crucial. Although satisfaction about the collaboration between pulmonologists and GPs was reasonably high, information exchange between primary care and the hospital was viewed as problematic. This finding is consistent with previous literature.[27] It is not merely a COPD specific problem: also letters from medical specialists to the GP about advanced cancer patients seldom contain advance care planning items.[28] Establishing work agreements between pulmonologists and GPs may help to determine what and when to communicate. A shared medical record, whether integrated into an electronic medical record system or via a standardized paper form, is a prerequisite. After a pulmonologist identifies a patient with COPD in the palliative phase, contact should be initiated with his/her GP to discuss the patient's situation, options for future care and alignment of responsibilities.

Limitations

This study had some limitations. We asked participants to provide estimates on the frequency and content provided to patients with COPD in the palliative phase in the previous year. While this was a feasible and straightforward method to obtain an approximation of the provided care, it might not be an accurate reflection of the actually provided care because of recall bias and social-desirability bias. Neither does it provide insights into the quality nor the timing of the provided care, e.g. whether treatments and discussions took place in the terminal or dying phase rather than early in the palliative phase. Although we achieved 76% coverage of pulmonology departments in the Netherlands, the response rate obtained among pulmonologists was lower than in previous studies.[7, 14, 19] Also, we faced significant item nonresponse for unknown reasons. Additionally, respondents may be more concerned with palliative care than the general population of physicians, which could have influenced the results. Therefore, caution is warranted when extrapolating the results to all pulmonologists and GPs in the Netherlands. Finally, we did not include specialized COPD-nurses or advanced nurse practitioners in the study, even though they play an essential role in the care of patients with COPD. Their views and practices should be investigated in future research.

Conclusions

Most pulmonologists and GPs regularly discuss palliative care topics, use opioids to treat dyspnea and involve specialist palliative care consultants, probably with increasing frequency compared to a decade ago. However, palliative care for patients with COPD remains unstructured and little formalized, and advance care planning discussions frequently take place in an acute care setting. Nevertheless, there seems to be a high willingness to improve this care. To continue the upward trend, clear guidance and standardization of practice may help to decide when and how to initiate discussions, when to involve specialist palliative care and how to optimize information exchange between care settings. Furthermore, training in palliative care communication can empower healthcare providers to discuss end-of-life related topics, caregiver burden and spiritual needs.

Abbreviations

COPD, chronic obstructive pulmonary disease; GP, general practitioner; SQ, surprise question.

Data availability

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

Funding

The authors disclosed receipt of the following financial support for the research, authorship and/or publication of this article: This work was financed by The Netherlands Organization for Health Research and Development (ZonMw) (project number: 844001401).

Competing interests

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

Author contributions

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

Acknowledgements

The authors would like to thank Mirjam Riedijk for her contribution in collecting the data.

References

1. Lozano R, Naghavi M, Foreman K, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*. Dec 15 2012;380(9859):2095-128. doi:10.1016/s0140-6736(12)61728-0
2. Janssen DJ, Spruit MA, Wouters EF, Schols JM. Daily symptom burden in end-stage chronic organ failure: a systematic review. *Palliat Med*. 12/2008 2008;22(8):938-948. Not in File. doi:0269216308096906 [pii];10.1177/0269216308096906 [doi]
3. Tavares N, Jarrett N, Hunt K, Wilkinson T. Palliative and end-of-life care conversations in COPD: a systematic literature review. *ERJ Open Res*. Apr 2017;3(2)doi:10.1183/23120541.00068-2016
4. Beernaert K, Cohen J, Deliens L, et al. Referral to palliative care in COPD and other chronic diseases: a population-based study. *Respir Med*. Nov 2013;107(11):1731-9. doi:10.1016/j.rmed.2013.06.003
5. Momen N, Hadfield P, Kuhn I, Smith E, Barclay S. Discussing an uncertain future: end-of-life care conversations in chronic obstructive pulmonary disease. A systematic literature review and narrative synthesis. *Thorax*. Sep 2012;67(9):777-80. doi:10.1136/thoraxjnl-2012-201835
6. Siouta N, van Beek K, Preston N, et al. Towards integration of palliative care in patients with chronic heart failure and chronic obstructive pulmonary disease: a systematic literature review of European guidelines and pathways. *BMC Palliat Care*. Feb 13 2016;15:18. doi:10.1186/s12904-016-0089-4
7. Duenk RG, Verhagen C, Dekhuijzen P, Vissers K, Engels Y, Heijdra Y. The view of pulmonologists on palliative care for patients with COPD: a survey study. *Int J Chron Obstruct Pulmon Dis*. 2017;12:299-311. doi:10.2147/copd.s121294
8. Siouta N, Clement P, Aertgeerts B, Van Beek K, Menten J. Professionals' perceptions and current practices of integrated palliative care in chronic heart failure and chronic obstructive pulmonary disease: a qualitative study in Belgium. *BMC Palliat Care*. Aug 24 2018;17(1):103. doi:10.1186/s12904-018-0356-7
9. Long Alliantie Nederland. *Richtlijn Palliatieve zorg voor mensen met COPD*. 2011.
10. Boddaert M. Netherlands Quality Framework for Palliative Care. IKNL/Palliactief; 2017.
11. WHO. Definition Palliative care. World Health Organization. http://www.who.int/cancer/palliative/definition/en/
12. Veigh CM, Reid J, Larkin P, Porter S, Hudson P. The provision of generalist and specialist palliative care for patients with non-malignant respiratory disease in the North and Republic of Ireland: a qualitative study. *BMC Palliat Care*. Jul 11 2017;17(1):6. doi:10.1186/s12904-017-0220-1
13. Roberts CM, Seiger A, Buckingham RJ, Stone RA. Clinician perceived good practice in end-of-life care for patients with COPD. *Palliat Med*. Oct 2008;22(7):855-8. doi:10.1177/0269216308096722
14. Ecenarro PS, Iguiniz MI, Tejada SP, et al. Management of COPD in End-of-Life Care by Spanish Pulmonologists. *COPD*. 2018;15(2):171-176. doi:10.1080/15412555.2018.1441274

15. Gaspar C, Alfarroba S, Telo L, Gomes C, Barbara C. End-of-life care in COPD: a survey carried out with Portuguese pulmonologists. *Revista portuguesa de pneumologia*. May-Jun 2014;20(3):123-30. doi:10.1016/j.rppneu.2014.01.008
16. Brożek B, Damps-Konstańska I, Pierzchała W, et al. End-of-life care for patients with advanced lung cancer and chronic obstructive pulmonary disease: survey among Polish pulmonologists. *Polish archives of internal medicine*. Apr 30 2019;129(4):242-252. doi:10.20452/pamw.4478
17. Janssen DJA, Spruit MA, Schols J, Wouters EFM. A call for high-quality advance care planning in outpatients with severe COPD or chronic heart failure. *Chest*. May 2011;139(5):1081-1088. doi:10.1378/chest.10-1753
18. Janssen DJ, de Hosson SM, bij de Vaate E, Mooren KJ, Baas AA. Attitudes toward opioids for refractory dyspnea in COPD among Dutch chest physicians. Chronic respiratory disease. May 2015;12(2):85-92. doi:10.1177/1479972315571926
19. Bloom CI, Slaich B, Morales DR, Smeeth L, Stone P, Quint JK. Low uptake of palliative care for COPD patients within primary care in the UK. *Eur Respir J*. Feb 2018;51(2) doi:10.1183/13993003.01879-2017
20. SONCOS. *Standardisation of Multidiscipinary Cancer Care in the Netherlands. SONCOS Standardisation Report 5*. 2017.
21. 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 2017;12:2795-2806. Not in File. doi:10.2147/COPD.S141974 [doi];copd-12-2795 [pii]
22. Strang S, Ekberg-Jansson A, Strang P, Larsson LO. Palliative care in COPD--web survey in Sweden highlights the current situation for a vulnerable group of patients. *Upsala journal of medical sciences*. Aug 2013;118(3):181-6. doi:10.3109/03009734.2013.801059
23. Wichmann AB, van Dam H, Thoonsen B, Boer TA, Engels Y, Groenewoud AS. Advance care planning conversations with palliative patients: looking through the GP's eyes. *BMC Fam Pract*. Nov 28 2018;19(1):184. doi:10.1186/s12875-018-0868-5
24. Noppe D, Veen HI, Mooren K. COPD patients in need of palliative care: Identification after hospitalization through the surprise question. *Chronic respiratory disease*. Jan-Dec 2019;16:1479972318796219. doi:10.1177/1479972318796219
25. Chang VT, Hwang SS, Feuerman M. Validation of the Edmonton Symptom Assessment Scale. *Cancer*. May 1 2000;88(9):2164-71. doi:10.1002/(sici)1097-0142(20000501)88:9<2164::aid-cncr24>3.0.co;2-5
26. Rietjens JAC, Sudore RL, Connolly M, et al. Definition and recommendations for advance care planning: an international consensus supported by the European Association for Palliative Care. *The Lancet Oncology*. Sep 2017;18(9):e543-e551. doi:10.1016/s1470-2045(17)30582-x
27. Herrmann A, Carey ML, Zucca AC, Boyd LAP, Roberts BJ. Australian GPs' perceptions of barriers and enablers to best practice palliative care: a qualitative study. *BMC Palliat Care*. Oct 31 2019;18(1):90. doi:10.1186/s12904-019-0478-6

28. Ermers DJM, van Bussel KJH, Perry M, Engels Y, Schers HJ. Advance care planning for patients with cancer in the palliative phase in Dutch general practices. *Family practice*. Oct 8 2019;36(5):587-593. doi:10.1093/fampra/cmy124

Supplementary material

Table S1. Survey items and nonresponse per item.

#	Item	Answer options	Missing n (%)	
			Pulmonologists	**GPs**
Introduction				
	In this survey, we talk about palliative care and the palliative phase. Palliative care is an approach that improves the quality of life of patients and their relatives facing a life-threatening condition, by preventing and relieving suffering, through early detection and careful assessment and treatment of problems of a physical, psychological, social and spiritual nature. The palliative phase in patients with COPD is determined according to the guideline Palliative care for people with COPD by, among others: • (a deterioration of) the clinical condition; • status after intensive treatments with no (lasting) effect; • the assessment of the need and desirability of palliative care from both patient and healthcare professional.			
Structure				
1	How do you determine whether the palliative phase has started in patients with COPD? (Multiple answers possible)	○ *This distinction is not made* ○ *On the basis of the GOLD classification* ○ *On the basis of clinical expertise* ○ *On the basis of information of/ transfer by the pulmonologist*** ○ *By using the surprise question ("Would I be surprised if this patient dies within 12 months?")* ○ *Using the SPICT (Supportive and Palliative Indicators Tool) indicators* ○ *Using the RADPAC (Radboud Identification Palliative Patients) indicators* ○ *Using the Prolong or ProPal-COPD indicators* ○ *Based on the following clinical indicators* ○ *Different, namely*	0 (0.0)	0 (0.0)
2	Is there a specific protocol or are there specific appointments in your department*/ practice** regarding the care of patients with COPD in the palliative phase?	*No – I don't know – Yes. Please explain briefly*	8 (6.2)	4 (1.3)
3	Are there any plans for the coming year to (further) develop a specific protocol or specific agreements?	*No – I don't know – Yes. Please explain briefly*	11 (8.5)	4 (1.3)
Experience				
4	How much experience do you have with palliative care for patients with COPD?	*None – Little – A reasonable amount – A lot*	6 (4.6)	1 (0.0)
5	How many patients with COPD in the palliative phase do you treat on average per year? (an estimate is sufficient)	*...... patients per year*	13 (10.0)	15 (4.9)
If you have not treated any patients with COPD in the palliative phase in the past year, please proceed to question 15.				
Symptom management				
6	For the patients with COPD in the palliative phase you treated in the past year, how often did you give the treatments below?			
	Morphine/opioid due to dyspnea	*Never – Rarely – Sometimes – Often – Always*	7 (5.4)	3 (1.0)
	Non-pharmacotherapeutic treatment for dyspnea	*Never – Rarely – Sometimes – Often – Always*	11 (8.5)	11 (3.6)
	Morphine / opioid due to pain	*Never – Rarely – Sometimes – Often – Always*	10 (7.7)	6 (2.0)
	Pharmacotherapeutic treatment for anxiety or depression	*Never – Rarely – Sometimes – Often – Always*	12 (9.2)	8 (2.6)
	Non-pharmacotherapeutic treatment for anxiety or depression	*Never – Rarely – Sometimes – Often – Always*	13 (10.0)	13 (4.3)
Communication				
7	For the patients with COPD in the palliative phase you treated in the past year, how often did you discuss the following topics with the patient and/or relatives?			
	Disease course and incurability	*Never – Rarely – Sometimes – Often – Always*	13 (10.0)	12 (3.9)
	Life expectancy	*Never – Rarely – Sometimes – Often – Always*	15 (11.5)	14 (4.6)
	Fear of choking	*Never – Rarely – Sometimes – Often – Always*	15 (11.5)	14 (4.6)
	Fear of death / dying	*Never – Rarely – Sometimes – Often – Always*	15 (11.5)	20 (6.6)
	Advantages and disadvantages of intensive life extension treatments (e.g. cardiopulmonary resuscitation)	*Never – Rarely – Sometimes – Often – Always*	15 (11.5)	19 (6.2)

Table S1. *Continued*

#	Item	Answer options	Missing n (%)	
			Pulmonologists	**GPs**
	Advantages and disadvantages of non-invasive ventilation (NIV)	*Never – Rarely – Sometimes – Often – Always*	14 (10.8)	18 (5.9)
	Desirability of hospitalization in case of a future lung attack	*Never – Rarely – Sometimes – Often – Always*	15 (11.5)	16 (5.2)
	Palliative treatment options for dyspnea (e.g. morphine)	*Never – Rarely – Sometimes – Often – Always*	17 (13.1)	17 (5.6)
	Preferred place of death	*Never – Rarely – Sometimes – Often – Always*	18 (13.8)	16 (5.2)
	Spiritual and existential needs	*Never – Rarely – Sometimes – Often – Always*	18 (13.8)	18 (5.9)
	Caregiver burden	*Never – Rarely – Sometimes – Often – Always*	19 (14.6)	17 (5.6)
	Goals of care	*Never – Rarely – Sometimes – Often – Always*	20 (15.4)	19 (6.2)
8	For the patients with COPD in the palliative phase you treated in the past year, where and when did you discuss treatment preferences with the patient and/or relatives?			
	In the emergency room*/ At the patient's home**	*Never – Rarely – Sometimes – Often – Always*	22 (16.9)	22 (7.2)
	At the outpatient clinic*/ In the general practice**	*Never – Rarely – Sometimes – Often – Always*	22 (16.9)	27 (8.9)
	During hospitalization*/ Just after hospitalization for an acute exacerbation**	*Never – Rarely – Sometimes – Often – Always*	23 (17.7)	23 (7.5)
	During a regular appointment	*Never – Rarely – Sometimes – Often – Always*	22 (16.9)	25 (8.2)
	During a specially scheduled appointment for this purpose	*Never – Rarely – Sometimes – Often – Always*	21 (16.2)	23 (7.5)
9	How often in the past year did you have a conversation about the palliative phase, palliative treatment options and/or treatment preferences with only the next of kin, without the presence of the patient with COPD?	*Never – Rarely – Sometimes – Often – Always*	21 (16.2)	21 (6.9)
Collaboration				
10	How satisfied are you with the exchange of information from the primary to the secondary care*/from the secondary to the primary care** in patients with COPD in the palliative phase?	*Very dissatisfied – Somewhat dissatisfied Neutral – Somewhat satisfied – Very satisfied*	13 (10.0)	15 (4.9)
11	How satisfied are you with the collaboration with general practitioners*/ pulmonologists** in the care of patients with COPD in the palliative phase?	*Very dissatisfied – Somewhat dissatisfied Neutral – Somewhat satisfied – Very satisfied*	15 (11.5)	15 (4.9)
12	For the patients with COPD in the palliative phase that you treated in the past year, how often did you collaborate with the following healthcare providers in the care of these patients?			
	general practitioner*/pulmonologist**	*Never – Rarely – Sometimes – Often – Always*	15 (11.5)	26 (8.5)
	palliative care nurse in primary care	*Never – Rarely – Sometimes – Often – Always*	15 (11.5)	25 (8.2)
	specialized COPD-nurse in primary care	*Never – Rarely – Sometimes – Often – Always*	17 (13.1)	27 (8.9)
	practice nurse	*Never – Rarely – Sometimes – Often – Always*	21 (16.2)	27 (8.9)
	specialized COPD-nurse or advanced nurse practitioner in hospital	*Never – Rarely – Sometimes – Often – Always*	20 (15.4)	27 (8.9)
	district nurse	*Never – Rarely – Sometimes – Often – Always*	20 (15.4)	27 (8.9)
13	For the patients with COPD in the palliative phase that you treated in the past year, how often did you consult or refer to the following healthcare providers?			
	palliative care consultant in hospital	*Never – Rarely – Sometimes – Often – Always*	21 (16.2)	21 (6.9)
	physiotherapist	*Never – Rarely – Sometimes – Often – Always*	21 (16.2)	16 (5.2)
	occupational therapist	*Never – Rarely – Sometimes – Often – Always*	22 (16.9)	20 (6.6)
	speech therapist	*Never – Rarely – Sometimes – Often – Always*	23 (17.7)	22 (7.2)
	psychologist	*Never – Rarely – Sometimes – Often – Always*	21 (16.2)	22 (7.2)
	dietician	*Never – Rarely – Sometimes – Often – Always*	23 (17.7)	24 (7.9)
	spiritual caregiver	*Never – Rarely – Sometimes – Often – Always*	22 (16.9)	24 (7.9)
	social worker	*Never – Rarely – Sometimes – Often – Always*	23 (17.7)	25 (8.2)

Table S1. *Continued*

#	Item	Answer options	Missing n (%)	
			Pulmonologists	**GPs**
Bereavement care				
14	Of your patients with COPD who died in the past year, how often did you provide aftercare (care/support) to the relatives?	*Never – Rarely – Sometimes – Often – Always*	26 (20.0)	27 (8.9)
Barriers				
15	In your opinion, what are the most important reasons that there is little or no discussion about the palliative phase, palliative treatment options and/or treatment preferences with a patient with COPD? (Multiple answer options possible)	○ *The difficulty of predicting the disease course of COPD* ○ *The lack of a clear definition of the palliative phase in COPD* ○ *Healthcare professionals find it difficult to discuss this topic with COPD patients* ○ *Insufficient knowledge about treatment options in the palliative phase* ○ *The fear of losing the patient's hope* ○ *Patients do not want to discuss this topic* ○ *Patients have insufficient insight in and knowledge of their disease* ○ *Relatives do not want to discuss this topic* ○ *Patients have difficulty specifying* ○ *what future care/treatment they want if their situation deteriorates* ○ *Patients' care/treatment wishes change over time* ○ *Suboptimal information exchange between primary and secondary care* ○ *No clear agreements between healthcare professionals on who is in the lead to discuss palliative care issues with the patient* ○ *Insufficient financial compensation* ○ *Lack of time* ○ *Different, namely:*	17 (13.1)	14 (4.6)
Demographics & education				
16	What is your age?	*……year*	18 (13.8)	20 (6.6)
17	What is your gender?	*Male – Female*	7 (5.4)	20 (6.6)
18*	What is your position?*	*Pulmonologist – Pulmonologist in training – Non-practicing pulmonologist*	19 (14.6)	N/A
18**	Do you work as an attending or permanent general practitioner?**	*Attending GP – Permanent GP*	N/A	24 (7.9)
19	How many years of experience do you have as a pulmonologist (i.t.)*/general practitioner**?	*……years*	18 (13.8)	20 (6.6)
20*	What type of hospital do you work in?*	*General hospital – Top clinical hospital – University medical center*	17 (13.2)	N/A
20**	Where do you work (first part of postal code)**	*N/A*	24 (7.9)	
21*	How many pulmonologists are working in your department?*	*…… pulmonologists*	21 (16.2)	N/A
21**	Have you followed the post graduate course in asthma/COPD?**	*No – Yes*	N/A	23 (7.5)
22	Have you received education and/or training in palliative care?	○ *No.* ○ *Yes, the Dutch postgraduate course palliative care (2 years) or Cardiff Palliative Medicine Course (post graduate)* ○ *Yes, 8-day palliative care course for medical specialists** ○ *Yes, 2-day course palliative care of KNMG*** ○ *Yes, different namely:*	18 (13.8)	28 (9.2)

* Item for pulmonologists only.

** Item for general practitioners only.

Table S2. Symptom management in patients with COPD in the palliative phase by physicians with (T) and without (NT) any training in palliative care.

			Never	Rarely	Sometimes	Often	Always	*p* Value[a]
Dyspnea using opioids	Pulmonologists	T	0 (0.0)	2 (5.1)	3 (7.7)	31 (79.5)	3 (7.7)	.891
		NT	0 (0.0)	1 (1.4)	14 (20.0)	45 (64.3)	10 (14.3)	
	GPs	T	1 (1.3)	1 (1.3)	15 (20.0)	38 (50.7)	20 (26.7)	.636
		NT	4 (2.2)	2 (1.4)	24 (17.1)	67 (47.9)	43 (30.7)	
Dyspnea using non-pharmacological treatment	Pulmonologists	T	0 (0.0)	3 (7.7)	8 (20.5)	23 (59.0)	5 (12.8)	.051
		NT	0 (0.0)	6 (9.0)	26 (38.8)	31 (46.3)	4 (6.0)	
	GPs	T	1 (1.4)	5 (6.8)	26 (35.6)	31 (42.5)	10 (13.7)	.078
		NT	10 (7.4)	18 (13.3)	43 (31.9)	49 (36.3)	15 (11.1)	
Pain using opioids	Pulmonologists	T	2 (5.3)	6 (15.8)	20 (52.6)	8 (21.1)	2 (5.3)	.663
		NT	4 (5.8)	17 (24.6)	28 (40.6)	17 (24.6)	3 (4.3)	
	GPs	T	4 (5.5)	14 (19.2)	29 (39.7)	22 (30.1)	4 (5.5)	**.048**
		NT	14 (10.1)	36 (25.9)	54 (38.8)	30 (21.6)	5 (3.6)	
Anxiety/depression using pharmacological treatment	Pulmonologists	T	2 (5.3)	5 (13.2)	20 (52.6)	10 (26.3)	1 (2.6)	.237
		NT	6 (8.7)	17 (24.6)	28 (40.6)	17 (24.6)	1 (1.4)	
	GPs	T	2 (2.8)	9 (12.5)	31 (43.1)	28 (38.9)	2 (2.8)	.196
		NT	11 (8.0)	18 (13.0)	62 (44.9)	43 (31.2)	4 (2.9)	
Anxiety/depression using non-pharmacological treatment	Pulmonologists	T	1 (2.8)	6 (16.7)	12 (33.3)	16 (44.4)	1 (2.8)	**.030**
		NT	4 (5.7)	17 (24.3)	32 (45.7)	16 (22.9)	1 (1.4)	
	GPs	T	0 (0.0)	7 (10.3)	35 (51.5)	22 (32.4)	4 (5.9)	**.011**
		NT	14 (10.1)	27 (19.6)	56 (40.6)	34 (24.6)	7 (5.1)	

Data are expressed as absolute values and percentages.

[a]*P*-Values based on Mann-Whitney *U*-test.

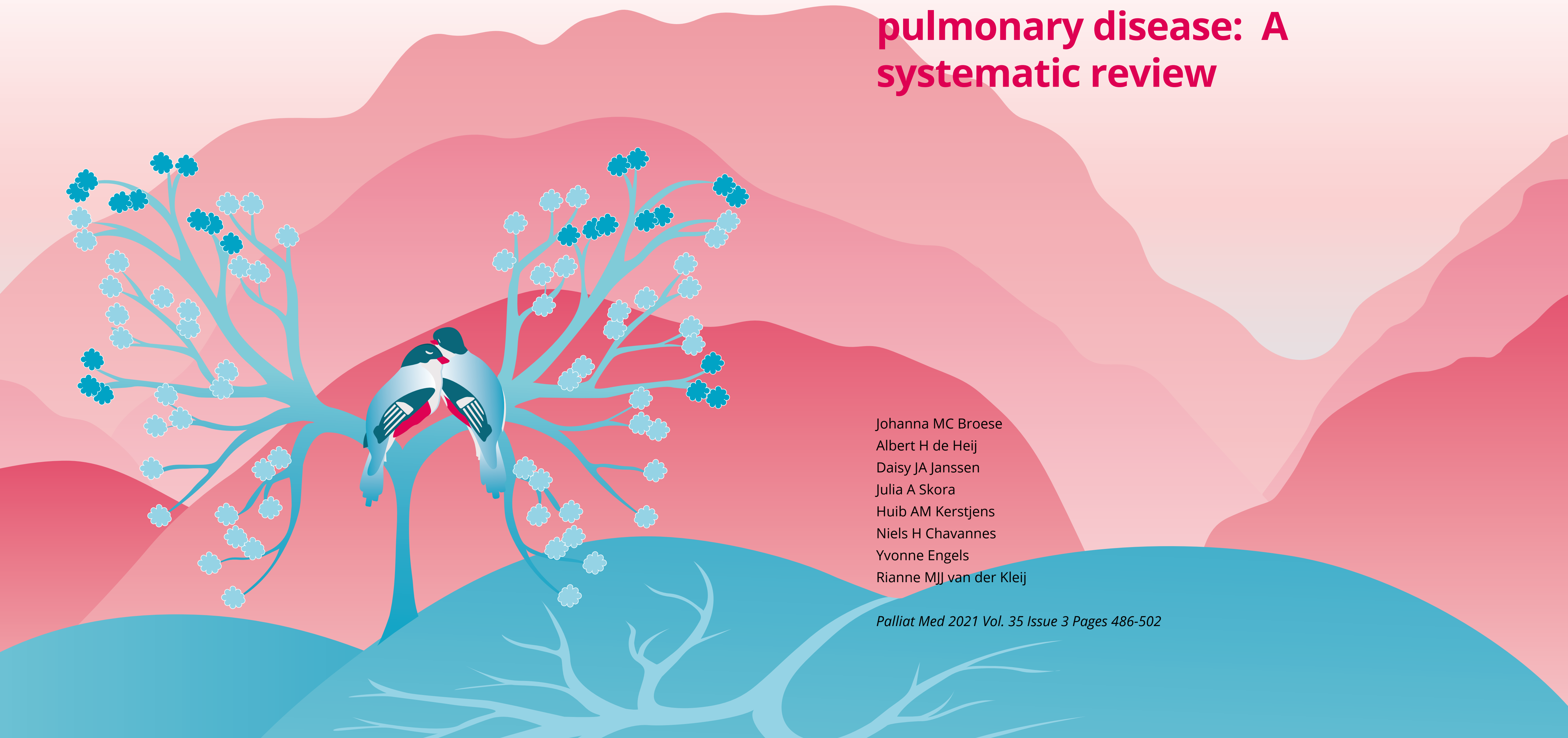
Table S3. Frequency of topics discussed by physicians, with (T) and without any training in palliative care (NT), in the previous year.

			Never	Rarely	Sometimes	Often	Always	*p* Value[a]
Disease course and incurability	Pulmonologists	T	0 (0.0)	1 (2.8)	2 (5.6)	20 (55.6)	13 (36.1)	.130
		NT	0 (0.0)	1 (1.4)	9 (12.9)	44 (62.9)	16 (22.9)	
	GPs	T	0 (0.0)	1 (1.4)	6 (8.6)	28 (40.0)	35 (50.0)	.314
		NT	2 (1.4)	1 (0.7)	16 (11.6)	59 (42.8)	60 (43.5)	
Life expectancy	Pulmonologists	T	0 (0.0)	5 (14.3)	11 (31.4)	13 (37.1)	6 (17.1)	.780
		NT	0 (0.0)	7 (10.1)	29 (42.0)	22 (31.9)	11 (15.9)	
	GPs	T	3 (4.3)	5 (7.1)	16 (22.9)	33 (47.1)	13 (18.6)	.737
		NT	5 (3.7)	10 (7.4)	34 (25.0)	54 (39.7)	33 (24.3)	
Fear of choking	Pulmonologists	T	0 (0.0)	0 (0.0)	3 (8.8)	20 (58.8)	11 (32.4)	**.015**
		NT	0 (0.0)	2 (2.9)	15 (21.4)	42 (60.0)	11 (15.7)	
	GPs	T	0 (0.0)	1 (1.4)	11 (15.7)	37 (52.9)	21 (30.0)	.406
		NT	1 (0.7)	6 (4.4)	18 (13.2)	57 (41.9)	54 (39.7)	
Fear of death/dying	Pulmonologists	T	0 (0.0)	1 (2.9)	9 (25.7)	15 (42.9)	10 (28.6)	**.025**
		NT	1 (1.4)	6 (8.7)	25 (36.2)	28 (40.6)	9 (13.0)	
	GPs	T	0 (0.0)	2 (3.0)	10 (14.9)	32 (47.8)	23 (34.3)	.440
		NT	2 (1.5)	4 (2.9)	14 (10.3)	62 (45.6)	54 (39.7)	
Advantages and disadvantages of life sustaining treatments	Pulmonologists	T	0 (0.0)	0 (0.0)	4 (11.4)	12 (34.3)	19 (54.3)	.119
		NT	0 (0.0)	1 (1.4)	4 (5.8)	41 (59.4)	23 (33.3)	
	GPs	T	0 (0.0)	0 (0.0)	8 (11.9)	28 (41.8)	31 (46.3)	.987
		NT	0 (0.0)	6 (4.4)	11 (8.1)	55 (40.4)	64 (47.1)	
Advantages and disadvantages of non-invasive ventilation	Pulmonologists	T	0 (0.0)	2 (5.7)	7 (20.0)	18 (51.4)	8 (22.9)	.479
		NT	0 (0.0)	2 (2.9)	18 (25.7)	40 (57.1)	10 (14.3)	
	GPs	T	12 (17.6)	14 (20.6)	24 (35.3)	11 (16.2)	7 (10.3)	.064
		NT	39 (28.7)	33 (24.3)	34 (25.0)	20 (14.7)	10 (7.4)	

Table S3. *Continued*

			Never	Rarely	Sometimes	Often	Always	*p* Value[a]
Desirability of hospitalization for acute exacerbation	Pulmonologists	T	0 (0.0)	2 (5.7)	12 (34.3)	17 (48.6)	4 (11.4)	.214
		NT	1 (1.4)	8 (11.6)	24 (34.8)	33 (47.8)	3 (4.3)	
	GPs	T	0 (0.0)	1 (1.4)	10 (14.5)	32 (46.4)	26 (37.7)	.597
		NT	2 (1.5)	2 (1.5)	14 (10.2)	63 (46.0)	56 (40.9)	
Palliative treatment options for dyspnea (e.g. morphine)	Pulmonologists	T	0 (0.0)	0 (0.0)	1 (2.9)	24 (70.6)	9 (26.5)	.283
		NT	0 (0.0)	0 (0.0)	8 (11.8)	45 (66.2)	15 (22.1)	
	GPs	T	0 (0.0)	0 (0.0)	4 (5.8)	28 (40.6)	37 (53.6)	.893
		NT	0 (0.0)	1 (0.7)	8 (5.9)	52 (38.2)	75 (55.1)	
Preferred place of death	Pulmonologists	T	0 (0.0)	3 (9.1)	10 (30.3)	15 (45.5)	5 (15.2)	**.005**
		NT	5 (7.4)	15 (22.1)	25 (36.8)	17 (25.0)	6 (8.8)	
	GPs	T	0 (0.0)	2 (2.9)	6 (8.7)	30 (43.5)	31 (44.9)	.638
		NT	1 (0.7)	4 (2.9)	17 (12.4)	44 (32.1)	71 (51.8)	
Spiritual and existential needs	Pulmonologists	T	3 (8.8)	7 (20.6)	17 (50.0)	5 (14.7)	2 (5.9)	**.007**
		NT	11 (16.4)	30 (44.8)	18 (26.9)	7 (10.4)	1 (1.5)	
	GPs	T	1 (1.5)	6 (8.8)	29 (42.6)	22 (32.4)	10 (14.7)	.257
		NT	9 (6.6)	20 (14.7)	48 (35.3)	40 (29.4)	19 (14.0)	
Caregiver burden	Pulmonologists	T	0 (0.0)	2 (5.7)	16 (45.7)	15 (42.9)	2 (5.7)	**.003**
		NT	1 (1.5)	15 (23.1)	34 (52.3)	13 (20.0)	2 (3.1)	
	GPs	T	1 (1.5)	0 (0.0)	13 (19.1)	37 (54.4)	17 (25.0)	.641
		NT	1 (0.7)	4 (2.9)	29 (21.2)	69 (50.4)	34 (24.8)	
Goals of care	Pulmonologists	T	0 (0.0)	0 (0.0)	15 (42.9)	15 (42.9)	5 (14.3)	**.020**
		NT	0 (0.0)	11 (17.2)	28 (43.8)	20 (31.3)	5 (7.8)	
	GPs	T	4 (6.0)	8 (11.9)	23 (34.3)	23 (34.3)	9 (13.4)	.302
		NT	16 (11.8)	15 (11.0)	51 (37.5)	35 (25.7)	19 (14.0)	

Data are expressed as absolute values and percentages.
[a] *P*-Values based on Mann-Whitney *U*-test.



Chapter 3

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

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Palliat Med 2021 Vol. 35 Issue 3 Pages 486-502

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.

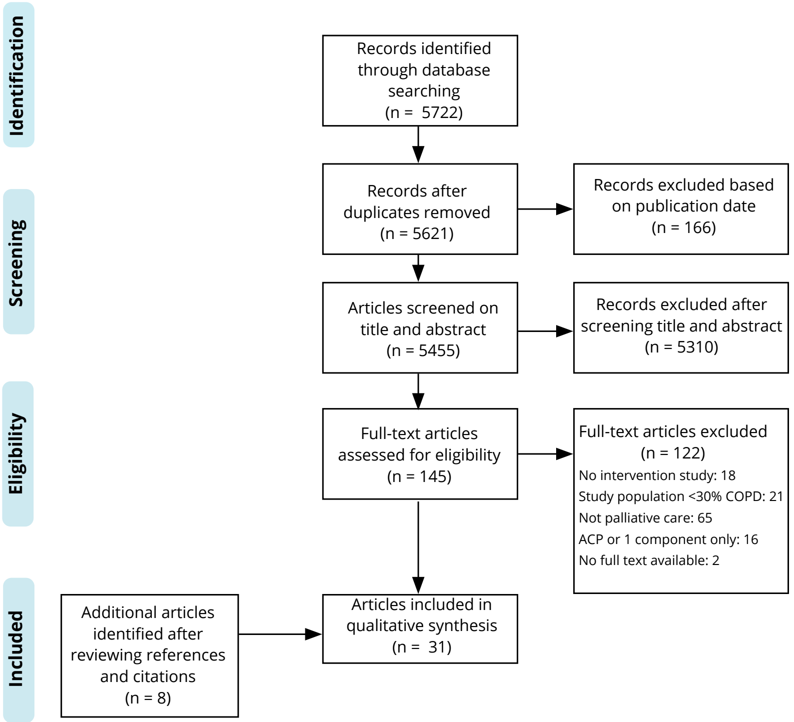

Figure 1. PRISMA flow diagram of the study selection process.

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 pulmonologists, 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 and alternative approaches such as relaxation, reflexology, massages	COPD	PCN and PCP	Monthly home visits	12
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 breathlessness, 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 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)
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.

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.

Data management and sharing

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

Declaration of conflicting interests

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

Funding

The authors disclosed receipt of the following financial support for the research, authorship and/or publication of this article: This work was financed by The Netherlands Organization for Health Research and Development (ZonMw).

References

1. WHO. Fact Sheet Top 10 global causes of deaths, 2016, http://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death (accessed 2018-09-04).
2. 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. 2009/04/28. DOI: 10.1016/j.jpainsymman.2008.07.010.
3. WHO. Definition Palliative care, http://www.who.int/cancer/palliative/definition/en/ (2002).
4. 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. 2016/11/29. DOI: 10.1001/jama.2016.16840.
5. Carlucci A, Guerrieri A and Nava S. Palliative care in COPD patients: is it only an end-of-life issue? *European respiratory review : an official journal of the European Respiratory Society* 2012; 21: 347-354. 2012/12/04. DOI: 10.1183/09059180.00001512.
6. 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. 2011/04/23. DOI: 10.1089/jpm.2010.0479.
7. 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. 2017/03/05. DOI: 10.1038/s41533-017-0017-y.
8. 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. 2005/01/26. DOI: 10.1111/j.1532-5415.2005.53011.x.
9. 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 2017/05/04. DOI: 10.1183/23120541.00068-2016.
10. 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. DOI: S0140-6736(17)32127-X [pii];10.1016/S0140-6736(17)32127-X [doi].
11. 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. 2008/04/09. DOI: 10.1164/rccm.200605-587ST.
12. IKNL/Palliactief. Netherlands Quality Framework for Palliative Care. 2017.
13. 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. 2016/01/01. DOI: 10.1177/1049909116674669.
14. 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. 2018/12/01. DOI: 10.1136/thoraxjnl-2018-211589.
15. Bausewein C, Booth S, Gysels M, et al. Non-pharmacological interventions for breathlessness in advanced stages of malignant and non-malignant diseases. *The Cochrane database of systematic reviews* 2008: Cd005623. 2008/04/22. DOI: 10.1002/14651858.CD005623.pub2.
16. 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. DOI: thoraxjnl-2016-209806 [pii];10.1136/thoraxjnl-2016-209806 [doi].
17. Ekström M, Nilsson F, Abernethy AA, et al. Effects of opioids on breathlessness and exercise capacity in chronic obstructive pulmonary disease. A systematic review. *Annals of the American Thoracic Society* 2015; 12: 1079-1092. 2015/03/25. DOI: 10.1513/AnnalsATS.201501-034OC.
18. 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. 2012/03/13. DOI: 10.1016/j.ijnurstu.2012.02.004.
19. 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. 2008/10/01. DOI: 10.1136/bmj.a1655.
20. Hong QN PP, Fàbregues S, Bartlett G, Boardman F, Cargo M, Dagenais P, Gagnon M-P, Griffiths F, Nicolau B, O'Cathain A, Rousseau M-C, Vedel I. . Mixed Methods Appraisal Tool (MMAT), version 2018. *Registration of Copyright (#1148552), Canadian Intellectual Property Office, Industry Canada* 2018.
21. Reeves BC DJ, Higgins JPT, Shea B, Tugwell P, Wells GA. Chapter 24: Including non-randomized studies on intervention effects. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). . *Cochrane Handbook for Systematic Reviews of Interventions version 60 (updated July 2019) Cochrane, 2019 Available from wwwtrainingcochraneorg/handbook*.
22. *Clinical Practice Guidelines for Quality Palliative Care, Third edition*. 2013. National Consensus Project for Quality Palliative Care.
23. *Quality standard for end of life care for adults. Issued: August 2011 last modified: October 2013.* 2013. National Institute for Health and Care Excellence.
24. Pope C, Ziebland S and Mays N. Qualitative research in health care. Analysing qualitative data. *BMJ (Clinical research ed)* 2000; 320: 114-116. 2000/01/22. DOI: 10.1136/bmj.320.7227.114.
25. Proctor E, Silmere H, Raghavan R, et al. Outcomes for implementation research: conceptual distinctions, measurement challenges, and research agenda. *Administration and policy in mental health* 2011; 38: 65-76. 2010/10/20. DOI: 10.1007/s10488-010-0319-7.
26. Fleuren MA, Paulussen TG, Van Dommelen P, et al. Towards a measurement instrument for determinants of innovations. *International journal for quality in health care : journal of the International Society for Quality in Health Care* 2014; 26: 501-510. 2014/06/22. DOI: 10.1093/intqhc/mzu060.
27. 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. 2009/08/12. DOI: 10.1186/1748-5908-4-50.

28. 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. DOI: 10.1089/jpm.2006.9.111 [doi].
29. 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. DOI: S2213-2600(14)70226-7 [pii];10.1016/S2213-2600(14)70226-7 [doi].
30. 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. DOI: 10.1186/s13063-016-1304-6 [doi];10.1186/s13063-016-1304-6 [pii].
31. 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. DOI: 10.2147/COPD.S141974 [doi];copd-12-2795 [pii].
32. 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. DOI: 10.1001/archinte.164.1.83 [doi];164/1/83 [pii].
33. 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. DOI: 10.1089/109662103322144862 [doi].
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. *Clinical and investigative medicine Medecine clinique et experimentale* 2014; 37: E311-319. 2014/10/06.
36. Iupati 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. DOI: 10.1111/imj.12947 [doi].
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. *Journal of Hospice & Palliative Nursing* 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. DOI: 10.1183/23120541.00102-2017 [doi];00102-2017 [pii].
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. *Chronic respiratory disease* 2014; 11: 111-119. 2014/04/15. DOI: 10.1177/1479972314529674.
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. DOI: 10.2147/COPD.S140043 [doi];copd-12-2157 [pii].
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. 2006/10/28.
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. 2015/08/28. DOI: 10.1177/0269216315600103.
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. DOI: 10.12968/ijpn.2016.22.11.549 [doi].
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...". *Journal of Pain and Symptom Management* 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. 2019/03/04. DOI: 10.1186/s12904-019-0410-0.
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 Palliative 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* 2017: 1479972317712720. DOI: 10.1177/1479972317712720 [doi].
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. DOI: 1472-684X-8-9 [pii];10.1186/1472-684X-8-9 [doi].
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. DOI: S1478951509990897 [pii];10.1017/S1478951509990897 [doi].
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. 2017/06/16. DOI: 10.2147/copd.s136183.
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. DOI: npjpcrm201520 [pii];10.1038/npjpcrm.2015.20 [doi].

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. DOI: 10.1089/jpm.2012.0285 [doi].
54. Qian MYY, Politis J, Thompson M, et al. Individualized breathlessness interventions may improve outcomes in patients with advanced COPD. *Respirology* 2018. DOI: 10.1111/resp.13324 [doi].
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. 2019/10/13. DOI: 10.1016/j.jpainsymman.2019.09.012.
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. 2018/09/27. DOI: 10.1089/jpm.2018.0321.
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. DOI: 10.1159/000495312.
58. Lockhart CA, Volk-Craft BE, Hamilton G, et al. The PhoenixCare Program. *J Palliat Med* 2003; 6: 1001-1012. 2004/01/22. DOI: 10.1089/109662103322654929.
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. 2019/07/17. DOI: 10.1177/0269216319859148.
60. Mannino DM and Buist AS. Global burden of COPD: risk factors, prevalence, and future trends. *Lancet* 2007; 370: 765-773. 2007/09/04. DOI: 10.1016/s0140-6736(07)61380-4.
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. 2015/07/15. DOI: 10.1038/npjpcrm.2015.43.
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. 2014/03/13. DOI: 10.1136/bmj.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. 2018/02/13. DOI: 10.1186/s12904-018-0274-8.
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. 2017/02/17. DOI: 10.1186/s13012-017-0552-5

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)
	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)

Chapter 4

A cluster randomized controlled trial on a multifaceted implementation strategy to promote integrated palliative care in COPD: study protocol of the COMPASSION study

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BMC Palliat Care 2020 Vol. 19 Issue 1 Pages 155

Abstract

Background

Despite the urgent need for palliative care for patients with advanced chronic obstructive pulmonary disease (COPD), it is not yet daily practice. Important factors influencing the provision of palliative care are adequate communication skills, knowing when to start palliative care and continuity of care. In the COMPASSION study, we address these factors by implementing an integrated palliative care approach for patients with COPD and their informal caregivers.

Methods

An integrated palliative care intervention was developed based on existing guidelines, a literature review, and input from patient and professional organizations. To facilitate uptake of the intervention, a multifaceted implementation strategy was developed, comprising a toolbox, (communication) training, collaboration support, action planning and monitoring. Using a hybrid effectiveness-implementation type 2 design, this study aims to simultaneously evaluate the implementation process and effects on patient, informal caregiver and professional outcomes. In a cluster randomized controlled trial, eight hospital regions will be randomized to receive the integrated palliative care approach or to provide care as usual. Eligible patients are identified during hospitalization for an exacerbation using the Propal-COPD tool. The primary outcome is quality of life (FACIT-Pal) at six months. Secondary outcome measures include spiritual well-being, anxiety and depression, unplanned healthcare use, informal caregiver burden and healthcare professional's self-efficacy to provide palliative care. The implementation process will be investigated by a comprehensive mixed-methods evaluation assessing the following implementation constructs: context, reach, dose delivered, dose received, fidelity, implementation level, recruitment, maintenance and acceptability. Furthermore, determinants to implementation will be investigated using the Consolidated Framework for Implementation Research.

Discussion

The COMPASSION study will broaden knowledge on the effectiveness and process of palliative care integration into COPD-care. Furthermore, it will improve our understanding of which strategies may optimize the implementation of integrated palliative care.

Trial registration

Netherlands Trial Register (NTR): NL7644. Registration date: April 7, 2019.

Keywords

COPD, exacerbation, proactive palliative care, advance care planning, quality of life, integrated care, implementation study, cluster randomized controlled trial

Background

Chronic Obstructive Pulmonary Disease (COPD) is a common illness characterized by persistent respiratory symptoms and airflow limitation.[1] When the disease progresses, many patients experience recurrent acute exacerbations, often requiring hospital admissions with a mortality rate of up to 23% within one year after admission.[2] COPD is the third leading cause of death in the world.[3] Moreover, in advanced stages of the disease, patients suffer from multiple symptoms, which are frequently undertreated.[4] Accordingly, their health-related quality of life is comparable to, or even worse than that of patients with advanced lung cancer.[5] Thus, patients with COPD have at least a similar need for palliative care.

In line with the WHO definition, palliative care should not be restricted to reactive care in the terminal phase of the disease.[6] Instead, it should be provided proactively and earlier in the course of the disease, complementing disease-modifying care. Its goal is to enhance quality of life through assessment and treatment of physical, psychological, social and spiritual problems. Additionally, it is advocated that palliative care should take into account the maintenance of the patient's autonomy, access to information and treatment options,[7] which requires ongoing communication including advance care planning and care coordination. In accordance with current recommendations, palliative care provision should principally be provided by generalist care professionals, i.e. general practitioners and respiratory care specialists in the case of COPD-care, whereas patients can be referred to specialist palliative care if needed.[7, 8] Consequently, palliative care should be an integrated part of regular COPD-care, in which professionals collaborate in multidisciplinary teams to optimize continuity of care.

However, it is not yet clear how palliative care can be successfully integrated into COPD-care. At the moment, discussions on prognosis, goals of care and advance care planning rarely occur or only at a very late stage of the disease.[9] Neither are patients with COPD regularly referred to specialist palliative care.[10] As a consequence, patients with COPD are less likely to die at their preferred place of death, and symptoms remain undertreated.[4, 11] Previous research revealed three major barriers to palliative care provision in COPD.[9, 12] First, the unpredictable disease trajectory of COPD makes it difficult to determine when to start palliative care and discuss advance care planning. The second barrier is the lack of palliative care communication skills of professionals. The third barrier is related to a lack of care continuity and collaboration between healthcare professionals.[12, 13]

In the COMPASSION (a central element in the provision of COPD-care[13] and acronym for COPD Palliative and Supportive care Implementation) study, we attempt to overcome these barriers towards the implementation of palliative care. In collaboration with patient and professional organizations, we developed an integrated palliative COPD care intervention that integrates existing scientific and practical knowledge. Moreover, to facilitate uptake of the intervention among healthcare professionals, a multifaceted implementation strategy was developed comprising a training, an online toolbox and support with planning and monitoring of implementation.

In this article, we will describe the aim, design and procedures of the COMPASSION study. Both the implementation process and clinical effectiveness of the integrated palliative care approach will be assessed. The COMPASSION study aims to:

1. investigate the effect of the implementation of integrated palliative care on patient, informal caregiver and healthcare professional outcomes;
2. investigate the effect of the multifaceted implementation strategy on implementation outcomes and explore what barriers hamper the implementation of integrated palliative care in routine COPD-care;
3. explore the relationship between implementation level and patient outcomes.

Methods

Design

We follow an effectiveness-implementation hybrid design type 2, as proposed by Curran et al.[14], which allows us to simultaneously test the implementation strategy and impact of the integrated palliative care intervention on health outcomes. To study effectiveness, a cluster randomized controlled trial will be performed in eight hospital regions in the Netherlands. Furthermore, the implementation process will be evaluated using mixed methods. Each hospital region will serve as a cluster. Randomization on this cluster level instead of one-to-one randomization was chosen to reduce contamination: it is likely that professionals exposed to the implementation strategy also would treat patients assigned to the control condition differently.[15]

Setting

This study will take place in eight pulmonary care departments of Dutch hospitals that collaborate with affiliated general practitioners, home care organizations and palliative care consultation teams further referred to as 'hospital regions'. To increase comparability, academic hospitals were excluded.

Participants

Healthcare professionals

Each participating hospital region forms an intervention group consisting of at least one of the following professions: pulmonologist, respiratory nurse of pulmonology care department, palliative care consultant in the hospital, general practitioner specialized in asthma and COPD, general practitioner specialized in palliative care, consultants from the regional palliative care consultation teams. The following professionals can be involved facultatively if present in that region: respiratory nurse in primary care, pulmonologists in training, practice nurse and other relevant professionals.

Patients

Patients diagnosed with COPD and admitted to the hospital for an acute exacerbation will be invited to participate in the study. Patients not able to complete questionnaires in Dutch, patients with severe cognitive decline (e.g. dementia) and patients on the waiting list for lung transplantation will be excluded. After completion of the baseline questionnaire, patients will be screened using the Propal-COPD tool.[16] Patients with a positive Propal-COPD score will be included in the effectiveness study. The Propal-COPD tool consists of seven indicators: Medical Research Council (MRC) dyspnea score of 5, Clinical COPD Questionnaire (CCQ) score >3, forced expiratory volume in 1 second lower than 30% predicted, presence of specific comorbidities, body-mass index lower than 21 kg/m2 or weight loss (>10% in the last six months or >5% in last month), previous hospitalization for acute exacerbation in the last two years (last two years ≥2 admissions or last year ≥1 admission), and a negative answer to the surprise question ("Will you be surprised if your patient would die in the next coming 12 months?") [16]. For each indicator, specific weight is given, together generating a total score. A score exceeding the previous published cut off value of -1.362 corresponds with a high probability for death within one year, which is considered a proxy for having palliative care needs.

Informal caregivers

Informal caregivers of included patients will be invited to participate by asking the patient to indicate who gives him or her the most help and support at home.

Recruitment of regions

To recruit hospital regions for participation, invitational letters will be sent to the heads of departments of respiratory medicine of all hospitals in the Netherlands. After agreement to take part in the study, eight hospital regions will be selected for randomization to the intervention or control group. Participating regions will be offered a small reimbursement of expenses (maximum €2.5K per region).

Randomization

Hospital regions will be randomly allocated by an independent statistician to the intervention or control condition, stratified by the number of COPD exacerbation hospital admissions per year.

Blinding

To minimize response bias, patients and informal caregivers will not be told whether their hospital is assigned to the intervention or control group. Also, the researcher will be blinded during the analysis process of effect outcomes, using recoded identification numbers of participants. Blinding of professionals for cluster group allocation will not be possible due to the nature of the implementation strategy and intervention. However, professionals of control regions will be blinded for the Propal-COPD score. As a consequence, it remains unknown to them which patients take part in the effectiveness study and receive follow-up questionnaires.

Project organization

This study is part of a national project coordinated by the Lung Alliance Netherlands, in cooperation with the Leiden University Medical Center and the Radboud University Medical Center, with financial support from The Netherlands Organization for Health Research and Development (ZonMw). A steering group for coordination and three expert groups is set up, representing the relevant patient, family and professional organizations in the Netherlands. In the development phase of the project, every 6 to 8 weeks meetings took place in which the three expert groups gave input on (i) patient-professional communication and compassionate care, (ii) identification of palliative care needs and professional's expertise, and (iii) implementation and future dissemination, respectively. Additionally, existing practical tools and useful links were selected for an online toolbox supporting professionals.

Intervention

Table 1 details the components of the integrated palliative care approach, consisting of an integrated palliative care intervention and an multifaceted implementation strategy. Figure 1 shows the causal assumptions of its outcomes and mechanisms of impact, based on the Medical Research Council framework.[17] The integrated palliative care intervention developed follows existing palliative care guidelines,[18, 19] the Quality Framework Palliative care of the Netherlands[20], a literature review and input from the expert groups. For the identification of patients that are likely to benefit from palliative care, the previously validated Propal-COPD tool will be used. This tool has been validated in patients admitted to the hospital for acute exacerbation and showed to have a high sensitivity of 90% and specificity of 73%.[16] Moreover, admission for an acute exacerbation of COPD is considered to be one of the key milestones for transition towards a palliative approach[21] and seems to be a feasible moment to start proactive palliative care.[22, 23] After identification, one or more consultations take place either in the outpatient clinic or in the general practice, depending on the patient's needs, for a multidimensional assessment, symptom management and advance care planning. The treatment plan and agreements made will be documented and shared with other involved professionals and discussed in a multidisciplinary meeting if needed. In case of preference for care at home, the responsibility will be transferred to the patient's general practitioner. If a patient deceases, the provided end-of-life care will be evaluated with the patient's informal caregiver and involved healthcare professionals.

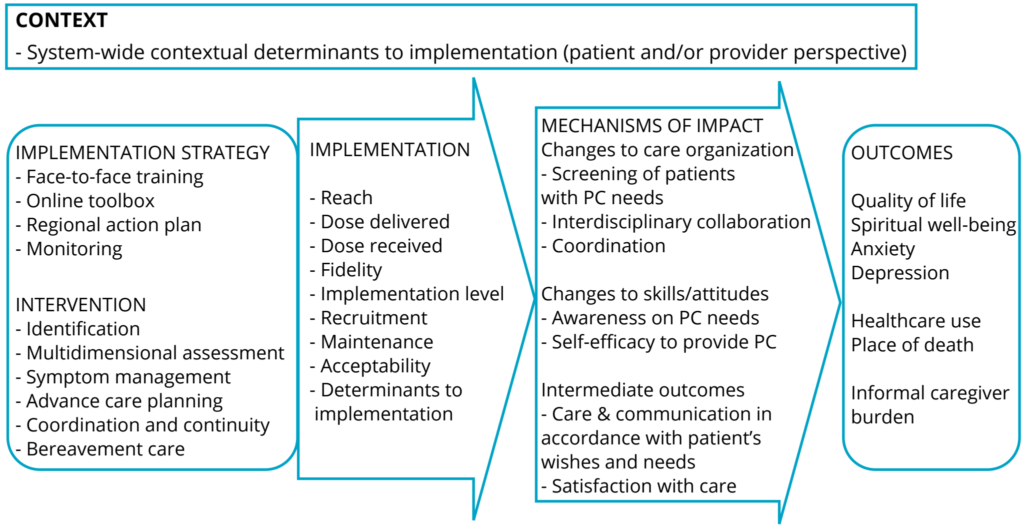

Figure 1. Medical Research Council derived model 17 illustrating causal assumptions of outcomes and mechanisms of impact
Abbreviation PC: palliative care

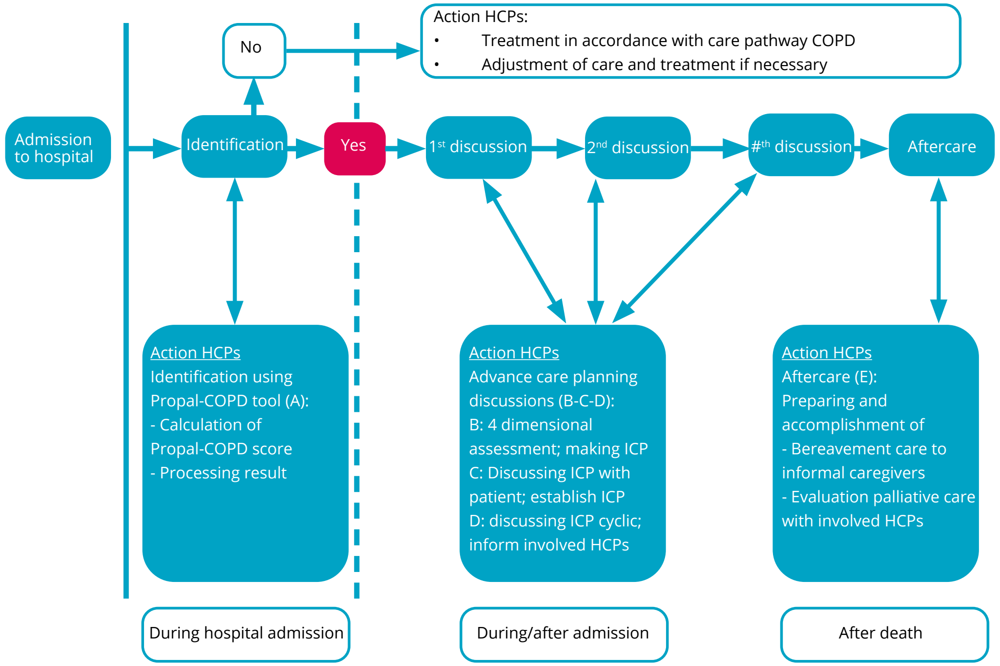

Figure 2. Flowchart on the care process for the individual patient.

Table 1. Description of the implementation strategy and integrated palliative care intervention of the Compassion study

Implementation strategy

Components	**Content of the component**	**Tools/materials/ underpinning theory**
Formation of regional intervention group	Multidisciplinary regional team	Implementation strategies integrated into multiple settings and directed to multiple professions involved are more effective[24]
Access to online toolbox	Website with information and guidance on the core elements of palliative care in COPD, including tools and links for facultative use	Quality Framework[7] Input from experts
Training session 1 (3 hours)	Introductory information on the project and research	n.a.
	Instruction the Propal-COPD tool to identify the palliative phase in patients with COPD	Propal-COPD tool[16]
	Multidimensional assessment (physical, psychological, social, spiritual)	Adapted version of Problems Square[26]
	Communication training on advance care planning in COPD including roleplay with actors	Training in palliative care communication with roleplay supports implementation[36-38]
	Non-pharmacological and pharmacological dyspnea management	Breathing Thinking Functioning model[39]
Training session 2 (3 hours)	Discussion current palliative care as organized in region vs. desired palliative care	7-phase model[40]
	Introductory information on implementing care pathway	7-phase model[40]
	Filling in formats A to E (who does what how and when) leading to first draft of regional action plan	Flowchart on patient care process (see Figure 2)
	Assigning local implementation leaders	7-phase model[40]
Completion of regional action plan	Agreement on who does what how and when	Format regional action plan Action planning stimulates behavior change 41 and assures the suitability of the intervention to the existing structure of the region
Monitoring	Monitoring meetings on site	Audit and provide feedback to monitor, evaluate, and modify provider behavior[42]
	Evaluation meetings with local implementation groups	Share local knowledge on how implementers and clinicians made something work in their setting and then share it with other sites[42]

Integrated palliative care intervention

Components	**Content of the component**
Identification	Calculation of Propal-COPD score
	Planning first consultation with patient and informal caregiver
Multidimensional assessment	Assessing palliative care needs on physical, psychological, social and spiritual dimension
Symptom management	Non-pharmacological and pharmacological treatment for breathlessness and other physical symptoms, smoking cessation, medication review, anxiety and depression
Advance care planning	Education about the illness trajectory and discussions with patient and informal caregiver on goals and preferences for future medical treatment
Coordination & continuity	Individual care plan, documentation of advance care directives Information exchange and cooperation with general practitioners and other involved professionals
	Regular multidisciplinary meetings
Dying phase & bereavement care	Planning a consultation with informal caregiver to evaluate care in the last phase
	Planning an evaluation of the provided palliative care with all involved professionals

To facilitate the uptake of the integrated palliative care intervention, an implementation strategy was developed that consists of multiple components.[24] An online toolbox describing the core elements of integrated palliative care and providing easy access to validated, existing tools was established. Also, we developed an interactive training including roleplay for participating healthcare professionals. The training consists of two sessions of three hours and addresses the core elements of integrated palliative care and its implementation. We collaborated with experienced training actors whose training sessions have been well received in previous research on advance care planning in dementia.[25] Also, the adapted version of the earlier developed Problems Square was used.[26] This tool is a practical translation of the WHO palliative care definition and helps professionals structuring the inventory of actual and possible future problems, and needs and wishes across multiple dimensions. Furthermore, non-pharmacological and pharmacological dyspnea management was discussed. In the second training session, each region collaboratively decides who should be involved, and which steps need to be performed by whom, how, where and when, leading to a regional action plan. In this plan, the different steps of the patient care process are elaborated (see Figure 2). In order to guide and monitor the implementation and execution of the regional action plans, there will be regularly monitoring meetings with the project leaders of each intervention region. During the study period, every four months meetings with participating professionals of the intervention regions will take place in which experiences and recommendations can be exchanged.

Following the recommendations of Mohr et al.,[27] we will not evaluate a locked-down version of the intervention, but the implementation of the essential, core elements of the integrated palliative care intervention that will be responsible for the intervention effect. This means that healthcare professionals of all participating settings are allowed to fine-tune the intervention to organizational, professional and patient characteristics. This iterative refinement will result in continuous improvement of the intervention during the study period. Similarly, small adaptations to the online toolbox can be made based on incoming process evaluation data.[27]

Control

Healthcare professionals of the control group will provide care as usual. For the Netherlands, this means that all healthcare professionals have online access to all existing guidelines on palliative care (including dyspnea) and COPD, possibility to consult specialized palliative care teams in primary care as well as in hospitals. After the recruitment of participants has been completed, professionals of the control group will be offered similar training as the intervention group received, and they will get access to the online toolbox.

Procedures

After randomization and formation of a regional intervention team, participating professionals of all eight hospital regions will be sent the baseline questionnaire by email. This will be repeated 3 and 12 months after the training (intervention regions) or the inclusion of the first patient (control regions). A physician or nurse with knowledge of the study will check all COPD-patients admitted to the pulmonology care department due to an acute exacerbation, and their informal caregiver if applicable, for eligibility. After the informed consent procedure, participating patients and informal caregivers complete the questionnaires required for the Propal-COPD tool and the baseline questionnaires during the hospital stay. A physician or nurse will enter the Propal-COPD tool indicators and baseline characteristics in an online data management system. The system automatically calculates the Propal-COPD score, based on the published algorithm.[16] For a patient of the intervention region, the score will be displayed as "positive" or "negative" and in the control regions it will be displayed as "xxx". A patient with a positive Propal-COPD score and, if present, his or her participating informal caregiver, will be sent follow-up questionnaires 3 and 6 months after inclusion. Questionnaires will be sent on paper or digitally via email, depending on personal preference. A flowchart of the cluster randomized controlled trial is shown in Figure 3.

Effect evaluation

An overview of the data collection process, detailing the timing of data collection and the outcome measures and instruments used, is provided in Table 2.

Primary effect outcome

The primary outcome is quality of life as measured with the Functional Assessment of Chronic Illness Therapy-Palliative care (FACIT-Pal) scale. This scale is a validated 46-item questionnaire comprising of a general part with four subscales on physical well-being, social/family well-being, emotional well-being and functional well-being, respectively, and a specific part regarding palliative care.[28] The total score ranges from 0 to 184; a higher score indicates a better quality of life. Since a Dutch version of the FACIT-Pal questionnaire was not yet available, the items of the palliative care subscale were first translated in collaboration with the FACIT organization, following the FACIT translation/linguistic validation methodology.[29] After a comprehensive forward-backwards translation process, the concept version of the translated FACIT-Pal questionnaire was tested through retrospective and cognitive interviews in ten patients: six with very severe COPD, three with lung cancer and one with both COPD and lung cancer. Recruitment of these patients took place in a pulmonology ward, outpatient clinic, as well as a pulmonary rehabilitation center.

Secondary effect outcomes

Secondary effect outcomes will be spiritual well-being, disease-specific health-related quality of life, unplanned healthcare use, date and place of death if applicable, informal caregiver burden and professionals' self-efficacy and role identity with providing palliative care and discussing end-of-life. Satisfaction with care will be assessed at the patient, informal caregiver and professional level. The measurement instruments to be used are detailed in Table 2.

Baseline measures

Demographic characteristics of patients that will be collected are sex, age, ethnicity (western and non-western), marital status, living situation, an education level (high, medium, low), smoking status, pack years. Also, characteristics of disease severity (long term oxygen use, home non-invasive ventilation use, previous ICU admissions, previous mechanical ventilation and opioid use before hospital admission) will be collected. Demographic characteristics of informal caregivers that will be collected are sex, age, education level (high, medium, low) and current job. Demographic characteristics of professionals that will be collected are function, years of experience, palliative care experience and education.

Sample size calculation

Our primary outcome measure is quality of life measured with the FACIT-Pal. The clinically relevant difference is suggested to be between 4% to 6% of a measure's overall score for the

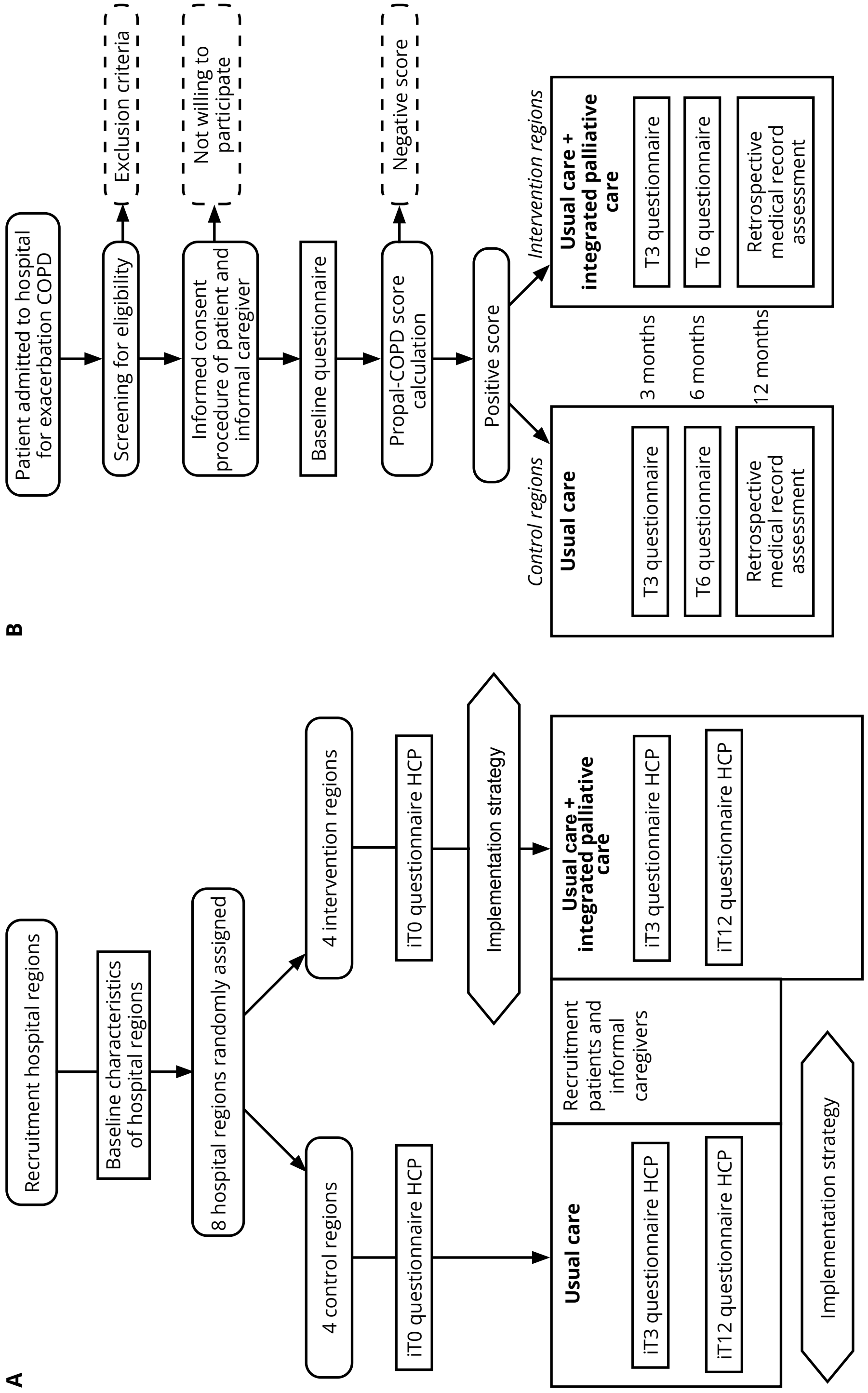

Figure 3. Flowchart of procedures with timelines of **(A)** healthcare professionals and **(B)** patients and informal caregivers. Abbreviations HCP: health care professionals; iT0: professional timeline at baseline (pre-implementation); iT3: 3 months after inclusion of first included patient (initial implementation); iT12: 12 months after training (intervention regions) or inclusion of first patient (control regions) (late implementation); T0: patient timeline at baseline; T3: patient timeline at 3 months; T6: patient timeline at 6 months; R: retrospectively

Functional Assessment of Cancer Therapy (FACT) scores, including the FACIT-Pal.[30] A previous systematic review on palliative care interventions used the 5% midrange bound, which equals 9 points on the FACIT-Pal.[31] Assuming a standard deviation of 25,[32] at least 121 patients per group are required to obtain a power of 80% (two-sided t-test, alpha = 0.05). To adjust for the clustering at hospital level (a previous study found an ICC = 0.01[23]) and to allow for an additional loss to follow up of 10% a total of 347 patients are needed (44 patients per region).

Table 2. Data collection schedule and measurement instruments for patients, informal caregivers and healthcare professionals

Patient	**Measurement instrument**	**T0**	**T3**	**T6**	**R**
Baseline characteristics	Questionnaire on demographic characteristics and case report form on disease severity	x			
Quality of life (primary outcome)	Functional Assessment of Chronic Illness Therapy-Palliative care (FACIT-Pal) scale 28	x	x	x	
Spiritual well-being	Functional Assessment of Chronic Illness Therapy - Spiritual Well-Being (FACIT-Sp-12) scale 43	x	x	x	
Anxiety and depression	Hospital Anxiety and Depression Scale (HADS) 44	x	x	x	
Disease-specific health-related quality of life	Clinical COPD Questionnaire (CCQ)	x	x	x	
Satisfaction with care	Single item question on satisfaction with provided care, self-rated on a numeric rating scale (NRS) from 0 to 10	x		x	
Unplanned healthcare use	Medical record assessment on number of ED visits (without admission), hospital admission (number and number of days), ICU admission (number and number of days), in the 12 months pre-enrollment up to 12 months after enrollment				x
Date and place of death, place of care in last week of life if applicable	Medical record assessment (and contact with general practitioner if needed)				x
Dose received	Questionnaire on received core elements, based on three validated questionnaires 45-47	x		x	
	Medical record assessment on core elements				x
Experiences and acceptability	Semi-structured interviews		x*		
Informal caregiver		**T0**	**T3**	**T6**	
Baseline characteristics	Questionnaire on demographic characteristics	x			
Caregiver burden	Caregiver Reaction Assessment (CRA) scale 48	x	x	x	

Table 2. *Continued*

	Measurement instrument			
Satisfaction with care	Single item question on satisfaction with provided care to the patient, self-rated on a NRS from 0 to 10	x		x
Experiences and acceptability	Semi-structured interviews		x*	
Health care professional		**iT0**	**iT3**	**iT12**
Self-efficacy	End-of-life professional caregiver survey (EPCS) 49	x	x	x
Role identity	Developed five-item question on role identity based on MIDI questionnaire 34	x	x	x
Satisfaction with care	Single item question on satisfaction with provided palliative care to patients with COPD, self-rated on a 5-point Likert scale	x	x	x
Dose delivered	Self-reported provision of delivered core elements	x	x	x
Experiences, acceptability and determinants to implementation	Semi-structured interviews			x

T0=patient timeline at baseline; T3=patient timeline at 3 months; T6=patient timeline at 6 months; R=retrospectively; iT0= pre-implementation (professional timeline at baseline); iT3= initial implementation (3 months after inclusion of first patient); iT12= late implementation (12 months after training (intervention regions) or inclusion of first patient (control regions)).
* Interviews will be held with a purposeful sample of patients and informal caregivers between 3 and 6 months after inclusion.

Implementation outcomes

Context refers to the larger physical, social, and political environment that either directly or indirectly affects the intervention. To study contextual characteristics of each intervention region, we will use field notes of training sessions, transcriptions of monitoring meetings, project meetings and interviews with implementation leaders and involved healthcare professionals.

Reach concerns the degree to which the intended audience participates in the intervention. Reach of the implementation strategy will be reported as the composition of the intervention teams, the absolute number and the proportion of professionals that participated in the training, using the attendance list of the training sessions. Reach of the intervention will be reported as numbers, proportions and characteristics of patients that received the integrated palliative care intervention.

Dose delivered is measured as the extent to which core elements of palliative care have been carried out by participating healthcare professionals, using questionnaires before and after the training. This measure reflects the effect of the implementation strategy on the care practices of each professional.

Dose received is measured as the extent to which core elements of palliative care are being received by participating patients, using patient questionnaires and medical chart review on received core elements.

Fidelity refers to the extent to which a patient was treated in accordance with the regional action plan. Fidelity checklists for each participating intervention patient will be filled out by the involved healthcare professional.

Implementation is a composite score indicating the extent to which the intervention has been implemented by professionals and received by patients. To compare the integrated palliative care provision between the intervention and control regions, the implementation score of delivered and received core elements of integrated palliative care will be calculated using the calculation method following Fleuren et al.[34]

Recruitment refers to the way we have recruited hospital regions to become involved in the implementation and evaluation of integrated palliative care in COPD.

Maintenance is the extent to which core elements of integrated palliative care is embedded in the routine organizational practices and policies.

Acceptability is the perception among healthcare professionals, patients and informal caregivers that the integrated palliative care intervention is agreeable, palatable, or satisfactory. We will perform semi-structured interviews with involved healthcare professionals on their experiences with the intervention and suggestions for improvement. A purposeful sample of patients and informal caregivers will be interviewed about their experiences with and perceptions about the care received and the information discussed with their healthcare professionals. Evaluation questionnaires will inquire on experiences with the training and toolbox and suggestions for improvement among participating professionals. The data will be used to make adaptations to the training and toolbox.

Barriers and facilitators to implementation

The Consolidated Framework For Implementation Research will be used to explore what determinants to implementation are across different contexts. This framework consists of 37 constructs in five major domains: intervention characteristics, outer setting, inner setting, characteristics of the individuals involved, and the process of implementation. We will use the constructs to develop topic lists for semi-structured interviews with involved professionals.

Data monitoring and management

All quantitative data will be collected using the online data management system Castor edc. For the management of participants, a secured Access database will be used. In case of errors or essential missing data, the participant or the concerning hospital will be contacted. Of eligible non-consenting patients their year of birth, sex and reasons for non-participation will be collected. The qualitative data gathered via monitoring and project meetings and interviews will all be audio-recorded and transcribed verbatim. The transcripts will be pseudonymized.

Also, field notes made during training sessions and contact with professionals of the regions will be written out in digital documents. All study data and meta-data will be stored on a secured place in the Leiden University Medical Center for 15 years.

Analysis

Analysis of effect evaluation

Data cleaning and all analyses will be carried out using statistical software that supports multilevel mixed model analyses, such as IMB SPSS Statistics 25. Baseline characteristics of region and study population will be analyzed using descriptive statistics. Continuous variables will be reported as mean and standard deviation and categorical variables as frequency or percentage. The statistical analyses will be done by an intention-to-treat approach. All analysis will be considered significant if $\alpha < 0.05$. We will analyze differences between the control and the intervention group for the primary and secondary outcomes on the patient, informal caregiver and professional level using multilevel mixed model analyses that will account for the clustered study design (i.e. patients and professionals nested within a region). We will check for eventual unbalances in baseline characteristics and adjust for these variables if needed.

Analysis of process evaluation

All quantitative process data will be analyzed using descriptive statistics. We will examine the association between the implementation score and each effect outcome measure at patient level, using linear regression analysis. For this analysis, the dependent variable is the implementation score. Independent variables are patient outcomes at measurement point T6 or T12. Transcriptions of the semi-structured interviews, monitoring sessions and project meetings will be analyzed using inductively and deductively content analysis techniques supported by the qualitative analysis software Atlas.ti. Subsequently, triangulation of quantitative and qualitative results will take place.

Ethical considerations

The study has been approved by the Medical Ethics Committee (CMO) of the Radboud University Medical Centre (number 2018-4833). Since palliative care is additional to disease-oriented care, we do not expect any risks of participation for patients. The integrated palliative care intervention is patient-centred (adapted to the needs of every individual patient) and based on existing guidelines and thus could be considered as regular care. However, participation in this study will require filling out questionnaires which can be burdensome. To minimize the burden, we therefore limited the length and frequency of used questionnaires. Moreover, when selecting and writing questionnaires and information letters, we took into account that most patients are older and have a low education level.

Discussion

This study protocol details the implementation and evaluation of an integrated palliative care approach into regular COPD-care in the Netherlands. The outcomes of this large-scale study will add to the evidence base on how to effectively implement palliative care for patients with COPD, a study population which long has been underrepresented in palliative care research.[31]

The integrated palliative care approach was co-created with a wide variety of stakeholders to incorporate scientific and practical knowledge. Also, we built upon previous experiences of national care pathway development for patients admitted to the hospital for an acute exacerbation COPD.[35] Moreover, since coordination between different professionals and transmural collaboration are vital requirements to provide good palliative care, our approach integrates COPD-care and palliative care and includes primary and secondary care professionals.

The effectiveness of integrating palliative care into regular COPD-care can only be tested when it is implemented in a real-world setting. An 'implementation momentum' had been created by the publication of the Quality Framework for palliative care in 2017, prescribing the organization and provision of palliative care in the Netherlands, independent of the type of disease.[7] Therefore, a hybrid study design which blends clinical effectiveness and implementation research, as proposed by Curran et al..[14] was chosen. A hybrid design might enable a more rapid translation of our research findings into routine practices, as it will provide information on both the prerequisites of integrating palliative care in routine COPD care and its clinical effectiveness. We are planning to disseminate the study findings and promote the scale-up of the approach if proven effective.

This study will have some methodological challenges. In hybrid effectiveness-implementation studies, implementation science terminology and methods need to be aligned to those of traditional, clinical effectiveness research. Regarding the design, a complex balance needs to be found between internal validity and factors that promote implementation. In our study, to facilitate uptake, the intervention will be tailored to regional needs. Although this resembles real practice and enables generalizability, the heterogeneity of provided intervention elements to patients may limit internal validity.

Furthermore, all hospital regions – including those randomized to the control group – wanting to participate in this study had a particular interest in this topic and were eager to change their care practice. Hence, this might lead to smaller differences between the provided care in the intervention and control group, and may decrease chances of detecting actual intervention effect. We attempt to deal with this by measuring and comparing the implementation score of delivered and received core elements of integrated palliative care between intervention and control groups.

Finally, it is uncertain what proportion of patients will score positively on the Propal-COPD tool and thus will be eligible for inclusion, as we made an assumption based on the development study.[16] Although the Propal-COPD tool is considered to be the best choice because it showed high sensitivity, its robustness and its feasibility in clinical practice need further testing. Therefore, we are planning to perform external validation with the data derived from this study.

Abbreviations

COPD: chronic obstructive pulmonary disease; FACIT-Pal: Functional Assessment Chronic Illness Therapy; Functional Assessment of Chronic Illness Therapy-Palliative care; RCT: randomized controlled trial.

Ethics approval and consent to participate

The study has been approved by the Medical Ethics Committee (CMO) of Radboud University Medical Centre (protocol number 2018-4833). After receiving oral and written information about the study, participating patients and informal caregivers are required to give their informed consent in writing. On the informed consent form, participants indicate whether they agree to be approached for an interview about their experiences with the care they received. All participants of semi-structured interviews (patients, informal caregivers and healthcare professionals) are given information on interview procedures and data protection. Subsequently, they are required to give their informed consent in writing.

Consent for publication

Not applicable.

Availability of data and materials

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Funding

This work was financed by The Netherlands Organization for Health Research and Development (ZonMw). This funding source had no role in the design of this study and will not have any role during its execution, analyses, interpretation of the data, or decision to submit results.

Acknowledgements

The authors would like to acknowledge all individuals representing the organizations that were involved in the expert groups and gave feedback on the core elements of the intervention and content of the online toolbox and training. Also, the authors thank Jason Bredle of the FACIT organization for the collaboration in the translation process of the FACIT-Pal questionnaire. Furthermore, the authors wish to thank the patients that helped to pretest the study questionnaires.

Authors' contributions

The Lung Alliance Netherlands, NH, RK and YE initiated the project. JB, RK, YE, NH and HK were involved in developing and refining the study design and EV helped with the operationalization. JB wrote the first draft of the manuscript. All authors drafted and revised sections of the manuscript and contributed to the content. All authors read and approved the final manuscript.

References

1. GOLD. Pocket Guide to COPD Diagnosis, Management, and Prevention. A Guide for Health Care Professionals 2017.
2. Groenewegen KH, Schols AM and Wouters EF. Mortality and mortality-related factors after hospitalization for acute exacerbation of COPD. Chest 2003; 124: 459-467. 2003/08/09.
3. WHO. Fact Sheet Top 10 global causes of deaths, 2016, http://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death (accessed 2018-09-04).
4. 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. 2011/04/23. DOI: 10.1089/jpm.2010.0479.
5. 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. 2009/04/28. DOI: 10.1016/j.jpainsymman.2008.07.010.
6. WHO. Definition Palliative care, http://www.who.int/cancer/palliative/definition/en/ (2002).
7. IKNL/Palliactief. Netherlands Quality Framework for Palliative Care. 2017.
8. 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. 2008/04/09. DOI: 10.1164/rccm.200605-587ST.
9. 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 2017/05/04. DOI: 10.1183/23120541.00068-2016.
10. Beernaert K, Cohen J, Deliens L, et al. Referral to palliative care in COPD and other chronic diseases: a population-based study. Respir Med 2013; 107: 1731-1739. 2013/07/03. DOI: 10.1016/j.rmed.2013.06.003.
11. 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. 2017/03/05. DOI: 10.1038/s41533-017-0017-y.
12. IKNL. Rapport IKNL Palliatieve zorg in beeld. 2014.
13. Oishi A and Murtagh FE. The challenges of uncertainty and interprofessional collaboration in palliative care for non-cancer patients in the community: a systematic review of views from patients, carers and health-care professionals. Palliat Med 2014; 28: 1081-1098. DOI: 0269216314531999 [pii];10.1177/0269216314531999 [doi].
14. Curran GM, Bauer M, Mittman B, et al. Effectiveness-implementation hybrid designs: combining elements of clinical effectiveness and implementation research to enhance public health impact. Med Care 2012; 50: 217-226. 2012/02/09. DOI: 10.1097/MLR.0b013e3182408812.
15. Eccles M, Grimshaw J, Campbell M, et al. Research designs for studies evaluating the effectiveness of change and improvement strategies. Quality & safety in health care 2003; 12: 47-52. 2003/02/07.

16. Duenk RG, Verhagen C, Bronkhorst EM, et al. Development of the ProPal-COPD tool to identify patients with COPD for proactive palliative care. Int J Chron Obstruct Pulmon Dis 2017; 12: 2121-2128. DOI: 10.2147/COPD.S140037 [doi];copd-12-2121 [pii].
17. 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. 2008/10/01. DOI: 10.1136/bmj.a1655.
18. Richtlijn Dyspneu in de palliatieve fase 3.0.
19. Nederland LA. Richtlijn Palliatieve zorg voor mensen met COPD. 2011. Amersfoort.
20. Boddaert M. Netherlands Quality Framework for Palliative Care. 2017.
21. Landers A, Wiseman R, Pitama S, et al. Severe COPD and the transition to a palliative approach. Breathe (Sheffield, England) 2017; 13: 310-316. 2017/12/07. DOI: 10.1183/20734735.013917.
22. 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. DOI: npjpcrm201520 [pii];10.1038/npjpcrm.2015.20 [doi].
23. 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. 2017/10/17. DOI: 10.2147/COPD.S141974.
24. van Riet Paap J, Vernooij-Dassen M, Sommerbakk R, et al. Implementation of improvement strategies in palliative care: an integrative review. Implement Sci 2015; 10: 103. 2015/07/27. DOI: 10.1186/s13012-015-0293-2.
25. Tilburgs B, Koopmans R, Vernooij-Dassen M, et al. Educating Dutch General Practitioners in Dementia Advance Care Planning: A Cluster Randomized Controlled Trial. J Am Med Dir Assoc 2019 2019/11/25. DOI: 10.1016/j.jamda.2019.09.010.
26. Thoonsen B, Vissers K, Verhagen S, et al. Training general practitioners in early identification and anticipatory palliative care planning: a randomized controlled trial. BMC Fam Pract 2015; 16: 126. DOI: 10.1186/s12875-015-0342-6 [doi];10.1186/s12875-015-0342-6 [pii].
27. Mohr DC, Schueller SM, Riley WT, et al. Trials of Intervention Principles: Evaluation Methods for Evolving Behavioral Intervention Technologies. Journal of medical Internet research 2015; 17: e166. 2015/07/15. DOI: 10.2196/jmir.4391.
28. Lyons KD, Bakitas M, Hegel MT, et al. Reliability and validity of the Functional Assessment of Chronic Illness Therapy-Palliative care (FACIT-Pal) scale. J Pain Symptom Manage 2009; 37: 23-32. 2008/05/28. DOI: 10.1016/j.jpainsymman.2007.12.015.
29. Eremenco SL, Cella D and Arnold BJ. A comprehensive method for the translation and cross-cultural validation of health status questionnaires. Eval Health Prof 2005; 28: 212-232. 2005/04/27. DOI: 10.1177/0163278705275342.
30. Ringash J, O'Sullivan B, Bezjak A, et al. Interpreting clinically significant changes in patient-reported outcomes. Cancer 2007; 110: 196-202. 2007/06/05. DOI: 10.1002/cncr.22799.

31. 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. 2016/11/29. DOI: 10.1001/jama.2016.16840.
32. Rogers JG, Patel CB, Mentz RJ, et al. Palliative Care in Heart Failure: The PAL-HF Randomized, Controlled Clinical Trial. Journal of the American College of Cardiology 2017; 70: 331-341. 2017/07/15. DOI: 10.1016/j.jacc.2017.05.030.
33. Steckler A and Linnan L. Process evaluation for public health interventions and research. San Francisco, CA, US: Jossey-Bass, 2002, p.xxviii, 400-xxviii, 400.
34. Fleuren MA, Paulussen TG, Van Dommelen P, et al. Towards a measurement instrument for determinants of innovations. International journal for quality in health care : journal of the International Society for Quality in Health Care 2014; 26: 501-510. 2014/06/22. DOI: 10.1093/intqhc/mzu060.
35. Westbroek LF, Klijnsma M, Salomé P, et al. Reducing the number of hospitalization days for COPD: setting up a transmural care pathway Int J Chron Obstruct Pulmon Dis; Forthcoming 2020.
36. Back AL, Arnold RM, Baile WF, et al. Efficacy of communication skills training for giving bad news and discussing transitions to palliative care. Arch Intern Med 2007; 167: 453-460. 2007/03/14. DOI: 10.1001/archinte.167.5.453.
37. Hales BM and Hawryluck L. An interactive educational workshop to improve end of life communication skills. The Journal of continuing education in the health professions 2008; 28: 241-248; quiz 249-255. 2008/12/06. DOI: 10.1002/chp.191.
38. Thoonsen B, Gerritzen SH, Vissers KC, et al. Training general practitioners contributes to the identification of palliative patients and to multidimensional care provision: secondary outcomes of an RCT. BMJ Support Palliat Care 2016. DOI: bmjspcare-2015-001031 [pii];10.1136/bmjspcare-2015-001031 [doi].
39. Spathis A, Booth S, Moffat C, et al. The Breathing, Thinking, Functioning clinical model: a proposal to facilitate evidence-based breathlessness management in chronic respiratory disease. NPJ Prim Care Respir Med 2017; 27: 27. 2017/04/23. DOI: 10.1038/s41533-017-0024-z.
40. Aeyels D, Van der Veken L and Vanhaecht K. 7-fasenmodel voor de ontwikkeling, implementatie, evaluatie en opvolging van zorgpaden. Uitdieping voor transmurale zorg. 2016. Leuven: Netwerk Klinische Paden.
41. Hagger MS and Luszczynska A. Implementation intention and action planning interventions in health contexts: state of the research and proposals for the way forward. Applied psychology Health and well-being 2014; 6: 1-47. 2014/03/05. DOI: 10.1111/aphw.12017.
42. Powell BJ, Waltz TJ, Chinman MJ, et al. A refined compilation of implementation strategies: results from the Expert Recommendations for Implementing Change (ERIC) project. Implement Sci 2015; 10: 21. 2015/04/19. DOI: 10.1186/s13012-015-0209-1.

43. Peterman AH, Fitchett G, Brady MJ, et al. Measuring spiritual well-being in people with cancer: the functional assessment of chronic illness therapy--Spiritual Well-being Scale (FACIT-Sp). Annals of behavioral medicine : a publication of the Society of Behavioral Medicine 2002; 24: 49-58. 2002/05/15. DOI: 10.1207/s15324796abm2401_06.
44. Zigmond AS and Snaith RP. The hospital anxiety and depression scale. Acta psychiatrica Scandinavica 1983; 67: 361-370. 1983/06/01. DOI: 10.1111/j.1600-0447.1983.tb09716.x.
45. Uittenbroek RJ, Reijneveld SA, Stewart RE, et al. Development and psychometric evaluation of a measure to evaluate the quality of integrated care: the Patient Assessment of Integrated Elderly Care. Health expectations : an international journal of public participation in health care and health policy 2016; 19: 962-972. 2015/08/01. DOI: 10.1111/hex.12391.
46. Heyland DK, D. P, P. D, et al. The Development and Validation of a Questionnaire to Audit Advance Care Planning. J Palliative Care Med 2012; 2. DOI: 10.4172/2165-7386.1000119.
47. Uijen AA, Schellevis FG, van den Bosch WJ, et al. Nijmegen Continuity Questionnaire: development and testing of a questionnaire that measures continuity of care. Journal of clinical epidemiology 2011; 64: 1391-1399. 2011/06/22. DOI: 10.1016/j.jclinepi.2011.03.006.
48. Nijboer C, Triemstra M, Tempelaar R, et al. Measuring both negative and positive reactions to giving care to cancer patients: psychometric qualities of the Caregiver Reaction Assessment (CRA). Social science & medicine (1982) 1999; 48: 1259-1269. 1999/04/29.
49. Lazenby M, Ercolano E, Schulman-Green D, et al. Validity of the end-of-life professional caregiver survey to assess for multidisciplinary educational needs. J Palliat Med 2012; 15: 427-431. 2012/04/17. DOI: 10.1089/jpm.2011.0246.

Chapter 5

The effect of an integrated palliative care intervention on quality of life and acute healthcare use in patients with COPD: results of the COMPASSION cluster randomized controlled trial

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Palliat Med 2023 Vol. 37 Issue 6 Pages 844-855

Abstract

Background

COPD causes high morbidity and mortality, emphasizing the need for palliative care.

Aim

To assess the effectiveness of palliative care in patients with COPD.

Design

Cluster randomised controlled trial (COMPASSION study; Netherlands Trial Register (NTR): NL7644, 07-04-2019). Healthcare providers within the intervention group were trained to implement palliative care components into routine COPD care. Patients completed questionnaires at baseline, after 3 and 6 months; medical records were assessed after 12 months. The primary outcome was quality of life (FACIT-Pal). Secondary outcomes were anxiety, depression, spiritual well-being, satisfaction with care, acute healthcare use, documentation of life-sustaining treatment preferences, and place of death. Generalised linear mixed modelling was used for analyses.

Setting

Eight hospital regions in the Netherlands.

Participants

Patients hospitalised for an acute exacerbation of COPD and positive ProPal-COPD score.

Results

Of 222 patients included, 106 responded to the questionnaire at six months. 36 of 98 intervention patients (36.7%) received the intervention. Intention-to-treat-analysis showed no effect on the primary outcome (adjusted difference: 1.09; 95% confidence interval: -5.44–7.60). In the intervention group, fewer intensive care admissions for COPD took place (adjusted odds ratio: 0.21; 95% confidence interval: 0.03–0.81) and strong indications were found for fewer hospitalisations (adjusted incidence rate ratio: 0.69; 95% confidence interval: 0.46–1.03).

Conclusions

We found no evidence that palliative care improves quality of life in patients with COPD. However, it can potentially reduce acute healthcare use. The consequences of the COVID-19 pandemic led to suboptimal implementation and insufficient power, and may have affected some of our findings.

Keywords

COPD, palliative care, clinical effectiveness, quality of life, cluster randomized controlled trial.

What is already known about the topic?

- Patients in advanced stages of COPD suffer from high symptom burden, limited physical functioning and low quality of life.
- In oncological patients, timely initiation of palliative care alongside usual care improves quality of life and reduces healthcare use.

What this paper adds

- We did not find improvements in quality of life, but saw fewer intensive care admissions and a trend toward fewer hospital admissions in intervention group patients with advanced COPD .
- Study power was insufficient and not all patients received the intended palliative care intervention elements, possibly hampering reliable measurement of the clinical effectiveness.

Implications for practice, theory or policy

- Quality of life is a broad construct and may be difficult to target in patients with advanced organ failure; Future studies should consider a more proximal outcome measure, e.g. coping with COPD.
- Lower acute healthcare use reduces healthcare costs and this is a relevant secondary outcome parameter to society as a whole; This finding needs further exploration.

Introduction

Chronic obstructive pulmonary disease (COPD) causes considerable morbidity and is the third leading cause of death worldwide.[1] As the disease progresses, acute exacerbations occur more frequently, requiring hospital admissions.[2] Many patients in advanced stages suffer from severe breathlessness and other problems such as fatigue, anxiety, depression, social isolation and existential suffering.[3, 4] Their symptom burden and functional status are similar to those of patients with lung cancer and severely affect their quality of life.[5]

In patients with cancer, quality of life can be improved and healthcare use reduced by timely initiation of palliative care.[6] Palliative care aims to enhance quality of life by addressing physical, psychological, social and spiritual problems.[7] In addition, it endeavours to tailor patient care to their needs and preferences through advance care planning and care coordination. Patients with advanced COPD may equally benefit from palliative care.[6, 8] However, the evidence of the effectiveness of palliative care for this patient group is still scarce.

In a recent systematic review, only four out of twenty palliative care interventions in COPD had been evaluated in a powered controlled trial, and the effects on health outcomes remained inconclusive.[9] Furthermore, guidelines recommend palliative care delivery by ‘generalists’ (i.e. respiratory care providers) in the first place, and only specialist palliative care involvement in case of complexity,[10, 11] but the integration of palliative care elements into routine COPD care (integrated palliative care)[12] has hardly been studied.

Therefore, in the COMPASSION study, in half of the participating hospital regions, primary and secondary healthcare providers were trained to integrate palliative care components into routine COPD care. We assessed the effect on quality of life, emotional and spiritual well-being, acute healthcare use and place of death of patients with COPD. We hypothesized that intervention group patients would score better on quality of life and well-being, use less acute healthcare, and have a lower rate of in-hospital deaths than patients of hospitals in the control group.

Methods

Design

A cluster randomised controlled trial was performed. A detailed study protocol has been published previously.[13]

Setting

This study took place in pulmonary care departments of eight hospitals in the Netherlands, that collaborated with affiliated general practitioners, primary care nurses, and palliative care consultation teams, further referred to as ‘hospital regions’ or ‘clusters’.

Randomisation

Hospital regions were randomised to the intervention or control condition (four clusters in each group) by an independent statistician, stratified by the number of COPD-related hospital admissions per year.

Intervention

An integrated palliative care intervention was developed following national guidelines, literature and stakeholders' input and comprised 1) palliative care conversations tailored to the patient's needs, 2) care coordination and continuity, and 3) aftercare if a patient had died (Table 1). To optimize uptake of the intervention in practice, an implementation strategy was developed (Table 1). Primary and secondary healthcare providers from the intervention group were provided with an online toolbox, received two training sessions, and received implementation guidance. Healthcare providers in the control group provided care as usual and were offered training after the formal study had ended.

Table 1. Description of the implementation strategy and integrated palliative care intervention of the Compassion study. Adapted from Broese et al. (2020).[13]

Components	**Content of the component**
Implementation strategy	
Formation of regional intervention group	Multidisciplinary regional team consisting of pulmonologists, general practitioners, COPD nurses and palliative care nurses
Access to online toolbox	Website with information and guidance on the core elements of palliative care in COPD, including tools and links for facultative use: www.palliatievezorgcopd.nl
Training session 1 (3 hours)	Introductory information on the project and research
	Instruction on the Propal-COPD tool to identify the palliative phase in patients with COPD
	Multidimensional assessment (physical, psychological, social, spiritual)
	Communication training on advance care planning in COPD including roleplay with actors
	Non-pharmacological and pharmacological dyspnea management based on the Breathing-Thinking-Functioning model[14]
Training session 2 (3 hours)	Discussion current palliative care as organized in region vs. desired palliative care
	Introductory information on implementing care pathway
	Filling in formats (who does what how and when) leading to first draft of regional action plan
	Assigning local implementation leaders
Completion of regional action plan	Agreement on who does what, how, and when
Monitoring	Monitoring meetings on site
	Evaluation meetings with local implementation groups
Integrated palliative care intervention	
1) Palliative care conversations	Consultation at outpatient clinic with patient and informal caregiver by pulmonologist and/or COPD nurse, including: • Multidimensional assessment • Symptom management • Advance care planning
If needed:	Follow up palliative care conversation(s)
	Specialist palliative care team consultation(s)
2) Coordination & continuity	Individual care plan and documentation of advance care directives
	Information exchange and collaboration with general practitioners and other involved professionals
	Regular multidisciplinary meetings
If a patient had died:	
3) Aftercare	Consultation with informal caregiver to evaluate care in the last phase
	Evaluation of the provided palliative care with all involved professionals

Participants

Between May 2019 and August 2020, patients admitted to the hospital for an acute exacerbation were invited by a pulmonologist or nurse to participate and subsequently screened with the ProPal-COPD tool (see Box 1).15 Patients with a positive score were considered having palliative care needs and were included in the study. Initially, the previously published cut-off value of – 1.362 was used.[15] However, as the rate of patients with a positive score was lower than anticipated, it was deemed necessary to lower the cut-off value by one point to – 2.4 after six months. Exclusion criteria for participation were the inability to complete questionnaires in Dutch, severe cognitive decline and being on the waiting list for lung transplantation (Table 2).

Box 1. ProPal-COPD tool

The ProPal-COPD tool was developed by Duenk et al. (2017) and consists of seven indicators: Medical Research Council (MRC) dyspnoea score of 5, Clinical COPD Questionnaire (CCQ) score > 3, forced expiratory volume in 1 s lower than 30% predicted, presence of specific comorbidities, body mass index lower than 21 kg/m2 or weight loss (> 10% in the last six months or > 5% in last month), previous hospitalisation for acute exacerbation in the last two years (last two years ≥2 admissions or last year ≥1 admission), and a negative answer to the surprise question ("Would you be surprised if your patient were to die in the next 12 months?").

Table 2. Inclusion and exclusion criteria of study participants.

Inclusion criteria	Exclusion criteria
• Patient diagnosed with COPD	• Inability to complete questionnaires in Dutch
• Being admitted with an acute exacerbation COPD	• Severe cognitive decline (e.g. dementia)
• ProPal-COPD score positive (i.e.above cut-off value)	• Being on the waiting list for lung transplantation

Blinding

Complete blinding of participants for group allocation was impossible, but patients were not explicitly told whether their hospital was assigned to the intervention or control group. Further, healthcare providers of control regions were blinded for the ProPal-COPD score (whether positive and thus needing palliative care, or negative).

Data collection

Demographics and patient-reported outcome measures were collected using a questionnaire at three time points. At baseline, patients completed a paper questionnaire during hospitalisation. After three and six months, a follow-up questionnaire was sent to the patient's home or email, depending on the patient's preference. Patients were called by phone to remind them to complete the follow-up questionnaires. However, this was not always possible due to staff shortages in the research team. Medical record assessment was performed after 12 months to retrieve data on healthcare use, documentation of treatment preferences and date and place of death. Also, we assessed how many patients had received intervention components. Intervention patients who had had at least one palliative care conversation at the outpatient clinic with their pulmonologist and/or COPD nurse within six months after inclusion were considered to have received the intervention with fidelity.

Outcome measures

The primary outcome was quality of life measured with the validated 46-item Functional Assessment of Chronic Illness Therapy-Palliative care (FACIT-Pal) scale.16 Total score ranges between 0 and 184, with a higher score indicating a better quality of life. Two subscores were calculated: the FACT-G sub score (a combination of the four general subscales on physical, social/family, emotional and functional well-being, consisting of 27 items) and the PALS sub score (the specific palliative care subscale, consisting of 19 items). Secondary outcomes were health-related quality of life (CCQ), spiritual well-being (FACIT–Spiritual Well Being scale (FACIT-Sp-12)), anxiety and depression symptoms (Hospital Anxiety and Depression Scale (HADS)), satisfaction with care received from the hospital and general practice, respectively (numerical rating scale (NRS) ranging from 0 to 10). Furthermore, the number of emergency department visits, hospital admissions (number and number of days) and intensive care unit (ICU) admissions were assessed. Also, we verified if any life-sustaining treatment preferences (e.g. cardiopulmonary resuscitation) had been documented. Lastly, the date and place of death of deceased patients were collected and whether any emergency department or hospital admission had occurred in the last month of life. We also intended to collect and analyse informal caregiver burden data. However, due to low recruitment rates and high non-response rates, the data obtained were insufficient to conduct analyses.

Data analyses

Data cleaning and descriptive statistics were performed using SPSS, version 25, and outcome analyses were conducted using R software, version 3.6.2. We calculated that 347 participants were required to find an effect of minimum 9 points at the primary outcome with an assumed standard deviation of 25, taking clustering at hospital level and a loss to follow-up of 10% into account.[13] Primary and secondary outcomes were analysed using generalized linear mixed modelling with a normal distribution with identity link for continuous variables, negative binomial distribution with log link for count outcomes and log regression analysis for binary outcomes. A Hurdle model consisting of two parts (a binomial distribution with logit link and negative binomial distribution with log link) was used to compare the number of hospitalisation days.

The binomial part estimates the difference in the likelihood of having any hospitalisation days by means of an odds ratio, while the negative binomial part estimates the ratio between the hospitalisation days per time if larger than 0 using an incidence rate ratio. In the case of skewed residuals of continuous outcomes, bootstrapping was used. In all models, the baseline value of the outcome was entered as covariate and follow-up values as a dependent variable. To adjust for clustering, hospital region was entered as a random factor. The intraclass cluster coefficient was about zero for all outcomes, except for satisfaction with care from the hospital (0.031) and general practice (0.037). We checked for any unbalances in baseline characteristics and considered adjustment for these variables not required. Survival within 12 months between the two groups was analysed using a Kaplan-Meier plot and a Log Rank test. Differences between the two groups regarding the place of death and acute healthcare use in the last month of life were analysed using Chi-square tests. All outcomes were analysed using the intention-to-treat principle. Additionally, the occurrence of palliative care conversations in the intervention and control group was compared using a Chi-square test. A sensitivity analysis was done by limiting intervention participants to those who received one or more palliative care conversations at the outpatient clinic within six months after inclusion. All tests were two-sided, and p-values ≤ 0.05 were considered statistically significant.

Ethics approval and consent

All participants received oral and written study information and gave written informed consent. Ethical approval was granted by the Medical Ethics Committee of Arnhem-Nijmegen (file number 2018-4833) on 15 October 2018.

Results

Participant characteristics

Between May 2019 and August 2020, 735 patients admitted to the hospital for an acute exacerbation COPD were screened for eligibility (Figure 1). Of 477 consenting patients, 222 had a positive ProPal-COPD score and were included in the study, 98 in the intervention group and 124 in the control group. Fifty-six patients dropped out within six months after inclusion because of death (n=40) or reluctance to complete the questionnaires (n=16). At three and six months, 91 of 179 (50.8%) and 106 of 166 (63.9%) patients responded to the follow-up questionnaires. Dropout and non-response rates were similar across the two groups, and baseline characteristics of responders did not differ from non-responders. Table 3 shows the baseline characteristics of all participants and of those with at least one complete FACIT-Pal score during follow-up. On average, patients of the intervention group had a lower lung function, higher education level and, more often, one or more comorbidities; other characteristics did not differ significantly.

Table 3. Demographic- and clinical characteristics of participants in the intervention and control group and participants with at least one complete follow-up FACIT-Pal score.

	Intervention	**Control**	**Intervention - complete scores**	**Control - complete scores**
	n=98	n=124	n=56	n=61
Demographic characteristics				
Age in years, mean±SD	69.4±8.7	69.8±9.1	67.2±9.0	69.5±8.6
Sex, female	57 (58.2)	75 (60.5)	35 (62.5)	36 (59.0)
Marital status				
Married	53 (57.6)	54 (44.3)	34 (64.2)	28 (46.7)
Unmarried	7 (7.6)	21 (17.2)	5 (9.4)	11 (18.3)
Divorced	11 (12.0)	21 (17.2)	4 (7.5)	9 (15.0)
Widow	21 (22.8)	26 (21.3)	10 (18.9)	12 (20.0)
Living situation				
Living alone	36 (39.1)	47 (47.5)	17 (32.1)	26 (44.1)
Living together	56 (60.9)	63 (52.5)	36 (67.9)	33 (55.9)
Place of living				
Home, without homecare	64 (70.3)	78 (64.5)	41 (78.8)	40 (66.7)
Home, with homecare	26 (28.6)	37 (30.6)	11 (21.2)	17 (28.3)
Residential home	1 (1.1)	4 (3.3)	0 (0.0)	3 (5.0)
Nursing home	0 (0.0)	2 (1.7)	0 (0.0)	0 (0.0)
Country of birth				
Netherlands	88 (95.7)	116 (95.9)	50 (94.3)	57 (95.0)
Other	4 (4.3)	5 (4.1)	3 (5.7)	3 (5.0)
Highest level of education				
No education or elementary school	15 (16.3)	30 (25.0)	6 (11.3)	11 (18.6)
Secondary school	19 (20.7)	40 (33.3)	12 (22.6)	21 (35.6)
Vocational education	48 (52.2)	40 (33.3)	29 (54.7)	20 (33.9)
Higher/university	10 (10.9)	10 (8.3)	6 (11.3)	7 (11.9)
Clinical characteristics				
Current smoker	19 (20.2)	31 (25.6)	10 (17.9)	12 (20.0)
Pack years, mean±SD	40.7±27.6	42.8±27.4	35.8±22.2	43.4±30.8
FEV1 % of predicted, mean±SD	36.6±13.4	38.1±15.5	34.8±13.6	39.8±15.4
GOLD stage				
1	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)
2	17 (17.3)	22 (17.7)	9 (16.1)	13 (21.3)
3	31 (31.6)	45 (36.3)	18 (32.1)	24 (39.3)
4	48 (49.0)	52 (41.9)	29 (51.8)	23 (37.7)
Unknown	2 (2.0)	4 (3.2)		1 (1.6)
ProPal-COPD tool indicators				
MRC dyspnea score = 5	71 (72.4)	103 (83.1)	42 (75.0)	53 (86.9)
CCQ score >3	72 (73.5)	92 (74.2)	43 (76.8)	50 (82.0)
Comorbidity	40 (40.8)	31 (25.0)	23 (41.1)	14 (23.0)
Non-curable malignancy	5 (5.1)	6 (4.8)	3 (5.4)	2 (3.3)
Cor pulmonale	14 (14.3)	8 (6.5)	10 (17.9)	3 (4.9)
Chronic heart failure	16 (16.3)	14 (11.3)	7 (12.5)	8 (13.1)
Diabetes with neuropathy	6 (6.1)	3 (2.4)	2 (3.6)	2 (3.3)
Renal failure	5 (5.1)	5 (4.0)	2 (3.6)	2 (3.3)
Previous hospitalisation	50 (51.0)	70 (56.5)	29 (51.8)	37 (60.7)
BMI < 21 or weight loss	35 (35.7)	48 (38.7)	22 (39.3)	20 (32.8)
FEV1% of predicted < 30%	33 (33.7)	40 (32.3)	23 (41.1)	17 (27.9)
Surprise question, negative	56 (57.1)	69 (55.6)	32 (57.1)	34 (55.7)

Data presented as percentage unless stated otherwise. Abbreviations: BMI, body mass index; FEV1, Forced expiratory volume in the first second; MRC, Medical Research Council; SD, standard deviation.

Intervention delivery

In the intervention group, an outpatient palliative care conversation occurred in 36 of 98 patients within six months after inclusion (36.7%). In 8 patients, a conversation took place later than after six months. Reasons for no outpatient palliative care conversation were: transferral to a different care setting (primary care, rehabilitation centre or nursing home) (n=9), postponement

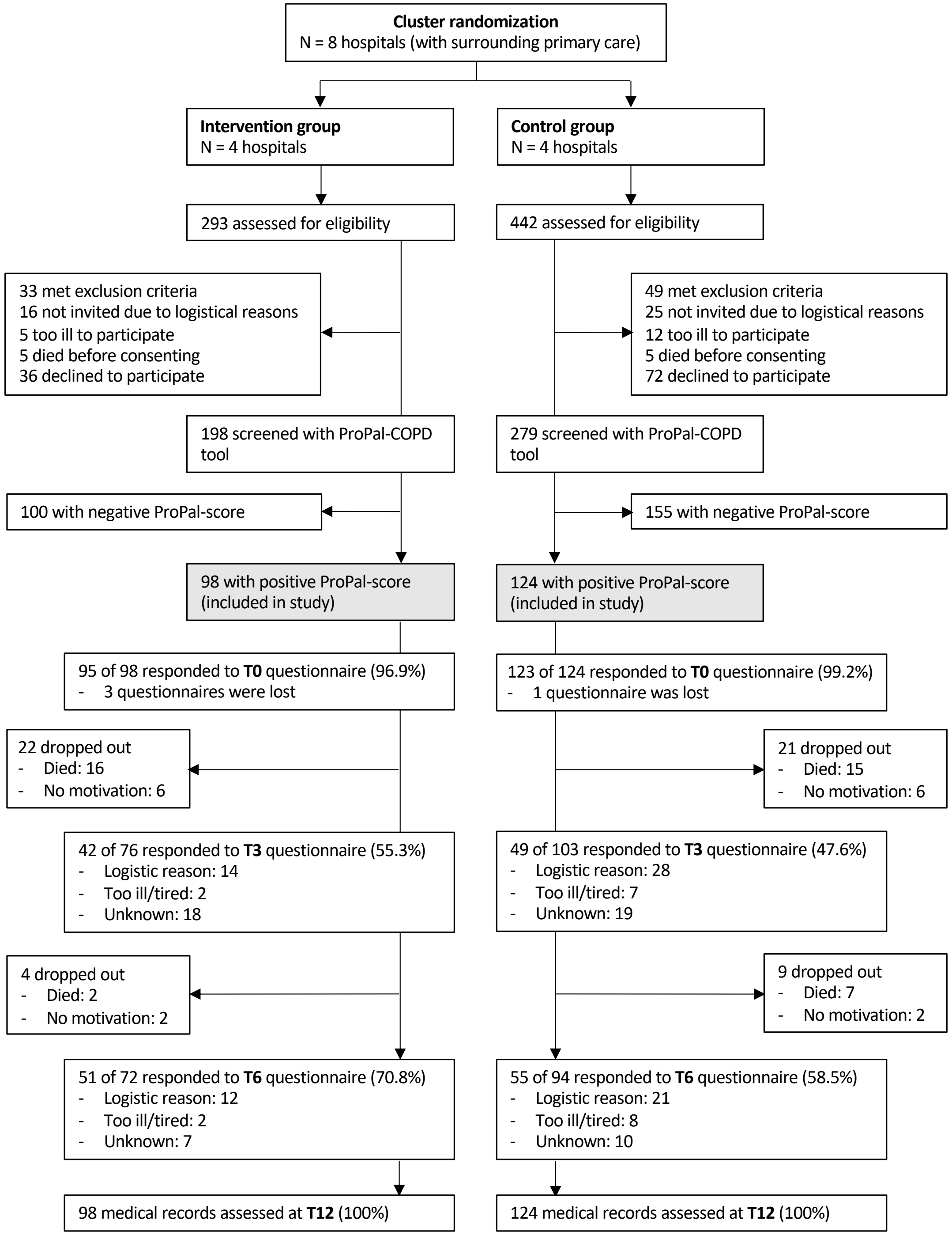


Figure 1. Flow diagram of inclusion of participants and response rates of questionnaires at baseline (T0), after three months (T3) and six months (T6).

due to the COVID-19 pandemic (n=6), death of patient before consultation took place (n=9), reluctance of patient (n=7) or psychiatric illness (n=1), initially negative ProPal-score (n=8), and unknown (n=14).

In the control group, an outpatient palliative care conversation occurred in 4 of 124 patients within six months after inclusion (3.2%). The occurrence of these conversations was in the intervention group statistically significantly higher than in the control group with an odds ratio of 17.42 (95 % CI: 5.93 to 51.17), p<0.001.

Outcomes

The FACIT-Pal score, the primary outcome, showed no difference between the intervention and control group in the intention-to-treat analysis (adjusted difference of 1.090 (95 % CI: -5.440 to 7.600), p=0.744). Also, no differences in secondary patient-reported outcome measures were found (Table 4). In the intervention group, the number of ICU admissions for COPD was lower (adjusted odds ratio of 0.212 (95 % CI: 0.032 to 0.813), p=0.047), and there was an indication of fewer hospitalisations for COPD (adjusted incidence rate ratio of 0.690 (95 % CI: 0.462 to 1.026); p=0.068). Other healthcare use outcome measures did not differ between the groups (Table 5). One year after inclusion, 54 patients (24.3%) had died; 21 in the intervention group and 33 in the control group. The Kaplan-Meier curve is shown in Figure 2. Survival did not differ between intervention and control patients (p=0.458). Place of death and acute healthcare use in the last month of life did not differ between the two groups (Table 6).

In the sensitivity analysis, limiting the intervention group to patients that received at least one outpatient palliative care conversation within six months (n=36), findings regarding the primary outcome and other secondary outcomes were similar, except for ICU admissions and documentation of life-sustaining treatment preferences (Supplementary Table 1 and 2). The effect on the number of ICU admissions disappeared (adjusted odds ratio of 0.591 (95 % CI: 0.088 to 2.352), p=0.508). Life-sustaining treatment preferences were more often documented in intervention patients than in controls (adjusted odds ratio of 4.817 (95 % CI: 1.930 to 12.026), p=0.001).

Discussion

Main findings

In this cluster randomized controlled trial, we assessed the effectiveness of palliative care components integrated into regular COPD care. We found no effects on quality of life nor other patient-reported outcome measures. However, intervention patients were less frequently admitted to the ICU than control patients, and there was a strong indication for fewer hospital admissions. Sensitivity analyses did not corroborate these findings but showed that the intervention increased documentation of life-sustaining treatment preferences.

Table 4. Response numbers and outcomes at baseline, after three and six months, and differences between intervention and control group.

	n	Intervention group Mean (SD)	n	Control group Mean (SD)	Adjusted difference* (95%-CI)	P value
Primary outcome						
FACIT-Pal total					1.090 (-5.440 to 7.600)	0.744
Baseline	94	104.0 (19.3)	120	106.6 (23.7)		
3 months	38	108.4 (25.2)	43	111.0 (22.2)		
6 months	49	113.3 (22.6)	51	111.7 (22.8)		
Secondary PROM outcomes						
FACT-G subscore					2.010 (-2.180 to 6.150)	0.379
Baseline	93	58.7 (11.9)	120	60.2 (15.9)		
3 months	39	61.9 (14.3)	44	62.7 (14.4)		
6 months	48	65.8 (14.8)	51	64.1 (15.0)		
PALS subscore					-0.815 (-3.540 to 1.910)	0.562
Baseline	95	45.3 (8.8)	123	46.4 (9.5)		
3 months	40	46.3 (11.5)	44	48.2 (8.8)		
6 months	50	47.1 (9.3)	54	47.4 (8.7)		
CCQ day score**					-0.225 (-0.572 to 0.123)	0.211
Baseline	97	3.60 (0.9)	123	3.68 (1.1)		
3 months	41	3.03 (1.1)	48	3.38 (1.0)		
6 months	50	2.94 (1.0)	55	3.29 (1.0)		
HADS anxiety**					-0.591 (-1.810 to 0.629)	0.347
Baseline	95	8.9 (4.6)	120	8.5 (5.3)		
3 months	41	7.8 (4.5)	43	7.7 (5.0)		
6 months	49	6.8 (4.7)	54	6.6 (4.5)		
HADS depression**					-0.378 (-1.660 to 0.903)	0.566
Baseline	95	8.7 (4.1)	120	8.1 (4.4)		
3 months	41	8.3 (4.3)	43	8.3 (4.4)		
6 months	49	7.2 (4.3)	54	7.2 (4.5)		
FACIT-Sp-12					0.068 (-1.72 to 1.86)	0.941
Baseline	89	22.9 (7.2)	113	26.2 (9.4)		
3 months	38	22.4 (7.8)	44	25.4 (8.3)		
6 months	44	22.7 (6.6)	51	24.7 (6.9)		
Satisfaction with hospital care					0.254 (-0.593 to 1.130)	0.592
Baseline	91	7.9 (1.5)	118	8.0 (1.6)		
6 months	46	8.1 (1.3)	48	7.9 (2.1)		
Satisfaction with GP care					-0.215 (-1.130 to 0.685)	0.711
Baseline						
6 months	87	7.2 (2.0)	118	7.3 (2.3)		
	42	6.9 (2.5)	48	7.4 (2.4)		

*Adjusted for baseline levels and clustering. **Higher score indicates worse. Abbreviations: CCQ, clinical COPD questionnaire; CI, confidence interval; FACIT-Pal, Functional Assessment of Chronic Illness Therapy Palliative care; FACT-G, Functional Assessment of Cancer Therapy General subscale; GP, general practitioner; HADS, Hospital Anxiety and Depression Scale; PALS, Palliative care subscale of the FACIT-Pal; PROM, patient-reported outcome measure.

Table 5. Numbers of acute healthcare use 1 year before and 1 year after inclusion and differences between intervention and control group.

	Intervention group n=98 Mean (SD)	Control group n=124 Mean (SD)	Adjusted Incidence Rate Ratio (95%-CI)	p Value
Number of ED visits total			1.558 (0.444 to 5.471)	0.489
Before	0.38 (0.73)	0.31 (0.78)		
After	0.27 (0.57)	0.20 (0.57)		
Number of ED visits COPD			1.577 (0.394 to 6.307)	0.520
Before	0.32 (0.67)	0.20 (0.60)		
After	0.16 (0.47)	0.10 (0.38)		
Number of hospitalisations total			0.757 (0.472 to 1.213)	0.247
Before	0.95 (1.26)	1.23 (1.60)		
After	0.96 (1.38)	1.37 (1.74)		
Number of hospitalisations COPD			0.690 (0.462 to 1.026)	0.068
Before	0.65 (1.02)	0.77 (1.11)		
After	0.65 (1.03)	0.98 (1.41)		
Number of hospital days COPD*			0.585 (0.315 to 1.02)**	0.074
Before	4.85 (8.84)	5.50 (8.75)	0.98 (0.717 to 1.29)	0.893
After	5.06 (8.48)	7.10 (10.07)		
			Adjusted Odds Ratio (95%-CI)	**p Value**
Number of ICU admission total			0.520 (0.178 to 1.425)	0.216
Before	0.10 (0.30)	0.11 (0.37)		
After	0.10 (0.44)	0.21 (0.93)		
Number of ICU admission COPD			0.212 (0.032 to 0.813)	0.047
Before	0.08 (0.28)	0.14 (0.55)		
After	0.02 (0.14)	0.09 (0.29)		
Patients with life-sustaining treatment preferences documented, n(%)	54 (55.1%)	61 (49.2%)	1.227 (0.720 to 2.092)	0.452

Abbreviations: CI, confidence interval; COPD, chronic obstructive pulmonary disease; ED, emergency department; GP, general practitioner, ICU, intensive care unit.
*For the number of hospital days COPD, the analysis was done using a Hurdle model, which gives two outcomes: the odds ratio for having any hospitalisation days and an incidence rate ratio for the ratio of hospitalisation days per time (if >0). **Adjusted odds ratio.

Table 6. Place of death and acute healthcare use in last month of life of participants in intervention and control group.

	Intervention group	Control group	Odds ratio (95%-CI)	p Value*
Patients who died	21/98 (21.4%)	33/124 (26.6%)	0.75 (0.40 – 1.41)	0.372
In-hospital death	5/21 (23.8%)	12/33 (36.4%)	0.55 (0.16 – 1.87)	0.336
Emergency department or hospital admission in last month	14/21 (66.6%)	22/33 (66.6%)	1.00 (0.31 – 3.19)	1.000

* *p*-Values based on Chi-square test.

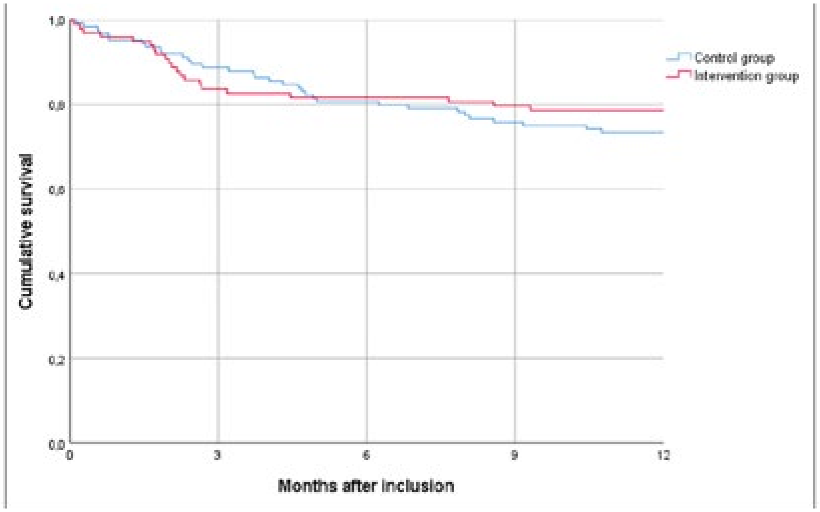


Figure 2. Kaplan-Meier plot of survival of the intervention and control group. Log Rank test: p= 0.458.

Interpretation of findings

Similar to our study, a recent systematic review found no effect of palliative care interventions on the quality of life of patients with COPD; effects on acute healthcare use were inconclusive.[9] It contrasts, however, with palliative care intervention studies in patients with cancer or chronic heart failure, in whom improved quality of life and less acute healthcare use was demonstrated.[6, 17, 18]

Our findings could be explained in several ways. First, we did not reach sufficient statistical power to detect effects on the primary outcome measure reliably. To increase recruitment, we lowered the cut-off value of the ProPal-COPD tool after six months, but then the COVID-19 pandemic again hampered recruitment rates.

Second, implementation was suboptimal. Because of several reasons, such as the COVID-19 pandemic, a significant part of the intervention group did not receive an outpatient palliative care conversation. Also, coordination and continuity of care between hospital and primary care remained challenging. The barriers and facilitators to successful implementation we encountered have been published in our process evaluation article separately.[19] Nevertheless, our rate of 37% is comparable to the average rate (33%) found across advance care planning intervention studies.[20]

Effects at the provider's level tended to be more prominent in our study, probably because our implementation strategy was at healthcare provider level: they were trained and guided to implement palliative care components. Indeed, many more outpatient palliative care conversations took place than in the control group, and treatment preferences were documented more often. Also, we found that self-efficacy in palliative care provision increased in trained healthcare providers.[19] Thus, although no effects were found at patient level, our implementation strategy effectively changed providers' behaviour.

Third, quality of life and other well-being outcomes are broad constructs influenced by many factors. The potential to improve overall quality of life may be limited in advanced organ failure, and the fluctuations in the disease course further complicate such outcome measurements.[21] It is probable that our intervention, mainly consisting of a single palliative care conversation, was insufficiently intensive to improve clinical outcomes. Also, these conversations may affect only certain aspects of quality of life. In previous palliative care trials, positive effects were found on outcomes related to 'coping with COPD': self-management,[22] mastery of breathlessness,[23] and the impact subscale of the St. George's Respiratory Questionnaire (SGRQ).[24] In interviews we held to assess the implementation process, healthcare providers indicated to highly value the intervention because of the positive effects of the palliative care conversations for their patients. According to them, patients expressed that knowing what would happen if the disease worsened and the care possibilities provided them clarity and peace of mind.[19] Feeling better equipped to cope with a severe chronic illness affects the patient's quality of life but may not be reflected in an overall quality of life measure.

Although we did not find an effect on quality of life, our study in COPD is the first controlled study that found a lower rate of ICU admissions in the palliative care group,[9] and is the second controlled trial that found a non-significant trend for fewer hospital admissions.[25] Even though these findings were not corroborated in the sensitivity analysis, trained healthcare providers of the intervention group may have become more aware of the disadvantages of invasive treatments making them more reluctant to refer patients to the ICU. The COVID-19 pandemic may have reinforced this reluctance. As intervention patients had more often comorbidities, this could also have caused a lower rate of ICU admissions found in this group. As ICU admissions contribute most to COPD-related healthcare costs,[26] palliative care may lower healthcare costs considerably, making it attractive to policymakers and healthcare insurers to encourage and reimburse palliative care.

Strengths and limitations

This study is the first large randomized controlled trial assessing the effectiveness of palliative care integrated into regular COPD care. As part of a hybrid type 2 effectiveness-implementation study,[27] the implementation was done in a real-world setting without additional human and financial resources and thus reflected naturalistic findings. Also, the multicentre design makes our findings generalizable to other hospital regions. Furthermore, we chose for cluster-level randomisation to prevent contamination between the intervention and control group.

However, our study also has limitations. Next to insufficient study power, we had a high rate of missing data due to the death of participants and high non-response to follow-up questionnaires. Missing data are expected in palliative care studies and increase with more items, quality of life questionnaires, and longer follow-up time.[28] Consistent with previous studies in this patient population,[24, 29] completing the questionnaire proved to be burdensome to some patients, and specific questions of the FACIT-Pal questionnaire were perceived as confrontational. Frequently, patients needed help from a healthcare provider to complete the questionnaire, as reflected by the high completion rate of baseline questionnaires during hospitalisation and low completion rates of follow-up questionnaires that had to be filled out at home. If sufficient resources are available, future studies could involve a research nurse administering the questionnaire at the patient's home to minimize missing data.[30] However, since both groups' attrition rates were similar and responders' characteristics did not significantly differ from those of non-responders, the risk of poor internal validity is low.

Conclusions

The effect of integrated palliative care on clinical outcomes in patients with COPD remains inconclusive. We found no evidence that palliative care improves quality of life in patients with COPD, but it can potentially reduce ICU admissions. Better implementation of palliative care components is needed to enhance reliable effect evaluation. Future research should consider using an outcome measure related to coping with COPD that is easy to complete by patients with advanced disease.

Acknowledgements

We are grateful to the patients and informal caregivers participating in the COMPASSION study. We thank all involved primary and secondary healthcare providers of the participating hospital regions Deventer Hospital, Haaglanden Medical Center, Langeland Hospital, Laurentius Hospital, Martini Hospital, Slingeland Hospital, Treant Zorggroep Hospital (Scheper) and Zaans Medical Center for their commitment and the pleasant collaboration. In particular, we want to thank Sandra Been-Buck, Anja Binnenmars, Wendy Blanck, Betty Bolink, Gerrit Bosman, Linda Brandjes, Leonie Bruil, Jasmijn van Campen, Erwina Cerimovic, Karin Eikenaar, Edith Goorhuis, Karin Groenewegen, Ellen Jacobs-Taag, Paul Janssen, Titia Klemmeier, Martijn Kross, Sarah van Oord, Steven Rutgers, Carla van de Spek, Maritha Spekschoor, and Veerle de Visser. Furthermore, we thank Jeroen de Blij of De Blij Trainen & Acteren for his support during the communication training sessions. We thank medical student Noortje van Vliet for her help in assessing medical records, and data managers Noortje Wesdorp, Nelleke van Deursen, and Brian Yothers for their help with data entry and data management.

Author contributions

J.B., R.K, H.K., Y.E. and N.H. designed the study protocol; J.B. and E.V. collected data; J.B. and E.B. performed data analyses; J.B. wrote the first draft; All authors contributed to critical revision and agreed with the final manuscript.

Declaration of conflicting interests

The authors declare no potential conflicts of interest concerning the research, authorship, and/or publication of this article.

Funding

This research project has been financially supported by The Netherlands Organization for Health Research and Development (ZonMw) (project no. 844001401). The funding source did not play any role in planning and implementing this study, interpreting its results, or writing the paper.

Data availability

Datasets of the COMPASSION study are available upon request via the online repository of DANS/EASY: https://doi.org/10.17026/dans-z83-58w8.

References

1. Lozano R, Naghavi M, Foreman K, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012; 380: 2095-2128. 2012/12/19. DOI: 10.1016/s0140-6736(12)61728-0.
2. Müllerova H, Maselli DJ, Locantore N, et al. Hospitalized exacerbations of COPD: risk factors and outcomes in the ECLIPSE cohort. Chest 2015; 147: 999-1007. DOI: 10.1378/chest.14-0655.
3. 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. 2011/04/23. DOI: 10.1089/jpm.2010.0479.
4. Bolton LE, Seymour J and Gardiner C. Existential suffering in the day to day lives of those living with palliative care needs arising from chronic obstructive pulmonary disease (COPD): A systematic integrative literature review. Palliat Med 2022: 2692163221074539. 20220217. DOI: 10.1177/02692163221074539.
5. Luckett T, San Martin A, Currow DC, et al. A systematic review and meta-analysis of studies comparing burden from lung cancer and chronic obstructive pulmonary disease. Palliat Med 2020; 34: 1291-1304. 20200728. DOI: 10.1177/0269216320940153.
6. 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. 2016/11/29. DOI: 10.1001/jama.2016.16840.
7. Sepúlveda C, Marlin A, Yoshida T, et al. Palliative Care: the World Health Organization's global perspective. J Pain Symptom Manage 2002; 24: 91-96. DOI: 10.1016/s0885-3924(02)00440-2.
8. Barnes-Harris M, Allingham S, Morgan D, et al. Comparing functional decline and distress from symptoms in people with thoracic life-limiting illnesses: lung cancers and non-malignant end-stage respiratory diseases. Thorax 2021; 76: 989-995. 20210216. DOI: 10.1136/thoraxjnl-2020-216039.
9. Broese JM, de Heij AH, Janssen DJ, et al. Effectiveness and implementation of palliative care interventions for patients with chronic obstructive pulmonary disease: A systematic review. Palliat Med 2021; 35: 486-502. 20201218. DOI: 10.1177/0269216320981294.
10. Boddaert M. Netherlands Quality Framework for Palliative Care. 2017.
11. 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. 2008/04/09. DOI: 10.1164/rccm.200605-587ST.
12. van der Eerden M, Csikos A, Busa C, et al. Experiences of patients, family and professional caregivers with Integrated Palliative Care in Europe: protocol for an international, multicenter, prospective, mixed method study. BMC Palliat Care 2014; 13: 52. 2014/12/05. DOI: 10.1186/1472-684x-13-52.
13. Broese JMC, van der Kleij R, Kerstjens HAM, et al. A cluster randomized controlled trial on a multifaceted implementation strategy to promote integrated palliative care in COPD: study protocol of the COMPASSION study. BMC Palliat Care 2020; 19: 155. 2020/10/12. DOI: 10.1186/s12904-020-00657-3.
14. Spathis A, Booth S, Moffat C, et al. The Breathing, Thinking, Functioning clinical model: a proposal to facilitate evidence-based breathlessness management in chronic respiratory disease. NPJ Prim Care Respir Med 2017; 27: 27. 2017/04/23. DOI: 10.1038/s41533-017-0024-z.
15. Duenk RG, Verhagen C, Bronkhorst EM, et al. Development of the ProPal-COPD tool to identify patients with COPD for proactive palliative care. Int J Chron Obstruct Pulmon Dis 2017; 12: 2121-2128. DOI: 10.2147/COPD.S140037 [doi];copd-12-2121 [pii].
16. Lyons KD, Bakitas M, Hegel MT, et al. Reliability and validity of the Functional Assessment of Chronic Illness Therapy-Palliative care (FACIT-Pal) scale. J Pain Symptom Manage 2009; 37: 23-32. 2008/05/28. DOI: 10.1016/j.jpainsymman.2007.12.015.
17. Diop MS, Rudolph JL, Zimmerman KM, et al. Palliative Care Interventions for Patients with Heart Failure: A Systematic Review and Meta-Analysis. J Palliat Med 2017; 20: 84-92. 2016/12/03. DOI: 10.1089/jpm.2016.0330.
18. Maqsood MH, Khan MS and Warraich HJ. Association of Palliative Care Intervention With Health Care Use, Symptom Burden and Advance Care Planning in Adults With Heart Failure and Other Noncancer Chronic Illness. J Pain Symptom Manage 2021; 62: 828-835. 20210222. DOI: 10.1016/j.jpainsymman.2021.02.017.
19. Broese JMC, van der Kleij R, Verschuur EML, et al. Implementation of a palliative care intervention for patients with COPD - a mixed methods process evaluation of the COMPASSION study. BMC Palliat Care 2022; 21: 219. 20221207. DOI: 10.1186/s12904-022-01110-3.
20. Houben CHM, Spruit MA, Groenen MTJ, et al. Efficacy of advance care planning: a systematic review and meta-analysis. J Am Med Dir Assoc 2014; 15: 477-489. 2014/03/07. DOI: 10.1016/j.jamda.2014.01.008.
21. Sanghera S and Coast J. Measuring Quality-Adjusted Life-Years When Health Fluctuates. Value in Health 2020; 23: 343-350. DOI: https://doi.org/10.1016/j.jval.2019.09.2753.
22. 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. DOI: 10.1089/jpm.2006.9.111 [doi].
23. 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. DOI: S2213-2600(14)70226-7 [pii];10.1016/S2213-2600(14)70226-7 [doi].
24. 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. DOI: 10.2147/COPD.S141974 [doi];copd-12-2795 [pii].

25. 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. DOI: 10.1159/000495312.
26. Mulpuru S, McKay J, Ronksley PE, et al. Factors contributing to high-cost hospital care for patients with COPD.
27. Curran GM, Bauer M, Mittman B, et al. Effectiveness-implementation hybrid designs: combining elements of clinical effectiveness and implementation research to enhance public health impact. Med Care 2012; 50: 217-226. 2012/02/09. DOI: 10.1097/MLR.0b013e3182408812.
28. Hussain JA, White IR, Langan D, et al. Missing data in randomized controlled trials testing palliative interventions pose a significant risk of bias and loss of power: a systematic review and meta-analyses. Journal of clinical epidemiology 2016; 74: 57-65. 2016/01/01. DOI: 10.1016/j.jclinepi.2015.12.003.
29. 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. DOI: 10.1089/jpm.2012.0285 [doi].
30. Houben CHM, Spruit MA, Luyten H, et al. Cluster-randomised trial of a nurse-led advance care planning session in patients with COPD and their loved ones. Thorax 2019; 74: 328-336. 20190119. DOI: 10.1136/thoraxjnl-2018-211943.

Supplementary material

Table S1. Outcomes of the sensitivity analyses limiting intervention patients to those who received the intervention within 6 months (n=36).

	n	Intervention patients who received intervention Mean (SD)	Adjusted difference (95%-CI)	p Value
Primary outcome				
FACIT-Pal total			-0.782 (-9.380 – 7.830)	0.860
Baseline	35	106.7 (17.4)		
3 months	16	105.2 (32.0)		
6 months	20	119.0 (19.8)		
Secondary PROM outcomes				
FACT-G subscore			1.590 (-3.930 – 6.980)	0.568
Baseline	35	60.8 (10.3)		
3 months	16	61.2 (18.1)		
6 months	20	70.7 (12.3)		
PALS subscore			-1.860 (-5.410 – 1.690)	0.311
Baseline	35	45.9 (8.4)		
3 months	16	44.0 (14.5)		
6 months	20	48.4 (8.0)		
CCQ day score			-0.115 (-0.569 – 0.338)	0.622
Baseline	36	3.6 (0.9)		
3 months	16	3.2 (1.2)		
6 months	20	2.8 (1.0)		
HADS anxiety			-0.843 (-2.450 – 0.763)	0.309
Baseline	35	7.9 (4.4)		
3 months	16	8.0 (4.2)		
6 months	20	4.9 (4.1)		
HADS depression			-0.337 (-2.050 – 1.380)	0.703
Baseline	35	7.7 (3.8)		
3 months	16	8.8 (4.4)		
6 months	20	6.1 (4.2)		
FACIT-Sp-12			-1.100 (-3.550 – 1.340)	0.384
Baseline	31	22.4 (6.2)		
3 months	15	21.2 (8.6)		
6 months	17	23.4 (5.4)		
Satisfaction with hospital care			0.360 (-0.884 – 1.610)	0.595
baseline	34	8.0 (1.3)		
6 months	18	8.2 (1.2)		
Satisfaction with GP care			0.135 (-1.040 – 1.340)	0.847
Baseline	31	7.6 (1.3)		
6 months	16	7.6 (2.2)		
Acute healthcare use			**Adjusted Incidence Rate Ratio (95%-CI)**	**P value**
Number of ED visits total			0.767 (0.166 – 3.552)	0.735
Before	36	0.36 (0.83)		
After	36	0.31 (0.71)		
Number of ED visits COPD			1.104 (0.259 – 4.712)	0.893
Before	36	0.14 (0.35)		
After	36	0.11 (0.32)		
Number of hospitalizations total			0.755 (0.472 – 1.208)	0.241
Before	36	1.19 (1.37)		
After	36	1.03 (1.34)		
Number of hospitalizations COPD			0.780 (0.455 – 1.320)	0.361
Before	36	0.83 (1.11)		
After	36	0.81 (1.14)		
Number of hospital days COPD*			0.780 (0.356 – 1.570)** 0.994 (0.664 – 1.430)	0.512 0.975
Before	36	5.58 (8.13)		
After	36	6.50 (9.69)		
			Adjusted Odds Ratio (95%-CI)	**P value**
Number of ICU admission total			0.580 (0.112 – 2.306)	0.469
Before	36	0.06 (0.23)		
After	36	0.08 (0.28)		
Number of ICU admission COPD			0.591 (0.088 – 2.352)	0.508
Before	36	0.03 (0.17)		
After	36	0.06 (0.23)		
Patients with life-sustaining treatment preferences documented, n(%)	36	28 (77.8%)	4.817 (1.930 – 12.026)	0.001

Abbreviations: CCQ, clinical COPD questionnaire; CI, confidence interval; COPD, chronic obstructive pulmonary disease; ED, emergency department; FACIT-Pal, Functional Assessment of Chronic Illness Therapy Palliative care; FACT-G, Functional Assessment of Cancer Therapy General subscale; GP, general practitioner; HADS, Hospital Anxiety and Depression Scale; ICU, intensive care unit; PALS, Palliative care subscale of the FACIT-Pal; PROM, patient reported outcome measure.

*For the number of hospital days COPD, the analysis was done using a Hurdle model, which gives two outcomes: the odds ratio for having any hospitalization days and an incidence rate ratio for the ratio of hospitalization days per time (if >0). **Adjusted odds ratio.

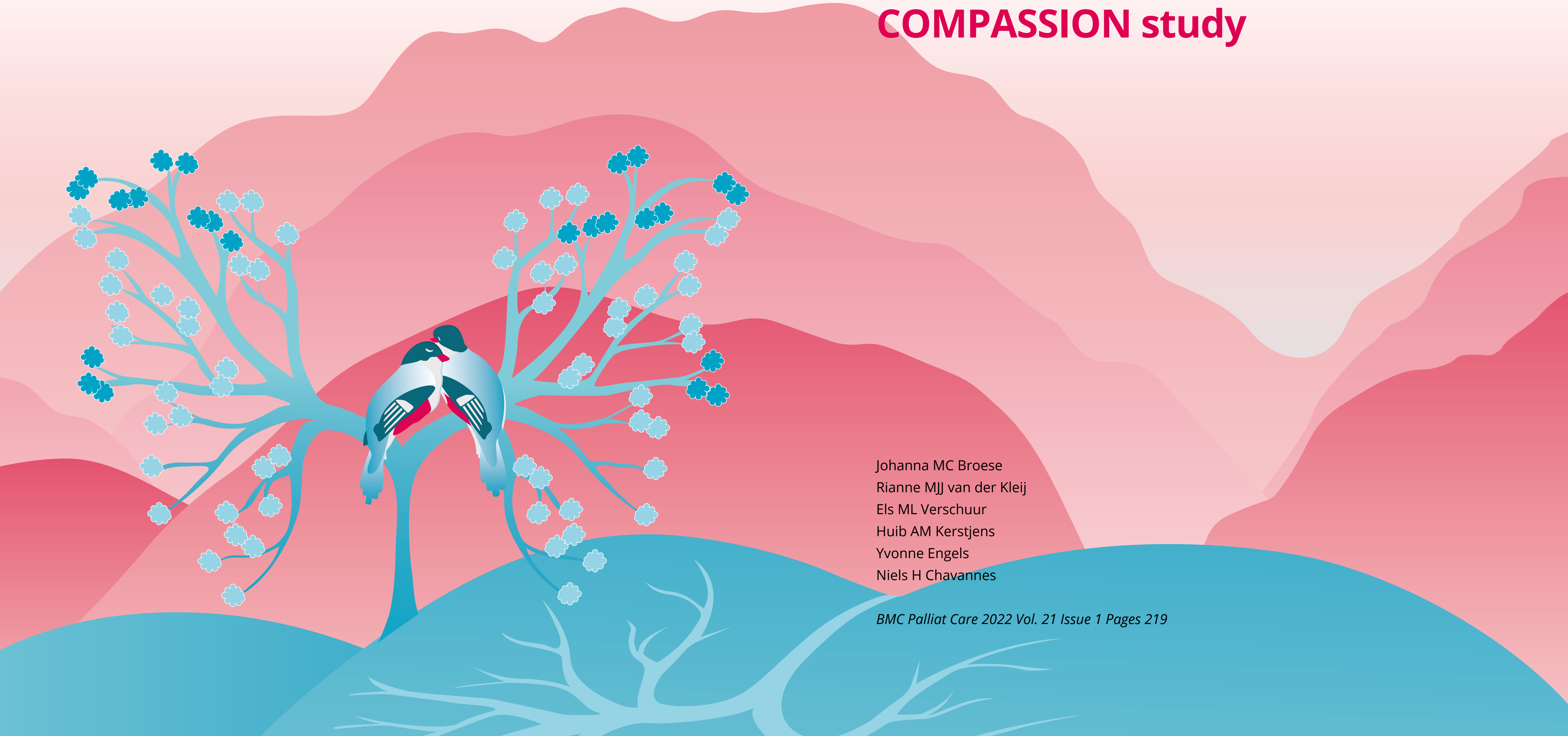
Table S2. Sensitivity analyses of place of death and acute healthcare use in last month.

	Intervention patients who received intervention	Control group	Odds ratio (95%-CI)	p Value*
Patients who died	4/36 (11.1%)	33/124 (26.6%)	0.345 (0.113 – 1.049)	0.052
In-hospital death	1/4 (25%)	12/33 (36.4%)	0.583 (0.054 – 6.251)	0.653
Emergency department or hospital admission in last month	2/4 (50%)	22/33 (66.6%)	0.500 (0.062 – 4.040)	0.510

* *p*-Values based on Chi square test.

Chapter 6

Implementation of a palliative care intervention for patients with COPD – a mixed methods process evaluation of the COMPASSION study



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BMC Palliat Care 2022 Vol. 21 Issue 1 Pages 219

Abstract

Objectives

Little direction exists on how to effectively implement palliative care for patients with COPD. In the COMPASSION study, we developed, executed, and evaluated a multifaceted implementation strategy to improve the uptake of region-tailored palliative care intervention components into routine COPD care. We evaluated the implementation strategy and assessed the implementation process, barriers, and facilitators.

Methods

A mixed methods process evaluation was performed. Primary and secondary healthcare providers in four hospital regions in the Netherlands were trained. Patients identified during hospitalisation for an acute exacerbation received palliative care and were followed for a year. Various sources were used: process data, questionnaires including the End-of-life Professional Caregiver Survey (EPCS), medical records, monitoring meetings, and interviews. The Consolidated Framework of Implementation Research (CFIR) was used to categorize implementation determinants.

Results

The training sessions with roleplay were positively evaluated and increased professionals' self-efficacy in providing palliative care statistically significantly. Of 98 patients identified, 44 (44.9%) received one or more palliative care conversations at the outpatient clinic. Having those conversations was highly valued by healthcare providers because it led to clarity and peace of mind for the patient and higher job satisfaction. Coordination and continuity remained suboptimal. Most important barriers to implementation were time constraints, the COVID-19 pandemic, and barriers related to transmural and interdisciplinary collaboration. Facilitators were the systematic screening of patients for palliative care needs, adapting to the patient's readiness, conducting palliative care conversations with a pulmonologist and/or a COPD nurse, and meeting regularly with a small team led by a dedicated implementation leader.

Conclusions

Providing integrated palliative care for patients with COPD is highly valued by healthcare providers but remains challenging. Our findings will guide future implementation efforts. Future research should focus on how to optimize transmural and interdisciplinary collaboration.

Keywords

Chronic obstructive pulmonary disease; palliative care; implementation; evaluation studies.

Introduction

Patients with advanced Chronic Obstructive Pulmonary Disease (COPD) suffer from a high symptom burden and low quality of life, emphasizing the need for palliative care.[1] Palliative care is an approach that aims to optimize the quality of life of patients with a life-limiting illness through assessment and treatment of physical, psychological, social and spiritual problems.[2] It includes advance care planning, allowing care to be tailored to the patient's goals and preferences.[3] Despite guideline recommendations,[4, 5] palliative care is only provided to a limited number of patients with COPD, and often, advance care planning is discussed in an acute care setting (e.g., when a patient visits the emergency department for an acute exacerbation) rather than proactively (e.g., during an outpatient visit to their regular doctor).[6, 7] Also, the involvement of specialist palliative care is limited and restricted to the terminal phase.[8] As a result, many symptoms, such as dyspnoea, fatigue, and depression, remain undertreated,[9] and care preferences are not timely discussed.[7]

Although the need for palliative care has been widely acknowledged, little direction exists on successfully implementing it into routine COPD care.[10] The key barriers to timely initiating palliative care in COPD are the prognostic uncertainty due to the unpredictable illness trajectory and the lack of training of healthcare providers (HCPs) to discuss end-of-life topics.[11, 12] These barriers may be addressed by using transition points, such as hospitalisation, to screen for palliative care needs[13] and communication training to increase HCPs' self-efficacy in discussing palliative care topics.[14] However, the empirical evidence on effective implementation strategies is still limited.[10]

Therefore, as part of the COMPASSION study, a multifaceted implementation strategy was developed, executed and evaluated.[15] HCPs across four hospital regions were trained to implement palliative care components into routine COPD care. Also, they were provided with access to an online toolbox, including a screening tool to identify palliative patients during hospitalisation, and implementation guidance. The aim of this study was 1) to evaluate the implementation strategy and its effect on reach and dose delivered of palliative care components and 2) to identify barriers and facilitators to successful implementation of integrated palliative care in COPD.

Methods

Design and setting

A comprehensive, mixed-method process evaluation was performed in four intervention hospital regions of the COMPASSION study. Each region was asked to form an intervention team consisting of primary and secondary care providers working in respiratory and palliative care (Table 1). We followed the Standards for Reporting Implementation Studies (StaRi) for reporting.[16]

Table 1. Setting characteristics at baseline, indicators in the year before implementation and characteristics of the intervention team of each hospital region.

	Region A	Region B	Region C	Region D
Characteristics of region				
Geographical setting	Large teaching hospital and surroundings	Regional hospital and surroundings	Regional hospital and surroundings	Regional hospital and surroundings
Pulmonologists / COPD nurses in hospital, n	6 / 4	5 / 2	5 / 4	5 / 3
COPD nurse in primary care present	No	Yes	No	Yes
Protocol for PC in COPD present	No	No	No	No
Indicators in the year before implementation (2018)				
COPD patients hospitalised for acute exacerbation, n	367	149	143	220
Hospitalised patients with ≥1 specialised PC team consultation, n/n (%)	18/367 (4.9%)	4/149 (2.7%)	0/143 (0.0%)	24/220 (10.9%)
Characteristics of formed intervention team				
Total team members, n	11	10	9	16
Team composition, n				
Pulmonologists	2	3	2	4
COPD nurses in hospital	2	4	4	2
PC nurses in hospital	2	1	0	2
GPs	3	1	1	4
COPD nurses in primary care	0	1	0	2
PC nurses in primary care	0	0	0	2
Other	2	0	2	0
Implementation leader(s)	pulmonologist + COPD nurse	pulmonologist + 2 COPD nurses + PC nurse	COPD nurse + pulmonologist	COPD nurse + pulmonologist

Abbreviations: COPD, chronic obstructive pulmonary disease; GP, general practitioner; PC, palliative care.

Intervention and implementation strategy

The intervention and multifaceted implementation strategy were developed in collaboration with many stakeholders and have previously been described in detail in the COMPASSION study protocol.[15] The intervention was based on national guidelines[2, 5] and consisted of the following core components (Figure 1A): 1) identification of palliative patients with COPD during hospitalisation, 2) one or more palliative care conversations consisting of advance care planning, multidimensional assessment, and symptom management, 3) coordination and continuity of care, and 4) if a patient died, aftercare comprising bereavement care and care evaluation with involved HCPs. According to the national guideline, palliative care was performed primarily by respiratory HCPs, whereas specialist palliative care team consultants could be involved in case of complex needs.[2] Regions were allowed to tailor the intervention to regional and individual patients' needs and preferences. The ProPal-COPD tool was used to facilitate providers to identify palliative patients admitted to the hospital for an exacerbation of COPD.[17] It consists of the surprise question ("Would you be surprised if your patient were to die in the next 12 months?") and six COPD-specific clinical indicators, which together produce a total score. Initially, the cut-off value as previously published was used.[17] After six months, in monitoring meetings it became clear that the rate of positive scores was lower than expected by HCPs and researchers. Therefore, the research group deemed it necessary to lower the cut-off value.

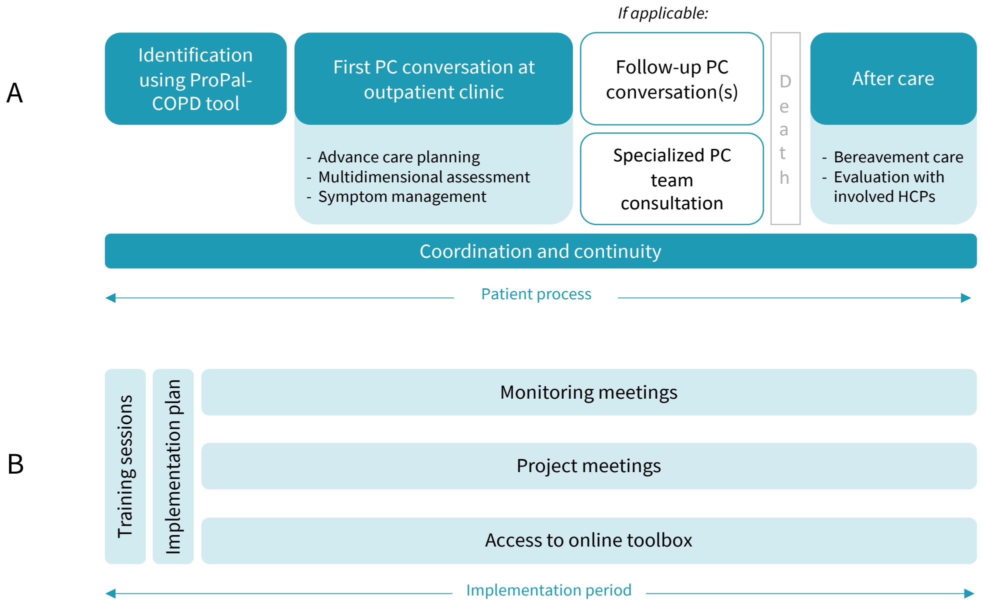


Figure 1. Components of the palliative care intervention (A) and implementation strategy (B). PC, palliative care.

To facilitate uptake of the intervention components, a multifaceted implementation strategy was developed (Figure 1B). Between April and September 2019, HCPs from the intervention team received two 3-hour training sessions on 1) content of palliative care in COPD, including communication training with roleplay and non-pharmacological dyspnoea management, and 2) implementation of palliative care. At the end of the second training session, HCPs were asked to complete a regional action plan detailing how, when and by whom different intervention components had to be performed. They received access to an online toolbox (www.palliatievezorgcopd.nl), comprising information on the content and practice of the intervention components, the ProPal-COPD tool, and other tools for facultative use. Furthermore, implementation leaders were guided for two years through four monitoring meetings per region and two project meetings, where regions exchanged experiences and best practices.

Data collection

The multifaceted implementation strategy was evaluated using process data (attendance rate of the training and use of regional action plans) and evaluation questionnaires administered at the end of each training session (appreciation of the training) and three and fifteen months later (use and appreciation of the toolbox). Also, HCPs' level of self-efficacy in providing palliative care was assessed using the End-of-life Professional Caregiver Survey (EPCS) before and 3 and 15 months after the training.[18] This scale is a validated questionnaire comprising 28 items on three domains: patient- and family-centred communication, cultural and ethical values, and effective care delivery. The total score ranges from 0 to 112, with higher scores reflecting better knowledge and comfort in providing end-of-life communication.

To determine reach and dose delivered, we assessed the medical records of patients participating in the COMPASSION study one year after inclusion. Reach was defined as the number of patients participating in the intervention. Dose was defined as the extent to which each component was delivered.[19] Information on the number, timing, and content of palliative care conversations, treatments started, referrals made, and life-sustaining treatment preferences documented were extracted. For each included patient, HCPs were asked to indicate the duration of palliative care conversations, who was present, and the reason if no conversation had taken place.

Barriers and facilitators to implementation were identified using transcripts of monitoring meetings with implementation leaders (held by EV and JB) and semi-structured interviews with implementation leaders and trained HCPs less actively involved in implementation (held by JB). Between fifteen to twenty months after the training, per region, six HCPs (n=24), were interviewed about care practices and work agreements, experiences with the implementation process, barriers and facilitators encountered, and experiences with the intervention. Interview duration varied between 20 and 85 minutes (mean 49 minutes). Monitoring meetings and interviews were audio-recorded and transcribed verbatim. All participants gave written informed consent, except for one GP due to time constraints, and this transcript was therefore excluded from analysis.

Data analyses

Quantitative data were analysed using descriptive statistics with IMB SPSS (Statistical Package for Social Science) version 25. EPCS total scores were calculated, and pre-post scores of HCPs with complete EPCS data were compared using Wilcoxon signed rank tests. Qualitative data were analysed using thematic analysis with a phenomenological approach.[20] Transcripts were first inductively coded via open and axial coding (JB). Initial codes and summaries were discussed with the research group multiple times, and codes were merged, split, and renamed until consensus was reached. Subsequently, the Consolidated Framework of Implementation Research (CFIR) was used to further categorize possible barriers and facilitators to implementation.[21] The CFIR contains 39 constructs across five domains: intervention characteristics, outer setting, inner setting, characteristics of the individuals involved, and the process of implementation. Each code was mapped to one of the constructs by JB and checked by RK, who has extensive expertise in implementation research. Differences between and within regions were compared. Finally, the interpretation of findings was discussed with the research group.

Results

Evaluation of implementation strategy

The first and second training session attendance rates were 38/46 (82.6%) and 36/46 (78.3%), respectively. HCPs evaluated the first training session high with a mean score of 8.4 out of 10 and the second training session with 7.9. The highest rated training elements were interactive communication training and dyspnoea management. After three months, 18/29 responding providers (62.1%) reported to have visited the online toolbox at least once, and 20/28 responding providers (71.4%) after fifteen months. The online toolbox was evaluated with a score of 7.1 for design and 7.8 for content. A draft of a regional action plan was completed by two regions, but not actively used in practice.

A statistically significant increase in EPCS total scores was observed three and fifteen months after the training (Table 2).

Table 2. Comparison of healthcare provider's End-of-life Professional Caregiver Survey (EPCS) scores at baseline and 3 and 15 months after the training.

	Number of complete cases	**Median score**	**Z***	***p*-Value**
Before training (baseline)	37	81.0		
After 3 months	26	89.5	4.03	<.001
After 15 months	23	92.0	3.44	.001

*Wilcoxon signed rank test.

Reach and dose of intervention components

Component 1. Identification

All 198 hospitalised patients eligible and consenting to participate in the COMPASSION study (100%) were screened with the ProPal-COPD tool (Table 3). Of these, 98 had a positive ProPal-score. HCPs also screened outpatients on their initiative, but as these patients did not participate in the COMPASSION study, they were not included in the numbers.

Component 2. Palliative care conversations

A palliative care conversation at the outpatient clinic within 1-year follow-up occurred in 44/98 patients with a positive ProPal-score (44.9%). The timing, duration, and content of the conversations are presented in Table 4. In some cases, a conversation was waived due to organisational factors: transferral to a different care setting (primary care, rehabilitation centre, or nursing home) (n=9) or postponement of outpatient visits due to the COVID-19 pandemic (n=6). In other cases, the patient had died (n=9), was reluctant (n=7), or was psychiatrically ill (n=1). Twenty-two of 98 patients (22.4%) received a specialist palliative care team consultation and were subsequently discussed in the multidisciplinary team meeting; the percentage varied between regions from 0 to 45% (Table 3).

Table 3. Reach and dose of palliative care intervention components per region.

Component		**Region A**	**Region B**	**Region C**	**Region D**	**Total**
1. Identification	Number of hospitalised patients screened using ProPal-COPD tool	48	73	45	32	198
	Number of patients with positive ProPal-score	29	31	17	21	98
2. Palliative care conversations	Patients who received ≥1 outpatient palliative care conversation	15/29	11/31	10/17	8/21	44/98
	Patients who received ≥1 specialist palliative care team consultation	3/29	14/31	0/17	5/21	22/98
3. Coordination and continuity	Number of letters to GP following an outpatient palliative care conversation	13/15	7/11	0/10	2/8	22/44
	Individual care plan	0/15	0/11	0/10	0/8	0/44
4. Aftercare	Conversation with bereaved family of deceased patients	0/7	0/9	0/1	0/4	0/21
	Evaluation by involved healthcare providers	0/7	0/9	0/1	1/4	1/21

Table 4. Timing, duration and content of 61 outpatient palliative care conversations in 44 patients.

	Findings
Palliative care conversations	
Timing of first palliative care conversation	Median 42 days (IQR 24.25 – 96.25) after inclusion 33/44 (75.0%) within 3 months 36/44 (81.8%) within 6 months
Average duration	Region A: 60 minutes Region B: 60 minutes Region C: 30 minutes Region D: 15 to 30 minutes
Number of conversations per patient	
1	32 (72.7%)
2	7 (15.9%)
3	5 (11.4%)
Healthcare providers present	Pulmonologist + COPD nurse: 32x (52.5%) Pulmonologist: 6x (9.8%) COPD nurse: 23x (37.7%)
Advance care planning	
Topics discussed	
Illness trajectory	19 (43.2%)
Incurability of the disease	7 (15.9%)
Life expectation	11 (25.0%)
Care goals	9 (20.5%)
Advantages and disadvantages of life-sustaining treatment	23 (52.3%)
Preferences for hospitalisation in case of a next exacerbation	16 (36.4%)
Preferred place of death	8 (18.2%)
Palliative sedation and/or euthanasia	10 (22.7%)
Documentation of life-sustaining treatment preferences	34 (77.3%)
Multidimensional assessment	
Domains addressed	
Physical	43 (97.7%)
Psychological	30 (68.2%)
Social	33 (75.0%)
Spiritual	27 (61.4%)
Symptom management	
Breathlessness treated with opioids	19 (43.2%)
Non-pharmacological breathlessness interventions	26 (59.1%)
Advice and breathing techniques	15
Oxygen therapy	11
Handheld fan	7
COPD action plan	2
Treatment for anxiety and depression	11 (25.0%)
Pharmacological treatment	7
Referral to psychologist	5
Breathing techniques	2
Involving palliative care nurse	1
Patients referred	32 (72.3%)
Physiotherapist	21
Tertiary pulmonary rehabilitation	12
Primary care COPD nurse	11
Psychologist	5
Dietician	5
Occupational therapist	2
Primary care palliative care nurse	2
Spiritual counsellor	1

Component 3. Coordination and continuity

In half (22/44) of patients receiving an outpatient palliative care conversation, a letter was sent to the GP to report the conversation, in which nine agreements about future care coordination were included. None of the regions noted creating an individual care plan.

Component 4. Aftercare

Of all 98 patients, 21 patients died within one year of follow-up. An aftercare conversation was occasionally offered to bereaved families but never occurred in practice, and an evaluation of HCPs involved took place once.

Barriers and facilitators to successful implementation

Characteristics of interview participants are described in Table 5. For each domain of the CFIR, the facilitators and barriers identified are summarised in Table 6. In the outer setting domain, no determinants were identified.

Intervention characteristics

Relative advantage - All HCPs highly appreciated the palliative care intervention because its implementation resulted in more clarity and peace of mind for patients, improved the relationship with patients, and provided HCPs with a sense of contributing in a meaningful way.

Table 5. Characteristics of interview participants (n=24).

Characteristic	Value
Mean age in years ±SD (range)	49.8±9.6 (33–62)
Age category, n(%)	
30-39	4 (16.7)
40-49	7 (29.2)
50-59	9 (37.5)
60-69	4 (16.7)
Female sex, n(%)	18 (75.0)
Profession, n(%)	
Pulmonologist	7 (29.2)
COPD nurse	9 (37.5)
General practitioner	4 (16.7)
Palliative care nurse	4 (16.7)
Years in profession, mean±SD (range)	10.9±9.3 (1–32)
Years in profession, n(%)	
<5	7 (29.2)
5-10	8 (33.3)
≥10	9 (37.5)

Table 6. Facilitators (F) and barriers (B) that affected the process of implementing palliative care into regular COPD care.

Domain	Constructs	F/B	Main findings
Intervention characteristics	Relative advantage	F	The intervention was highly valued because it provided clarity, peace of mind, and less anxiety to the patient, improved the relationship with the patient, and increased job satisfaction.
		F	Systematic screening of patients helped HCPs to become aware of palliative care needs.
	Perceived difficulties of the intervention	B	Patients responded differently to the intervention. It was relieving for some and it was confronting for others. It was considered essential to adapt to the patient's level of readiness.
		B	All HCPs felt that transmural collaboration was still inadequate. Raised issues were: challenge to have phone contact due to busy schedules, lack of an appropriate communication tool, doubt about what and how to communicate, and lack of COPD nurses in primary care.
Inner setting	Tension for change	F	Almost all HCPs believed that (better structured) palliative care for patients with COPD was highly necessary.
		B	Two HCPs found that they already did many things well and that change was not needed.
	Available resources	B	Due to busy schedules, it was challenging to schedule palliative care conversations.
	Networks and communications	B	The division of roles between HCPs of the pulmonary department and the specialist palliative care team was unclear.
	Relative priority	B	The COVID-19 pandemic caused changed priorities, resulting in the postponement of palliative care conversations.
Characteristics of individuals	Knowledge and beliefs about the intervention	F	The observed positive effects on patients motivated to continue with the intervention.
		F	Sharing experiences in implementing and organizing integrated palliative care between regions was considered useful and inspiring to continue the intervention.
	Self-efficacy	F	Communication training and being provided with example phrases were perceived as helpful.
		F	Conducting palliative care conversations (in part) together with a COPD nurse helped the pulmonologist to discuss non-medical topics and it saved time.
Implementation process	Planning	B	HCPs found it challenging to formulate clear implementation goals and to plan actions.
	Reflecting & Evaluating	F	Regular meetings with a small team helped to make implementation agreements.
	Engaging	B	Implementation was primarily focused on planning palliative care conversations in the outpatient clinical setting. Team members from primary care and palliative care were not actively involved in the implementation process because their potential role was unclear.
	Implementation leaders	F	A dedicated implementation leader feeling responsible for the implementation was essential.
		B	Without someone explicitly made responsible, implementation was hampered.

Abbreviations: HCP, healthcare provider.

Pulmonologists and COPD nurses across all regions indicated that systematic screening of patients had enhanced their awareness of palliative care needs.

> *"[...] in the past, I often thought, oh, it'll be fine, he'll still have years. And now I'm more alert to it, so I think that's a really important factor, which makes me think more quickly that we need to have a conversation." - Pulmonologist 2*

Perceived difficulties of the intervention - HCPs across all regions experienced that most patients were open to discussing palliative care topics. However, reactions differed, and adapting to the patient's level of readiness was found essential.

> *"Um, at the beginning of the project, I did it quite abruptly [...]. I also noticed that people were a bit frightened, [...] that I thought, oh yes, this has to be done more gradually." - COPD nurse 7*

Across all regions, the collaboration between the hospital and primary care was perceived inadequate due to time constraints and lack of an appropriate communication tool. Also, some pulmonologists had doubts about what to communicate to GPs, as the level of palliative care expertise varied greatly between GPs. COPD nurses in primary care were found to be important for adequate transmural communication, but they were not always available due to staff shortages and budget cuts.

Inner setting

Tension for change - Almost all HCPs felt that improvement in palliative care was highly needed and they were willing to improve care.

Available resources - Busy schedules made planning palliative care conversations challenging, particularly when both a pulmonologist and COPD nurse were involved. In one region, this was solved by reserving a weekly set time in the pulmonologist's agenda. Whether conversations were scheduled depended greatly on clear working arrangements and staff continuity.

Relative priority - When the COVID-19 pandemic broke out in March 2019, HCPs experienced that priorities changed. Multidisciplinary meetings were cancelled, and palliative care conversations were postponed to keep patients out of the hospital.

Networks and communications - In each region, a COPD nurse became part of the specialist palliative care team to exchange knowledge. However, the extent of and satisfaction with collaboration between pulmonary and palliative care providers varied between regions. In one region, friction arose because palliative care providers had expected to become involved more often, but pulmonary care providers found them too direct in their approach to patients with COPD.

Characteristics of the individuals

Knowledge and beliefs about the intervention - Experiencing the positive effects on the patient motivated HCPs across all regions to continue implementing the intervention.

> *"Because you do the questionnaire [ProPal-score] with the patient, is it positive or not? And you also schedule appointments with the patient in a really clear way, it gives it all structure and clarity and by doing it you gain self-confidence and the reaction of the patient is generally very positive and yes, that also gives us a reason to continue, well, the way we took is just the right way." - COPD nurse 5*

Also, sharing experiences with other regions during the project meetings was reported by four HCPs to be very helpful.

Self-efficacy - Most pulmonologists and two COPD nurses reported initially feeling uncomfortable starting a palliative care conversation, but their confidence increased the more they did it. The communication training and example phrases were perceived as helpful. Most pulmonologists and COPD nurses preferred to hold the conversations partly together because it was more efficient and made it easier to start the conversation.

> *"That actually really helped me, I think, it also supported me a bit, that I found it a little less scary. Because it is quite difficult to start a conversation like that." - Pulmonologist 2*

> *"Because [...] I do the introductory talk, it's easier for the pulmonologist to continue the conversation in that half hour. Um, and in this way it's a bit more structured, the pulmonologist doesn't have to block a full hour for it, and in this way, we complement each other well." - COPD nurse 2*

Implementation process

Planning, Reflecting and Evaluating – Regional action plans were not used to guide implementation, but HCPs of three regions indicated that they made verbal work agreements. Working together in a small team helped to make those agreements and keep them. HCPs of one region noticed that it worked well to schedule weekly meetings at a fixed time.

> *"The big stick is that you just get together every week, [...] to implement the actions that each person is assigned." - COPD nurse 2*

Engaging – In all regions, implementation was primarily focused on identification and palliative care conversations. As a result, transmural collaboration only came into focus later in the project. To the disappointment of some, team members from primary care and specialist palliative care were not actively involved in the implementation process because their potential contribution was unclear.

> *"I didn't notice so much here the role of the specialised general practitioner. I had a different expectation." - General Practitioner 2*

Implementation leader - A dedicated implementation leader feeling responsible for the implementation and keeping everyone engaged was deemed essential by HCPs across all regions. In one region, no one was explicitly made responsible, which hampered implementation.

Discussion

Main findings

This mixed-method study provides a detailed understanding of the implementation process of palliative care components into routine COPD care, how a multifaceted strategy can influence this process, and essential factors for successful implementation. Training sessions with roleplay were positively evaluated and increased the self-efficacy in providing palliative care. Of all patients screened, around half received an outpatient palliative care conversation, on average six weeks after inclusion and mostly held by a pulmonologist and COPD nurse together. Continuity and coordination of care remained limited, and aftercare was not done at all. The most important implementation barriers were time constraints, the COVID-19 pandemic, and barriers related to interdisciplinary and transmural collaboration. Factors facilitating implementation were: the systematic screening of palliative patients, adapting to the patient's readiness, conducting palliative care conversations together with a pulmonologist and COPD nurse, and meeting regularly with a small team led by a dedicated implementation leader. Our findings will guide future implementation efforts to integrate a palliative care approach into COPD care and provide insights into the most effective components.

Implementation strategies

A multifaceted implementation strategy was used to optimize uptake of the intervention,[22] but the appropriateness varied per individual strategy. In line with previous research, communication training with roleplay by actors was positively evaluated by HCPs and increased their self-efficacy in providing palliative care.[14, 23, 24] Also, sharing best practices between regions during project meetings was positively evaluated and perceived as inspiring to continue implementation. However, the online toolbox and regional action plans were less used than anticipated. Filling in the plans proved too abstract and time-consuming for busy HCPs. As a result, implementation proceeded largely unstructured and depended greatly on the implementation leader's enthusiasm. For future implementation efforts, we recommend providing HCPs with clear instructions and practical ready-to-use tools and scheduling frequent team meetings led by a dedicated implementation leader.

Palliative care conversations

Systematic screening of patients appeared to be an essential intervention component. It raised HCPs' awareness and made them more ready to initiating palliative care conversations. However, the ProPal-COPD tool's performance appeared to be unsatisfactory. External validation results and user experiences will be discussed in a separate publication. With 45% of patients identified, a palliative care conversation was held. Despite of the COVID-19 pandemic, this percentage is comparable to previous studies. In the systematic review of Houben et al. on advance care planning interventions,[25] the occurrence of palliative care conversations in intervention groups of included studies ranged from 18 to 64%.[26-30] HCPs were very positive about the palliative care discussions, but alignment with patient readiness was deemed important as COPD is not considered as 'potentially lethal' by most patients.[31] It is less confronting to patients if advance care planning is initiated gradually with topics related to dying and death introduced step-by-step over multiple conversations. In our study, using a dual-track approach ("hope for the best, and prepare for the worst"),[32] it was possible to introduce such topics already in an earlier stage. Pulmonologists highly valued collaboration with a COPD nurse as it helped them discuss sensitive topics and saved time. Indeed, blocking enough time for the palliative care conversations was challenging. Therefore, scheduling conversations at the end of the consultation hour to allow for possible extension or scheduling a fixed time in the week is recommended.

Interdisciplinary collaboration

In line with guideline recommendations and care practices in the Netherlands,[4, 5, 33, 34] our intervention was delivered by respiratory HCPs (so-called generalist care providers), while specialist palliative care providers were only involved in the case of complex care needs. In our study, the level of involvement varied across regions. Respiratory HCPs were reluctant to involve the specialist palliative care team because they lacked COPD-specific knowledge regarding treatment and communication practices. Specialist palliative care providers are mainly involved with oncology patients,[35] whereas patients with COPD require a different approach.[36] Therefore, it should be further explored how respiratory and palliative care HCPs optimally collaborate and learn from each other's expertise.

Transmural collaboration

The intervention component coordination & continuity was less well implemented across all regions. Although providers from primary care and the hospital were involved in the training, implementation leaders first focused on organizing outpatient palliative care conversations. Consequently, transmural collaboration received insufficient attention, as reflected by the low number of letters sent from hospital to the GP. Although HCPs expressed that contact by phone is preferred to optimize care coordination and continuity after a patient was identified, this was not always done due to time constraints and lack of a shared electronic medical record.

Therefore, a communication tool to facilitate bidirectional communication (ideally digital, linked to medical files, and always accessible) is needed. Further, COPD nurses in primary care play an essential role in linking primary and secondary care and should be available in every region. Moreover, to optimize coordination and guarantee continuity of care, financial structures that allow flexibility and 'shared care' are warranted.

Strengths & limitations

This is the first comprehensive study assessing palliative care implementation in a real-world outpatient COPD care setting. We used different data sources to provide a broad and in-depth understanding of the implementation process. Furthermore, the intervention and implementation strategy were designed using theory, guidelines, and input of many stakeholders, ensuring that barriers from the field were addressed.[15] However, our study also has some limitations. First, the COVID-19 pandemic had severe implications that may have biased our findings. HCPs had less time for implementation activities, multidisciplinary meetings were put on hold, and palliative care conversations were cancelled to prevent contamination. Second, our implementation results were somewhat constrained because it was performed alongside a cluster randomised controlled trial (as part of a hybrid type 2 effectiveness-implementation study).[15] Next to the positive aspects of combining these two study objectives, such as faster knowledge development,[37] it limited our flexibility to adapt to new insights that emerged during the study. For example, the fixed inclusion criteria required for effectiveness evaluation limited the measured reach because palliative patients identified at the outpatient clinic could not be included. Also, HCPs were focused on enrolling patients for sufficient power of the effectiveness study, limiting their time for implementation activities. Finally, we did not assess the quality of implementation, e.g. the quality of palliative care conversations. In future studies, this could be assessed using conversation analysis, as was found to be a viable method by Otte et al.[38]

Conclusion

Implementation is a complex process, and dedicated action is needed to ensure theoretically promising and highly needed interventions, such as palliative care for patients with COPD, are delivered as intended. The multifaceted implementation strategy evaluated in the COMPASSION study demonstrated the importance of communication training in discussing palliative care topics with patients with COPD in a sensitive way, systematic screening of patients with palliative care needs, and a structured implementation process led by a dedicated implementation leader. It also highlighted that we are not there yet; future research should focus on optimizing transmural and interdisciplinary collaboration, to ensure optimal integration and continuity of palliative COPD care.

Abbreviations

CFIR, Consolidated Framework of Implementation Research; COPD, chronic obstructive pulmonary disease; EPCS, End-of-life Professional Caregiver Survey; HCP, healthcare provider.

Trial registration

The COMPASSION study is registered in the Netherlands Trial Register (NTR): NL7644. Registration date: 07/04/2019.

Ethics approval

This study was performed according to the Dutch law, the principles outlined in the Declaration of Helsinki, and Good Clinical Practice guidelines. The Medical Ethics Committee of the Radboud University Medical Centre approved the study protocol and concluded that the study was not subject to the Medical Research Involving Human Subjects act (number 2018–4833). All participating patients gave their written informed consent to use their medical data.

Data availability

The datasets generated and analysed during the current study are not publicly available due to the confidentiality and the traceability of the data but are available from the corresponding author on reasonable request.

Declaration of conflicting interests

The authors declared no potential conflicts of interest concerning the research, authorship, or publication of this article.

Funding

This research project has been financially supported by The Netherlands Organization for Health Research and Development (ZonMw) (project no. 844001401).

Author contributions

J.B., R.K, H.K., Y.E. and N.H. designed the study protocol; E.V. and J.B. led the development and implementation of the training and toolbox and held monitoring meetings; Y.E. led project meetings; J.B. and E.V. collected data; J.B. and R.K. performed data analyses, and the research group discussed preliminary and definitive findings; J.B. wrote the first draft; All authors contributed to critical revision and agreed with the final manuscript.

Acknowledgements

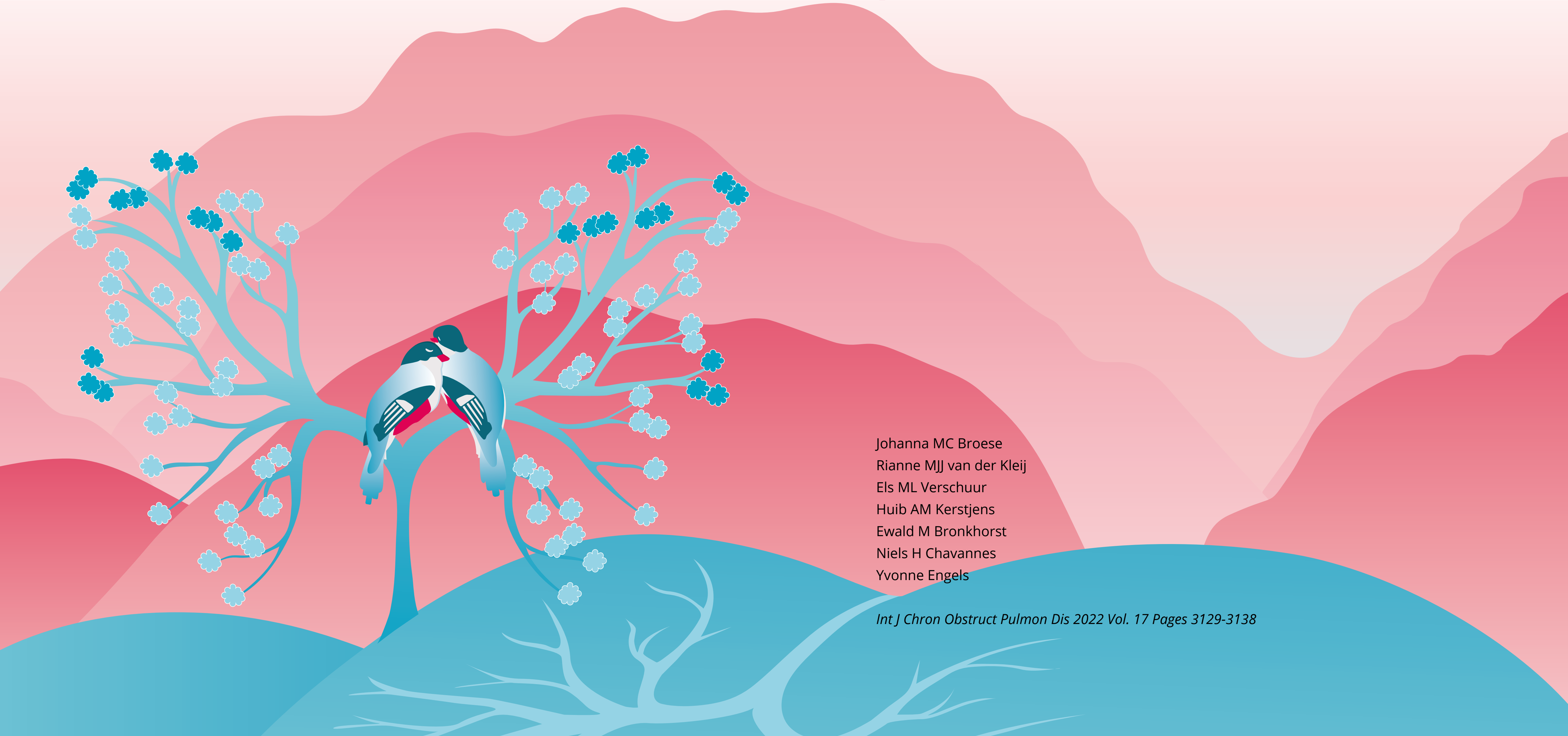
We thank all patients, informal caregivers, and healthcare providers who participated in the COMPASSION study. We are very grateful for the enthusiasm, effort, and dedication of all involved primary and secondary healthcare providers of the four intervention regions: Langeland

Hospital in Zoetermeer, Martini Hospital in Groningen, Slingeland Hospital in Doetinchem, and Zaans Medisch Centrum in Zaandam. In particular, we would like to thank Sandra Been-Buck, Gerrit Bosman, Linda Brandjes, Leonie Bruil, Karin Eikenaar, Ellen Jacobs-Taag, Titia Klemmeier, Martijn Kross, Sarah van Oord, Carla van de Spek, and Maritha Spekschoor. We thank Noortje van Vliet for her help in collecting data from medical records.

References

1. 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. 2009/04/28. DOI: 10.1016/j.jpainsymman.2008.07.010.
2. IKNL/Palliactief. Netherlands Quality Framework for Palliative Care. 2017.
3. Rietjens JAC, Sudore RL, Connolly M, et al. Definition and recommendations for advance care planning: an international consensus supported by the European Association for Palliative Care. The Lancet Oncology 2017; 18: e543-e551. 2017/09/09. DOI: 10.1016/s1470-2045(17)30582-x.
4. 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. 2008/04/09. DOI: 10.1164/rccm.200605-587ST.
5. IKNL/LAN. National guideline Palliative care in COPD, version 2.0. 2021. Utrecht, The Netherlands.
6. Broese JMC, van der Kleij R, Verschuur EML, et al. Provision of Palliative Care in Patients with COPD: A Survey Among Pulmonologists and General Practitioners. Int J Chron Obstruct Pulmon Dis 2021; 16: 783-794. 2021/04/06. DOI: 10.2147/COPD.S293241.
7. 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. DOI: thoraxjnl-2016-209806 [pii];10.1136/thoraxjnl-2016-209806 [doi].
8. Reipas KM, Grossman DL, Lock K, et al. Examining the Characteristics of Patients With Non-Malignant Lung Disease at the Time of Referral to An Inter-Professional Supportive Care Clinic. Am J Hosp Palliat Care 2021; 38: 1329-1335. 20210407. DOI: 10.1177/10499091211005698.
9. 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. 2011/04/23. DOI: 10.1089/jpm.2010.0479.
10. Broese JM, de Heij AH, Janssen DJ, et al. Effectiveness and implementation of palliative care interventions for patients with chronic obstructive pulmonary disease: A systematic review. Palliat Med 2021; 35: 486-502. 20201218. DOI: 10.1177/0269216320981294.
11. 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 2017/05/04. DOI: 10.1183/23120541.00068-2016.
12. Aldridge MD, Hasselaar J, Garralda E, et al. Education, implementation, and policy barriers to greater integration of palliative care: A literature review. Palliat Med 2016; 30: 224-239. 20150924. DOI: 10.1177/0269216315606645.
13. Meehan E, Foley T, Kelly C, et al. Advance Care Planning for Individuals With Chronic Obstructive Pulmonary Disease: A Scoping Review of the Literature. J Pain Symptom Manage 2020; 59: 1344-1361. 20191216. DOI: 10.1016/j.jpainsymman.2019.12.010.

14. Chung HO, Oczkowski SJ, Hanvey L, et al. Educational interventions to train healthcare professionals in end-of-life communication: a systematic review and meta-analysis. BMC Med Educ 2016; 16: 131. 20160429. DOI: 10.1186/s12909-016-0653-x.
15. Broese JMC, van der Kleij R, Kerstjens HAM, et al. A cluster randomized controlled trial on a multifaceted implementation strategy to promote integrated palliative care in COPD: study protocol of the COMPASSION study. BMC Palliat Care 2020; 19: 155. 2020/10/12. DOI: 10.1186/s12904-020-00657-3.
16. Pinnock H, Barwick M, Carpenter CR, et al. Standards for Reporting Implementation Studies (StaRI) Statement. BMJ (Clinical research ed) 2017; 356: i6795. 2017/03/08. DOI: 10.1136/bmj.i6795.
17. Duenk RG, Verhagen C, Bronkhorst EM, et al. Development of the ProPal-COPD tool to identify patients with COPD for proactive palliative care. Int J Chron Obstruct Pulmon Dis 2017; 12: 2121-2128. DOI: 10.2147/COPD.S140037 [doi];copd-12-2121 [pii].
18. Lazenby M, Ercolano E, Schulman-Green D, et al. Validity of the end-of-life professional caregiver survey to assess for multidisciplinary educational needs. J Palliat Med 2012; 15: 427-431. 2012/04/17. DOI: 10.1089/jpm.2011.0246.
19. Steckler A and Linnan L. Process evaluation for public health interventions and research. San Francisco, CA, US: Jossey-Bass, 2002, p.xxviii, 400-xxviii, 400.
20. Braun V and Clarke V. Using thematic analysis in psychology. Qual Res Psychol 2006; 3: 77-101.
21. 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. 2009/08/12. DOI: 10.1186/1748-5908-4-50.
22. van Riet Paap J, Vernooij-Dassen M, Sommerbakk R, et al. Implementation of improvement strategies in palliative care: an integrative review. Implement Sci 2015; 10: 103. 2015/07/27. DOI: 10.1186/s13012-015-0293-2.
23. Back AL, Arnold RM, Baile WF, et al. Efficacy of communication skills training for giving bad news and discussing transitions to palliative care. Arch Intern Med 2007; 167: 453-460. 2007/03/14. DOI: 10.1001/archinte.167.5.453.
24. Tilburgs B, Koopmans R, Vernooij-Dassen M, et al. Educating Dutch General Practitioners in Dementia Advance Care Planning: A Cluster Randomized Controlled Trial. J Am Med Dir Assoc 2020; 21: 837-842.e834. 2019/11/25. DOI: 10.1016/j.jamda.2019.09.010.
25. Houben CHM, Spruit MA, Groenen MTJ, et al. Efficacy of advance care planning: a systematic review and meta-analysis. J Am Med Dir Assoc 2014; 15: 477-489. 2014/03/07. DOI: 10.1016/j.jamda.2014.01.008.
26. Au DH, Udris EM, Engelberg RA, et al. A randomized trial to improve communication about end-of-life care among patients with COPD. Chest 2012; 141: 726-735. DOI: S0012-3692(12)60163-9 [pii];10.1378/chest.11-0362 [doi].
27. Clayton JM, Butow PN, Tattersall MH, et al. Randomized controlled trial of a prompt list to help advanced cancer patients and their caregivers to ask questions about prognosis and end-of-life care. Journal of clinical oncology : official journal of the American Society of Clinical Oncology 2007; 25: 715-723. DOI: 10.1200/jco.2006.06.7827.
28. Heffner JE and Barbieri C. Effects of advance care education in cardiovascular rehabilitation programs: a prospective randomized study. J Cardiopulm Rehabil 2001; 21: 387-391. DOI: 10.1097/00008483-200111000-00008.
29. Jacobsen J, Robinson E, Jackson VA, et al. Development of a cognitive model for advance care planning discussions: results from a quality improvement initiative. J Palliat Med 2011; 14: 331-336. 20110119. DOI: 10.1089/jpm.2010.0383.
30. Pearlman RA, Starks H, Cain KC, et al. Improvements in advance care planning in the Veterans Affairs System: results of a multifaceted intervention. Arch Intern Med 2005; 165: 667-674. DOI: 10.1001/archinte.165.6.667.
31. Knauft E, Nielsen EL, Engelberg RA, et al. Barriers and facilitators to end-of-life care communication for patients with COPD. Chest 2005; 127: 2188-2196. 2005/06/11. DOI: 10.1378/chest.127.6.2188.
32. Back AL, Arnold RM and Quill TE. Hope for the best, and prepare for the worst. Ann Intern Med 2003; 138: 439-443. DOI: 10.7326/0003-4819-138-5-200303040-00028.
33. Quill TE and Abernethy AP. Generalist plus specialist palliative care--creating a more sustainable model. The New England journal of medicine 2013; 368: 1173-1175. 20130306. DOI: 10.1056/NEJMp1215620.
34. Henderson JD, Boyle A, Herx L, et al. Staffing a Specialist Palliative Care Service, a Team-Based Approach: Expert Consensus White Paper. J Palliat Med 2019; 22: 1318-1323. 20190726. DOI: 10.1089/jpm.2019.0314.
35. Beernaert K, Cohen J, Deliens L, et al. Referral to palliative care in COPD and other chronic diseases: a population-based study. Respir Med 2013; 107: 1731-1739. 2013/07/03. DOI: 10.1016/j.rmed.2013.06.003.
36. Ngwenya N, Crang C, Farquhar M, et al. Communicating uncertainty: contrasting the communication experiences of patients with advanced COPD and incurable lung cancer. Family practice 2021; 38: 637-643. DOI: 10.1093/fampra/cmab024.
37. Curran GM, Bauer M, Mittman B, et al. Effectiveness-implementation hybrid designs: combining elements of clinical effectiveness and implementation research to enhance public health impact. Med Care 2012; 50: 217-226. 2012/02/09. DOI: 10.1097/MLR.0b013e3182408812.
38. Otte R, Roodbeen R, Boland G, et al. Affective communication with patients with limited health literacy in the palliative phase of COPD or lung cancer: Analysis of video-recorded consultations in outpatient care. PLoS One 2022; 17: e0263433. 20220210. DOI: 10.1371/journal.pone.0263433.



Chapter 7

External validation and user experiences of the ProPal-COPD tool to identify the palliative phase in COPD

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Int J Chron Obstruct Pulmon Dis 2022 Vol. 17 Pages 3129-3138

Abstract

Background

Difficulty predicting prognosis is a major barrier to timely palliative care provision for patients with COPD. The ProPal-COPD tool, combining six clinical indicators and the Surprise Question (SQ), aims to predict 1-year mortality as a proxy for palliative care needs. It appeared to be a promising tool for healthcare providers to identify patients with COPD who could benefit from palliative care.

Objective

To externally validate the ProPal-COPD tool and to assess user experiences.

Methods

Patients admitted with an acute exacerbation COPD were recruited across 10 hospitals. Demographics, clinical characteristics and survival status were collected. Sensitivity, specificity, positive and negative predictive values of the tool using two cut-off values were calculated. Also, predictive properties of the SQ were calculated. In monitoring meetings and interviews, healthcare providers shared their experiences with the tool. Transcripts were deductively coded using six user experience domains: Acceptability, Satisfaction, Credibility, Usability, User-reported adherence and Perceived impact.

Results

523 patients with COPD were included between May 2019 and August 2020, of whom 100 (19.1%) died within 12 months. The ProPal-COPD tool had an AUC of 0.68 and a low sensitivity (55%) and moderate specificity (74%) for predicting 1-year all-cause mortality. Using a lower cut-off value, sensitivity was higher (74%), but specificity lower (46%). Sensitivity and specificity of the SQ were 56% and 73%, respectively (AUC 0.65). However, healthcare providers generally appreciated using the tool because it increased awareness of the palliative phase and provided a shared understanding of prognosis, although they considered its outcome not always correct.

Conclusions

The accuracy of the ProPal-COPD tool to predict 1-year mortality is limited, although screening patients with its indicators increases healthcare providers' awareness of palliative care needs and encourages them to timely initiate appropriate care.

Keywords

chronic obstructive pulmonary disease; prognostication; palliative care; advance care planning; surprise question.

Introduction

Despite severe morbidity and high mortality,[1, 2] most patients with advanced chronic obstructive pulmonary disease (COPD) do not receive timely, adequate palliative care.[3-5] Palliative care aims to enhance quality of life of patients with a life-threatening disease through the assessment and treatment of physical, psychological, social and spiritual problems.[6] It includes advance care planning (ACP), which enables individuals to define goals and preferences for current and future care.[7]

Identification of the palliative phase is a prerequisite to provide palliative care,[6, 8] particularly in patients with organ failure like COPD.[9] However, a major barrier is the unpredictable disease course in COPD, hampering accurate prediction of the timing of death.[3, 10, 11] Lung function parameters, such as forced expiratory volume in 1 second (FEV1) % of predicted do not correlate well with mortality of individual patients.[12] Also, survival models that have been developed to predict prognosis in stable patients, such as ADO, BODEx and DOSE, were not very accurate.[13, 14]

Palliative care guidelines recommend using the Surprise Question (SQ), a single-item tool: 'Would I be surprised if this patient were to die in the next 12 months?'[8, 15] It proved to be a useful tool to increase awareness among healthcare providers that patients are nearing the end of life.[16] In hospitalized patients with COPD, however, its sensitivity was only 47%, indicating that many patients needing palliative care were missed.[17] Furthermore, several tools including general as well as disease specific indicators have been developed: the Gold Standards Framework Prognostic Indicator Guidance (GSF-PIG), the Supportive and Palliative Care Indicators Tool (SPICT) and the RADPAC indicators.[15, 18, 19] However, these tools are rather focused on the terminal phase and have not been validated for COPD.

To create a compact, practical guidance for healthcare providers to identify patients with COPD in need of proactive palliative care, the Propal-COPD tool was developed.[20] The tool combines the SQ with six clinical indicators. It was validated for patients admitted to the hospital for an acute exacerbation, as hospitalization increases mortality significantly and is a clear transition point in the disease course.[21, 22] A high probability of death within one year was used as a proxy for palliative care needs, as they generally increase towards the end of life. Predicting 1-year mortality with high sensitivity (90%), the ProPal-COPD tool showed to be a promising tool to urge healthcare providers to initiate palliative care provision.

However, before implementing a prediction tool in clinical practice, it is essential to test the performance in another dataset than used for model development.[23] Additionally, it is relevant to examine the benefits of using the tool in practice and how the implementation can be optimized. Therefore, we aimed to externally validate the ProPal-COPD tool in a prospective cohort of hospitalized patients with COPD and to assess user experiences of healthcare providers.

Methods

Design

This validation study is part of the COMPASSION study, a cluster randomized trial in eight hospital regions across the Netherlands aiming to assess the effectiveness and implementation process of integrated palliative care.[24] Patients were recruited in the eight participating hospitals of the COMPASSION study and in two additional hospitals. Patients diagnosed with COPD and hospital admission for an acute exacerbation were invited to participate. Patients not able to complete questionnaires in Dutch, patients with severe cognitive decline (e.g. dementia) and patients on the waiting list for lung transplantation were excluded. After receiving oral and written information about the study, written informed consent was obtained of all participants. The study was performed according to the Dutch law and Good Clinical Practice guidelines. The Research Ethics Committee of the Radboud University Medical Center Nijmegen concluded that this study does not fall within the remit of the Medical Research Involving Human Subjects Act (file number 2018-4390). The board of each participating hospital approved data collection. All data were stored and analyzed anonymized.

ProPal-COPD tool

The ProPal-COPD tool consists of seven dichotomous indicators, of which each has a specific weight, together generating a total score (Table 1).[20] Two indicators are patient reported outcome measures: Medical Research Council (MRC) dyspnea score of 5 and Clinical COPD Questionnaire (CCQ) score higher than 3. Four indicators relate to clinical characteristics: FEV1 lower than 30% of predicted, presence of specific comorbidities, body mass index lower than 21 kg/m2 or weight loss and previous hospitalization for acute exacerbation. The last indicator is a negative answer to the SQ ("Would I be surprised if this patient were to die in the next 12 months?"). A score exceeding the cut-off value of -1.362 was previously published and corresponded in the development cohort with a high sensitivity (90%) and moderate specificity (73%) to predict death within 1 year. To create an online tool, we set the intercept to 0, resulting in a cut-off value of 2.539. During the first months of the study, the tool identified fewer patients than expected, and therefore after six months the cut-off value was lowered with one point to 1.5 (Table 2).

Data collection

Participants filled in a questionnaire including demographic characteristics, smoking status, the MRC dyspnea score and CCQ score. A pulmonologist or COPD-nurse, involved in the care for the respective patient, gave their answer to the SQ and collected data on the four clinical ProPal-COPD indicators. Clinical baseline characteristics and all seven ProPal-COPD indicators were then entered by a healthcare provider in an electronic data management program (Castor edc). After twelve months of follow-up, survival status and, if applicable, date of death was collected from the medical records.

Table 1. Indicators of the ProPal-COPD tool and their corresponding weights

Indicator	Weight
MRC dyspnea score = 5	1.475
CCQ score > 3	0.257
FEV1 <30% of predicted	0.565
One or more severe comorbidities (non-curable malignancy, cor pulmonale, heart failure, diabetes mellitus with neuropathy, or renal failure with eGFR < 40 mL/min) present	1.479
BMI < 21 kg/m2 or weight loss > 10% in the last 6 months or > 5% in last month	1.005
In last 2 years ≥2 or last year ≥1 hospital admission for acute exacerbation of COPD	0.102
Negative answer to Surprise Question	0.959

Abbreviations: BMI, body mass index; CCQ, Clinical COPD Questionnaire; eGFR, estimated glomerular filtration rate; FEV1%, forced expiratory volume in 1 second; MRC, Medical Research Council.

Table 2. Intercepts and cut-off values of the original, converted and adapted model

	Original model	Model without intercept	Model with adapted cut-off value
Intercept	-3.901	0	0
Cut-off value	-1.362	2.539	1.500

Experiences with the use of the ProPal-COPD tool were assessed using transcripts of monitoring meetings and semi-structured interviews with healthcare providers within the four intervention hospitals of the COMPASSION study.[24] They had been using the ProPal-COPD tool to identify patients who were offered palliative care conversations. To evaluate the implementation process, four monitoring meetings per region were held by EV and JB over the course of the study, and interviews were held by JB at study completion.[25] In these meetings and interviews, providers were asked to reflect on their experiences with the ProPal-COPD tool using open questions about the practical use, appropriateness of the patient selection, and the perceived effects of its use. Experiences with both the original as well as the adapted cut-off value were inquired. All participants provided written informed consent for participation in the study and anonymous use of their data.

Data analyses

Participant characteristics were analyzed using descriptive statistics in SPSS version 25. Ordinary 2x2 tables were used to calculate sensitivity, specificity, positive and negative predictive values of the ProPal-COPD tool to predict 1-year all-cause mortality (calibration). These outcomes were calculated using the original cut-off value of the tool, the adapted, lower cut-off value and the SQ. We used a receiver operating characteristic (ROC) curve to calculate the area under the curve (AUC). An AUC (synonym for C-statistic) of 0.5 reflects no discriminative ability, and 1 reflects perfect discrimination. Differences in baseline characteristics between survivors and non-survivors were assessed using t-tests for continuous variables, Mann–Whitney U-tests for categorical variables and Chi-square tests for dichotomous variables.

Interview and monitoring meeting transcripts were deductively coded using user experience domains for eHealth interventions as proposed by Newton et al (2021).[26] They established working definitions for six domains. *Acceptability* refers to whether the intervention content, features, and delivery meet user expectations. *Satisfaction* refers to the user's overall impression of the intervention and whether it meets their needs. *Credibility* refers to the extent to which the user perceives the intervention trustworthy and has the potential to work. *Usability* refers to the user's perceived ease of use of the intervention based on technical factors. *User-reported adherence* refers to how and why the user did or did not follow the intervention or research protocol. Lastly, *Perceived impact* refers to the extent to which the user perceives the effect of the intervention's impacts. Due to considerable overlap between Acceptability and Satisfaction, these domains were merged. Coding was done by one researcher (JB) and checked by a second researcher (YE). Disagreements were discussed until consensus was reached. Subsequently, a summary of each code was created and relevant quotations were selected. Findings were discussed within the research group until consensus was reached on the interpretation of findings.

Results

Participant characteristics

Between May 2019 and August 2020, 825 patients admitted to the hospital due to an acute exacerbation of COPD were screened for eligibility. Eventually, 523 patients were included for analysis (Figure 1). Mean age was 70 years and 55.8% was female. Demographics and clinical characteristics of participants are presented in Table 3. Hundred patients (19.1%) died within 12 months after inclusion. Non-survivors were on average older, more often lived alone and more often received homecare, and had a lower lung function (FEV1 % of predicted) than survivors.

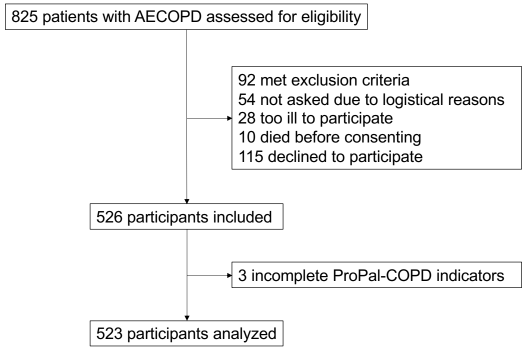

Figure 1. Flow diagram of study participants. AECOPD, acute exacerbation of chronic obstructive pulmonary disease.

Sensitivity and specificity of the ProPal-COPD tool

The ProPal-COPD tool had a low sensitivity (55.0%), and a medium to high specificity (73.3%) for predicting 1-year mortality. The positive predictive value was 32.7%, and the negative predictive value 87.3%. Using the lower cut-off value, sensitivity was higher (74.0%), but specificity lower (46.1%). The positive predictive value was 24.5%, and the negative predictive value was 88.2%. The ROC curve of the ProPal-COPD tool is presented in Figure 2. The AUC was 0.68 (95% confidence interval: 0.62-0.74).

Sensitivity and specificity of the Surprise Question

Sensitivity and specificity of the SQ alone were 56.0 and 73.0% respectively. The positive predictive value was 32.9%, and the negative predictive value was 87.5%. The AUC was 0.65 (95% confidence interval: 0.58-0.71).

Table 3. Demographics and clinical characteristics of survivors and non-survivors and ProPal-COPD tool indicators

Characteristic	**All participants n=523**	**Survivors n=423**	**Non-survivors n=100**
Demographics			
Age in years, mean±SD	70.0±9.1	69.4±9.2	72.5±8.4
Sex, female	292 (55.8)	239 (56.5)	53 (53.0)
Marital status			
Married	269 (53.3)	226 (55.3)	43 (44.8)
Unmarried	61 (11.9)	48 (11.7)	12 (12.5)
Divorced	73 (14.5)	57 (13.9)	16 (16.7)
Widow	103 (20.4)	78 (19.1)	25 (26.0)
Living situation			
Living alone	206 (41.1)	158 (39.0)	48 (50.0)
Living together	295 (58.9)	247 (61.0)	48 (50.0)
Place of living			
Home, without homecare	363 (72.7)	310 (76.4)	53 (57.0)
Home, with homecare	123 (24.6)	85 (20.9)	38 (40.9)
Residential home	11 (2.2)	9 (2.2)	2 (2.2)
Nursing home	2 (0.4)	2 (0.5)	0 (0.0)
Country of birth			
Netherlands	482 (95.6)	394 (96.6)	88 (91.7)
Other	22 (4.4)	14 (3.4)	8 (8.3)
Highest level of education			
No / elementary school	96 (19.4)	74 (18.5)	22 (23.2)
Secondary school	146 (29.5)	124 (31.0)	22 (23.2)
Vocational education	208 (42.0)	165 (413)	43 (45.3)
Higher / University	45 (9.1)	37 (9.3)	8 (8.4)

Table 3. *Continued*

Characteristic	**All participants** **n=523**	**Survivors** **n=423**	**Non-survivors** **n=100**
Clinical characteristics			
Current smoker	127 (24.9)	108 (26.2)	19 (19.4)
Pack years, mean±SD	39.5±26.6	38.4±26.1	44.3±28.4
FEV1 % of predicted, mean±SD	42.4±16.4	43.2±16.6	38.8±15.1
GOLD stage			
1	15 (2.9)	14 (3.3)	1 (1.0)
2	120 (23.0)	99 (23.5)	21 (21.0)
3	201 (38.5)	169 (40.0)	32 (32.0)
4	160 (30.7)	118 (28.0)	42 (42.0)
Unknown	26 (5.0)	22 (5.2)	4 (4.0)
Long term oxygen treatment	70 (14.8)	50 (13.0)	20 (22.7)
ProPal-COPD indicators			
MRC dyspnea score = 5	249 (47.6)	187 (44.2)	62 (62.0)
CCQ score >3	319 (61.0)	250 (59.1)	69 (69.0)
Comorbidity	100 (19.1)	72 (17.0)	28 (28.0)
Non-curable malignancy	15 (2.9)	7 (1.7)	8 (8.0)
Cor pulmonale	29 (5.5)	21 (5.0)	8 (8.0)
Chronic heart failure	45 (8.6)	34 (8.0)	11 (11.0)
Diabetes with neuropathy	10 (1.9)	6 (1.4)	4 (4.0)
Renal failure	15 (2.9)	9 (2.1)	6 (6.0)
Previous hospitalization	241 (46.1)	195 (46.1)	46 (46.0)
BMI < 21 or weight loss	123 (23.5)	93 (22.0)	30 (30.0)
FEV1 < 30% of predicted	107 (20.5)	77 (18.2)	30 (30.0)
Surprise Question, negative	170 (32.5)	114 (27.0)	56 (56.0)

Data are presented in absolute values and valid percentages, unless stated otherwise. Abbreviations: BMI, body mass index; CCQ, Clinical COPD Questionnaire; FEV1, forced expiratory volume in 1 second; MRC, Medical Research Council; SD, standard deviation.

User experiences

Seven pulmonologists, nine COPD-nurses and one general practitioner shared their experiences about using the ProPal-COPD tool in interviews and monitoring meetings.

Acceptability/Satisfaction – Almost all participants liked having a tool to help them evaluate whether a patient entered the palliative phase.

> *"In the hustle and bustle of the day, it's nice if you get a reminder from time to time, so then I'm going to look differently." – COPD-nurse 5*

Four participants found it particularly useful for less experienced healthcare providers. Two pulmonologists expressed that it helped them to make the decision more

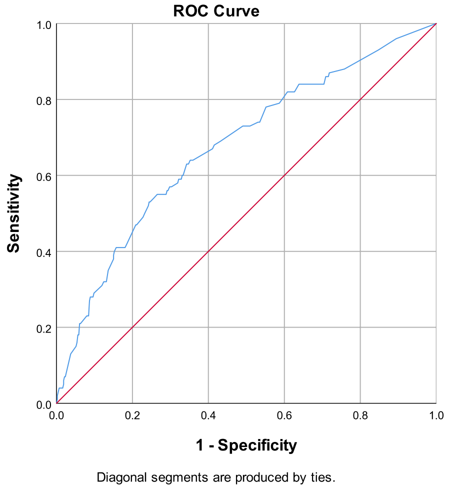

Figure 2. Receiver operating characteristic (ROC) curve of the ProPal-COPD tool.

objectively, resulting in a shared understanding of prognosis. It was perceived essential by two pulmonologists to be able to screen not only hospitalized patients but outpatients as well.

Credibility – Before modification of the cut-off value, the tool was found to be too strict by healthcare providers across all four regions, resulting in missed patients in need of palliative care. After lowering the cut-off value, most of them indicated that the tool sometimes selected patients that were still too good for a palliative care conversation.

> *"Sometimes I thought* [the tool] *underestimated and sometimes overestimated it. Because I've had patients with whom I've had advance care discussions and I've thought to myself, why am I having an advance care discussion here? And the next time, that patient comes hopping in." – Pulmonologist 2*

Usability – Almost all pulmonologists and COPD-nurses considered the tool easy to use. Three of them preferred integrating the tool in the electronic medical record, obviating the need to open a separate webpage. According to the general practitioner, the tool was less suitable for use in primary care, because data are not available there for each indicator, e.g. lung function. The SQ was perceived as difficult to answer by three COPD-nurses. Furthermore, statements of two pulmonologists and two COPD-nurses suggested that the SQ was sometimes (wrongly) interpreted as a life-expectancy of less than one year.

> *"What I did notice about the tool is that the surprise question is quite difficult for some, especially the nurses. To be able to estimate whether someone is still alive or not after a year." – Pulmonologist 1*

User-reported adherence – After the study had ended, most participants indicated that with increasing experience they had stopped filling out the ProPal tool, but instead used some of its indicators, such as the SQ, to make their own assessment. They had gained more experience in recognizing palliative care needs, memorized the indicators, and realized that "it is not black and white", partly because the tool did not perform as well as expected.

> *"I don't think I would hold it so strictly to negative or positive, but rather that by looking at it that way, you judge a patient differently." – COPD-nurse 7*

Healthcare providers of one region entered the ProPal-COPD indicators only for study purposes, but did not use them for identification. They preferred to initiate palliative care if it became clear that treatment options such as pulmonary rehabilitation and bronchoscopic lung volume reduction were not possible anymore.

Perceived impact – Around half of the participants expressed that using the tool had made them look at their patients differently, as their awareness of the palliative phase had increased.

> *"If you mark it huh, that palliative phase, that gives you some more insight that you can actually do something more instead of accepting that it's just chronically bad with that patient. – COPD-nurse 2*

Discussion

Main findings

We externally validated and assessed user experiences of the ProPal-COPD tool to facilitate healthcare providers identifying the palliative phase in patients with COPD, hospitalized for an acute exacerbation. The ProPal-COPD tool showed to have mediocre predictive properties. Although healthcare providers considered the outcome of the tool not always correct, they generally did appreciate having such a tool, particularly for less experienced colleagues, because it increases awareness of the palliative phase and provides a shared understanding of prognosis.

Interpretation and implications

There are several potential reasons why the ProPal-COPD tool did not confirm the promising data of the internal validation study and did not increase prediction of 1-year mortality compared to previously developed survival prediction models in COPD.[14] First, prediction models always perform better in the derivation cohort than in a new population.[23] In the study of Duenk et al, the model was built with 11 indicators using data from 155 patients of which 30 died.[20] This relatively small number of 'events' might have led to overfitting of the model, limiting its performance in a new group. Second, the tool comprises dichotomous instead of continuous indicators, making the model less accurate as not all available information is used. For example, an MRC dyspnoea score of 4 or 5 reflects a small difference in clinical practice, but results in a big difference in the total score. Third, all deaths, regardless of cause, have been used. In previous research on the SQ and SPICT, leaving out acute and unexpected deaths led to increased sensitivity.[27] Fourth, our data collection took place during the COVID-19 pandemic. The pandemic may have caused changed mortality patterns due to COVID-19 infections and reduced transmission of common respiratory virus infections following public health measures, which may have influenced our results.[28, 29]

Despite the suboptimal performance, the systematic screening of patients using the ProPal-COPD tool was appreciated by healthcare providers as it made them more aware of palliative care needs. Examining the indicators in each patient, apart from calculating the score, proved to be beneficial in itself. Furthermore, the ProPal-COPD tool was found to be easy-to-use in the hospital, which could be further enhanced by integration of the tool into the electronic medical record.

The SQ had a similar low sensitivity and specificity as the ProPal-COPD tool using the original cutoff value. It is a simple tool, but was easily confused with life-expectancy, as was demonstrated by some interview statements. This confusion may be solved by use of the 'Double Surprise Question', adding a second question "Would I be surprised if this patient will be still alive after 12 months?" to the original SQ.[30, 31]

Although we used 1-year mortality to validate the ProPal-COPD tool, the primary use of the tool is to facilitate healthcare providers to proactively identify patients whose quality of life could be improved by a holistic palliative care approach. As palliative care needs in organ failure do not necessarily start one year before death and may fluctuate over time, it has been advocated not to pursue accurate mortality prediction but to use a needs based tool instead.[32] For patients with heart failure, the I-HARP has recently been developed.[33] Finamore et al. attempted to cluster patients with COPD by their symptoms, which could be a first step to development of such a tool specific for COPD.[34] However, due to limited time and financial resources, it is not attainable to provide a comprehensive person-centered assessment to all patients with COPD. Making a selection of patients most in need, could help to distribute resources efficiently. Also, poor prognosis may define palliative care goals and topics to be discussed, in order to align care to the patient's wishes. Further, it helps to overcome healthcare providers' reluctance to talk about the end-of-life. Therefore, a tool that both identifies patients in need of palliative care and accurately predicts prognosis would activate healthcare providers to discuss end-of-life topics. Additionally, the shared understanding of prognosis may align goals and facilitate collaboration between healthcare providers in different care settings.

Strengths and weaknesses of the study

This multicenter and prospective study with a naturalistic and heterogenous population makes our findings generalizable to other COPD patient populations. With a relatively large sample size with 100 'events', we met the minimum requirement for external validation studies, making our findings reliable.[35] Our study also has some limitations. First, following the development cohort of the ProPal-COPD tool, we only included hospitalized patients. This inhibits the generalizability of our findings to outpatients and primary care patients. Second, death rates were based on registration in medical records, since we had no access to official death certificates, and could have been incomplete. However, the risk of a missed deceased patient is very low because we assessed survival status of most patients in the medical records well beyond one year of follow-up and additionally we searched the internet for death advertisements (www.mensenlinq.nl). Third, we included patients from four intervention hospitals. The intervention could have theoretically influenced survival. However, in our effect evaluation we did not observe any differences in survival between the intervention and control group.[36] Fourth, the SQ was answered by pulmonologists as well as by COPD-nurses. Interpersonal and interprofessional differences might have led to less precise prediction,[16, 37] but reflect normal clinical practice. Fifth, as we used existing qualitative data of the COMPASSION study for assessing user preferences, we may not have reached data saturation on all user experience domains.

Conclusion

The ProPal-COPD tool is easy-to-use and appreciated by healthcare providers, because screening with its indicators increases their awareness of the palliative phase and facilitates a shared understanding of the prognosis. However, the validity of the ProPal-COPD tool in predicting all-cause mortality within one year appears to be hardly superior than previously developed prediction models and the SQ. Future research should explore whether the predictive properties improve when using respiratory-related deaths or palliative care needs as outcome instead.

Acknowledgements
We are grateful to all participating patients. We wish to thank all involved healthcare providers of the participating hospitals: Deventer Hospital, Haaglanden Medical Center, Langeland Hospital, Laurentius Hospital, Martini Hospital, Medisch Spectrum Twente, Ommelander Hospital Groningen, Slingeland Hospital, Treant Zorggroep Hospital (Scheper), and Zaans Medical Center. In particular, we want to thank Sandra Been-Buck, Wendy van Beurden, Anja Binnenmars, Wendy Blanck, Betty Bolink, Gerrit Bosman, Linda Brandjes, Leonie Bruil, Jasmijn van Campen, Erwina Cerimovic, Karin Eikenaar, Edith Goorhuis, Karin Groenewegen, Wies Groothoff, Ellen Jacobs-Taag, Paul Janssen, Jan Willem de Jong, Titia Klemmeier, Martijn Kross, Sarah van Oord, Angelique Puntman, Jaap Ruivenkamp, Steven Rutgers, Carla van de Spek, Maritha Spekschoor, and Veerle de Visser.

Author contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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
This research project has been financially supported by The Netherlands Organization for Health Research and Development (ZonMw) (project no. 844001401).

References

1. Lozano R, Naghavi M, Foreman K, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012; 380: 2095-2128. 2012/12/19. DOI: 10.1016/s0140-6736(12)61728-0.
2. Habraken JM, van der Wal WM, Ter Riet G, et al. Health-related quality of life and functional status in end-stage COPD: a longitudinal study. *Eur Respir J* 2011; 37: 280-288. 2010/06/10. DOI: 10.1183/09031936.00149309.
3. 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 2017/05/04. DOI: 10.1183/23120541.00068-2016.
4. Vermylen JH, Szmuilowicz E and Kalhan R. Palliative care in COPD: an unmet area for quality improvement. *Int J Chron Obstruct Pulmon Dis* 2015; 10: 1543-1551. 2015/09/09. DOI: 10.2147/copd.s74641.
5. Beernaert K, Cohen J, Deliens L, et al. Referral to palliative care in COPD and other chronic diseases: a population-based study. *Respir Med* 2013; 107: 1731-1739. 2013/07/03. DOI: 10.1016/j.rmed.2013.06.003.
6. *Quality standard for end of life care for adults. Issued: August 2011 last modified: October 2013.* 2013. National Institute for Health and Care Excellence.
7. Rietjens JAC, Sudore RL, Connolly M, et al. Definition and recommendations for advance care planning: an international consensus supported by the European Association for Palliative Care. *The Lancet Oncology* 2017; 18: e543-e551. 2017/09/09. DOI: 10.1016/s1470-2045(17)30582-x.
8. Boddaert M. *Netherlands Quality Framework for Palliative Care*. 2017.
9. Duenk RG, Verhagen C, Dekhuijzen P, et al. The view of pulmonologists on palliative care for patients with COPD: a survey study. *Int J Chron Obstruct Pulmon Dis* 2017; 12: 299-311. 2017/02/09. DOI: 10.2147/copd.s121294.
10. Momen N, Hadfield P, Kuhn I, et al. Discussing an uncertain future: end-of-life care conversations in chronic obstructive pulmonary disease. A systematic literature review and narrative synthesis. *Thorax* 2012; 67: 777-780. 2012/07/18. DOI: 10.1136/thoraxjnl-2012-201835.
11. Broese JMC, van der Kleij R, Verschuur EML, et al. Provision of Palliative Care in Patients with COPD: A Survey Among Pulmonologists and General Practitioners. *Int J Chron Obstruct Pulmon Dis* 2021; 16: 783-794. 2021/04/06. DOI: 10.2147/COPD.S293241.
12. GOLD. Pocket Guide to COPD Diagnosis, Management, and Prevention. A Guide for Health Care Professionals 2017.
13. Marin JM, Alfageme I, Almagro P, et al. Multicomponent indices to predict survival in COPD: the COCOMICS study. *Eur Respir J* 2013; 42: 323-332. 20121206. DOI: 10.1183/09031936.00121012.
14. Bellou V, Belbasis L, Konstantinidis AK, et al. Prognostic models for outcome prediction in patients with chronic obstructive pulmonary disease: systematic review and critical appraisal. *BMJ (Clinical research ed)* 2019; 367: l5358. 20191004. DOI: 10.1136/bmj.l5358.
15. Thomas K and Armstrong WJ. *Gold standards framework proactive identification guidance. 6th edition.* 2016. London: Gold Standards Framework and Royal College of General Practitioners.
16. White N, Kupeli N, Vickerstaff V, et al. How accurate is the 'Surprise Question' at identifying patients at the end of life? A systematic review and meta-analysis. *BMC Med* 2017; 15: 139. 20170802. DOI: 10.1186/s12916-017-0907-4.
17. Tripp D, Janis J, Jarrett B, et al. How Well Does the Surprise Question Predict 1-year Mortality for Patients Admitted with COPD? *Journal of general internal medicine* 2021 2021/01/08. DOI: 10.1007/s11606-020-06512-8.
18. Casale G, Magnani C, Fanelli R, et al. Supportive and palliative care indicators tool (SPICT™): content validity, feasibility and pre-test of the Italian version. *BMC Palliative Care* 2020; 19: 79. DOI: 10.1186/s12904-020-00584-3.
19. Thoonsen B, Engels Y, van RE, et al. Early identification of palliative care patients in general practice: development of RADboud indicators for PAlliative Care Needs (RADPAC). *Br J Gen Pract* 2012; 62: e625-e631. DOI: 10.3399/bjgp12X654597 [doi].
20. Duenk RG, Verhagen C, Bronkhorst EM, et al. Development of the ProPal-COPD tool to identify patients with COPD for proactive palliative care. *Int J Chron Obstruct Pulmon Dis* 2017; 12: 2121-2128. DOI: 10.2147/COPD.S140037 [doi];copd-12-2121 [pii].
21. Müllerova H, Maselli DJ, Locantore N, et al. Hospitalized exacerbations of COPD: risk factors and outcomes in the ECLIPSE cohort. *Chest* 2015; 147: 999-1007. DOI: 10.1378/chest.14-0655.
22. Meehan E, Foley T, Kelly C, et al. Advance Care Planning for Individuals With Chronic Obstructive Pulmonary Disease: A Scoping Review of the Literature. *J Pain Symptom Manage* 2020; 59: 1344-1361. 20191216. DOI: 10.1016/j.jpainsymman.2019.12.010.
23. Bleeker SE, Moll HA, Steyerberg EW, et al. External validation is necessary in prediction research: a clinical example. *Journal of clinical epidemiology* 2003; 56: 826-832. DOI: 10.1016/s0895-4356(03)00207-5.
24. Broese JMC, van der Kleij R, Kerstjens HAM, et al. A cluster randomized controlled trial on a multifaceted implementation strategy to promote integrated palliative care in COPD: study protocol of the COMPASSION study. *BMC Palliat Care* 2020; 19: 155. 2020/10/12. DOI: 10.1186/s12904-020-00657-3.
25. Broese JMC, Van der Kleij RMJJ, Verschuur EML, et al. Implementation of palliative care into routine COPD-care – mixed-method evaluation of the COMPASSION study. *Submitted* 2022.
26. Newton AS, March S, Gehring ND, et al. Establishing a Working Definition of User Experience for eHealth Interventions of Self-reported User Experience Measures With eHealth Researchers and Adolescents: Scoping Review. *Journal of medical Internet research* 2021; 23: e25012. 20211202. DOI: 10.2196/25012.

27. van Wijmen MPS, Schweitzer BPM, Pasman HR, et al. Identifying patients who could benefit from palliative care by making use of the general practice information system: the Surprise Question versus the SPICT. *Family practice* 2020; 37: 641-647. DOI: 10.1093/fampra/cmaa049.
28. Tan JY, Conceicao EP, Wee LE, et al. COVID-19 public health measures: a reduction in hospital admissions for COPD exacerbations. *Thorax* 2021; 76: 512-513. 20201203. DOI: 10.1136/thoraxjnl-2020-216083.
29. Gerayeli FV, Milne S, Cheung C, et al. COPD and the risk of poor outcomes in COVID-19: A systematic review and meta-analysis. *EClinicalMedicine* 2021; 33: 100789. 20210318. DOI: 10.1016/j.eclinm.2021.100789.
30. Veldhoven CMM, Nutma N, De Graaf W, et al. Screening with the double surprise question to predict deterioration and death: an explorative study. *BMC Palliat Care* 2019; 18: 118. 2019/12/29. DOI: 10.1186/s12904-019-0503-9.
31. Ermers DJ, Kuip EJ, Veldhoven C, et al. Timely identification of patients in need of palliative care using the Double Surprise Question: A prospective study on outpatients with cancer. *Palliat Med* 2021; 35: 592-602. 20210111. DOI: 10.1177/0269216320986720.
32. Epiphaniou E, Shipman C, Harding R, et al. Avoid ‘prognostic paralysis’--just get ahead and plan and co-ordinate care. *NPJ Prim Care Respir Med* 2014; 24: 14085. 20141009. DOI: 10.1038/npjpcrm.2014.85.
33. Ament SMC, van den Beuken-Everdingen M, Maessen JMC, et al. Professionals guidance about palliative medicine in chronic heart failure: a mixed-method study. *BMJ Support Palliat Care* 2020 20201126. DOI: 10.1136/bmjspcare-2020-002580.
34. Finamore P, Spruit MA, Schols J, et al. Clustering of patients with end-stage chronic diseases by symptoms: a new approach to identify health needs. *Aging Clin Exp Res* 2021; 33: 407-417. 20200411. DOI: 10.1007/s40520-020-01549-5.
35. Collins GS, Ogundimu EO and Altman DG. Sample size considerations for the external validation of a multivariable prognostic model: a resampling study. *Statistics in medicine* 2016; 35: 214-226. 20151109. DOI: 10.1002/sim.6787.
36. Broese JMC, Van der Kleij RMJJ, Verschuur EML, et al. The effect of integrated palliative care on quality of life and acute healthcare use in patients with COPD: results of the COMPASSION cluster randomized controlled trial. *Submitted* 2022.
37. Straw S, Byrom R, Gierula J, et al. Predicting one-year mortality in heart failure using the ‘Surprise Question’: a prospective pilot study. *Eur J Heart Fail* 2019; 21: 227-234. 20181211. DOI: 10.1002/ejhf.1353.

Chapter 8

General discussion

Patients with COPD may benefit from palliative care including advance care planning (ACP), because of their severe symptom burden and high mortality rates.[1,2] However, when I started my PhD trajectory, there was little evidence for the effectiveness of palliative care interventions for this patient group specifically.[3,4] Furthermore, it was unclear how palliative care could be organized for this patient group and which requirements could facilitate successful implementation.[5] Therefore, this thesis aimed to study how palliative care for patients with COPD and their informal caregivers could be effectively improved and organized. Several studies with various methodologies were conducted to broaden the knowledge of the effectiveness and process of palliative care integration into COPD care.

In this final chapter of this thesis, I will answer the research questions and critically discuss the methodologies used and implications of the main research findings. Finally, recommendations for clinical practice, education, policy and future research are provided.

Main findings

1. To what degree is palliative care for patients with COPD currently implemented and formalized in primary and secondary care in the Netherlands?

In a survey study (chapter 2), many pulmonologists and general practitioners stated that they frequently talk with patients about topics related to palliative care. They tend to prescribe opioids to treat dyspnea and involve palliative care specialists probably more often than a decade ago, indicating a growing recognition of the importance of palliative care for patients with COPD. Nonetheless, palliative care for patients with COPD and their informal caregivers is not well-structured or formalized, and ACP discussions often just happen in the context of acute care.

2. Have palliative care interventions been developed for patients with COPD and what evidence is available on the effectiveness and implementation outcomes?

The systematic review as described in chapter 3 identified twenty interventions, spanning both short-term and longitudinal approaches in diverse care settings, designed to improve the delivery of palliative care to individuals with COPD. Only four interventions (20%) were evaluated in sufficiently vigorous controlled trials, and findings on efficacy were found to be inconclusive and inconsistent. However, qualitative data indicated that having someone to call for support and education about breathlessness were most valued characteristics to patients. Most frequently named barriers were uncertainty about the timing of referral due to the unpredictable disease trajectory (referrers), time availability (providers) and accessibility (patients).

3. What is the effect of the implementation of integrated palliative care on patient, informal caregiver and healthcare provider outcomes?
In the COMPASSION study, a cluster randomized controlled trial in which eight hospital regions participated (chapter 5), we found no evidence that palliative care integrated into regular COPD care improves patient's quality of life or other well-being outcomes. However, our findings suggest that it can potentially reduce ICU admissions. We aimed to assess the effect on informal caregiver burden, but the response rates to questionnaires was insufficient to conduct analyses. Regarding healthcare providers, self-efficacy for delivering palliative care increased (chapter 6).

4. What is the effect of a multifaceted implementation strategy on implementation outcomes and what barriers hamper the implementation of integrated palliative care in routine COPD care?
With a combination of quantitative and qualitative data (chapter 6), we found that approximately half of the screened patients received an outpatient palliative care conversation, on average six weeks post-inclusion, primarily conducted by a pulmonologist and COPD nurse together. However, care continuity and coordination, and aftercare remained limited. Key barriers to implementation included time constraints, the COVID-19 pandemic, and barriers related to interdisciplinary and transmural collaboration. Implementation facilitators encompassed systematic screening of palliative patients, adapting to the patient's readiness, conducting joint palliative care conversations with a pulmonologist and COPD nurse, and regular meetings with a small team under the leadership of a dedicated implementation leader.

5. What is the accuracy of the ProPal-COPD tool in predicting 1-year mortality, and what are user-experiences of healthcare providers?
In a prospective validation cohort, the ProPal-COPD tool's ability to predict all-cause mortality within one year did not appear to be substantially better than previously established prediction models and the Surprise Question (chapter 7). However, the tool appeared user-friendly and found valuable by healthcare providers, as its indicators enhance their comprehension of the palliative phase and foster a shared understanding of the prognosis.

Combining clinical effectiveness and implementation research

From the first two studies conducted within this PhD project (the survey study and the systematic review as described in chapters 2 and 3), it became clear that there were gaps in practice and knowledge regarding structurally integrating palliative care into COPD care. Moreover, robust evidence on the clinical effectiveness in patients with COPD was lacking. Therefore, we set up a trial with a hybrid effectiveness-implementation design (described in chapter 4) in which we were able to simultaneously study the clinical effectiveness and the implementation process.[6] Doing so, we were able to address various research objectives and make efficient use of the limited time in this 4-year project to guarantee sufficient time needed for the inclusion and follow-up of patients.

Despite the benefits, designing a hybrid type 2 effectiveness-implementation study led to methodological challenges. It demands a complex balance between internal validity to assess clinical effectiveness on the one hand and factors facilitating implementation on the other. Various concessions had to be made, as already discussed in chapters 4 and 6. For instance, to facilitate implementation, the intervention was heterogenous across regions because intervention components were allowed to be tailored to regional needs. However, this limited the internal validity and thus, optimal effectiveness evaluation. On the other hand, healthcare providers had to focus on enrolling sufficient patients and informal caregivers for the effectiveness trial. This limited their time to implement intervention components. Given these drawbacks, combining the two objectives in one study should be done thoughtfully. By focusing on either clinical effectiveness or implementation, choices on methodologies may be easier to make, and a study can potentially become more robust and produce clearer study results. For future research, I would recommend to choose a hybrid type 1 design, combining a clinical effectiveness study with a process evaluation, or a type 3 design, testing one or more implementation strategies combined with collecting some relevant clinical outcomes.

Although our study provided valuable insights in implementation processes, the effectiveness evaluation of our intervention was hampered by implementation failure due to several implementation barriers including significant external factors like the COVID-19 pandemic. However, in hindsight, part of the implementation failure could possibly been prevented by testing the feasibility and study procedures before the trial, and providing a longer implementation period. Indeed, as good palliative care encompasses various aspects,[7] we had developed an intervention comprising different components: 1) identification using the ProPal-COPD tool, 2) one or more palliative care conversations including ACP, multidimensional assessment, and symptom management, 3) coordination and continuity of care, and 4) aftercare when a patient had died. However, during the trial it became clear that regions had difficulties implementing all components simultaneously (chapter 6). Screening with the ProPal-COPD tool went well, but with a significant proportion of patients no palliative care conversation had taken place, and transmural collaboration and aftercare remained inadequate. Furthermore, the inclusion of patients had already started while intervention components were still being implemented, resulting in patients filling out questionnaires without receiving the intervention. Future research should consider testing the feasibility of the complex intervention before the formal evaluation takes place, as is recommended by the Medical Research Council Framework,[8] or testing the different intervention components separately and implementing them consecutively, each with its matching outcome.[9] The question is though, whether this would have been attainable in a project funded for four years.

The impact of palliative care on patients with COPD

Unfortunately, we were unable to draw definitive conclusions about the effectiveness of our intervention (chapter 5). Next to implementation failure, factors related to the primary outcome measure played a role. We chose for quality of life as a primary outcome measure, as this is the ultimate aim of palliative care, according to its definition.[10] However, the fact that no previous study to date has found an effect of palliative care on quality of life in patients with COPD[11-19] raises the question whether this outcome measure is appropriate to assess the intervention effect in this patient group. First, quality of life is a broad outcome influenced by many factors. Moreover, it may be difficult to improve in advanced disease. Our intervention mostly consisted of only one outpatient conversation, which may have been insufficient to affect quality of life measurably. Also, as transmural collaboration remained poor, probably treatments were not continued in primary care. Second, the timing of the follow up questionnaires was not related to the occurrence of the palliative care conversations. Also, as COPD is characterized by occurrence of acute exacerbations, the capricious disease course may have influenced our measurements that were defined at fixed time points. Third, in line with previous studies,[13, 20] filling in questionnaires and returning them (despite multiple reminders by phone) appeared to be burdensome and difficult for patients with advanced COPD due to their frequent lack of energy and the fact that half of them have low literacy skills.[21] We chose to use the FACIT-Pal questionnaire as it covers all four palliative care dimensions (physical, psychological, social and spiritual), but some of its 46 items are abstract in nature and may be difficult to interpret.[22] Also, we included too many secondary outcome measures. As a result, we faced a high number of non-returned questionnaires. Either a new and short questionnaire appropriate for this patient group needs to be developed, a research nurse needs to be involved, or data on patient outcomes should be collected qualitatively instead of quantitatively, as was already suggested earlier by Horton et al. and Farquhar et al.[20, 23]

An outcome measure less broad and more specific related to the goal and timing of the intervention may have led to different results.[24] In a systematic review, Fleuren et al. identified five distinctive underlying goals of ACP that may be informative when selecting an outcome measure in future studies: 1) respecting individual patient autonomy, 2) improving quality of care, 3) strengthening relationships, 4) preparing for end-of-life, and 5) reducing overtreatment.[25] Depending on the goal emphasized in a palliative care intervention, future research could choose an appropriate outcome measure. For example, in relation to the goal of respecting patient autonomy, the documentation of care preferences could be studied, as was previously done in a randomized controlled trial involving ACP in patients with dementia.[26] To address the goal of improving quality of care, an outcome measure could focus on coping with COPD or mastery of breathlessness, which was evaluated in a breathlessness support service.[12] Regarding strengthening relationships, this could be qualitatively assessed by using the Content Coding for Contextualization of Care (4C) method.[27] When the goal is preparation for end-of-life, the Quality of end-of-life care Communication questionnaire (QOC) can be considered,[28] as was previously done in a trial testing a nurse-led ACP intervention.[29] Finally, to address the goal of reducing overtreatment, the number of hospital admissions and days could be assessed.

As COPD patients are far from a homogenous group, research is needed on what does work for whom, including studying the needs of patients from different cultural contexts. It is interesting to consider measuring patient tailored goals and assess whether these personalized goals have been reached. Finally, as advanced COPD significantly affects the patient's informal caregivers,[30] it is important to study how informal caregiver support can be integrated into palliative care interventions. We recommend to set up a separate study addressing informal caregivers' needs, as we experienced that their recruitment needs a different approach than the study inclusion of patients.

Although we failed to measure a positive effect on quality of life quantitatively, this does not mean that palliative care is unbeneficial for patients with advanced COPD. In a study where patients with COPD were presented with a standardized description of early palliative care, they were willing to receive this care.[31] In another study, patients with COPD preferred discussions during intervals of good health in contrast to last minute crisis-type decision-making.[32] Moreover, various qualitative studies found positive psychological effects, and no negative reactions have been described.[15, 16, 33, 34] In our interviews, patients and informal caregivers participating in the COMPASSION study stated that the palliative care conversations had given them clarity and peace of mind. (These data have not been published due to insufficient data saturation.) Healthcare providers unanimously described similar reactions of their patients to the conversations in interviews, and they definitely wanted to continue providing palliative care conversations (chapter 6). Therefore, we are still convinced that with optimized implementation patients with COPD and their informal caregivers can benefit from integrated palliative care.

Initiating palliative care in patients with COPD

In the literature, there has yet to be a consensus on *when* it is appropriate to start palliative care in patients with COPD. Various tools have been developed to predict prognosis and facilitate healthcare providers to identify patients needing palliative care.[35-37] The ProPal-COPD tool was previously developed by Duenk et al. in 2017, and with its short completion time and high sensitivity, as measured in an internal validity study, it seemed to be a promising tool.[38] Also, it combined clinical indicators with the Surprise Question, leaving space for 'the clinical view' of pulmonologists, and provided a binary outcome, making it feasible to use it as a clear inclusion criterion in a controlled trial. Therefore, we chose in the COMPASSION project to use the ProPal-COPD tool. In chapter 7, however, we found that the predictive validity to predict death within one year was disappointing.

Due to the failure to predict prognosis in COPD and the ambiguous relation between life expectancy and palliative care needs, it has been advocated to use needs-based tools instead. Recently, the I-HARP for COPD has been developed.[39] Furthermore, as COPD treatments cannot be divided into curative and palliative treatments searching for a transition point might seem superfluous. Ideally, palliative care components such as multidimensional assessment, optimal symptom management, and ACP are fully integrated into regular COPD care from diagnosis, with a gradually shifting focus over time, tailored to the patient's needs. Indeed, by using a two-track approach ('hope for the best, prepare for the worst'), ACP could be initiated in any stage of the disease. However, the reality of daily practice with limited time and financial resources, makes it infeasible to provide a comprehensive person-centered assessment to all COPD patients. Since palliative care discussions rarely take place and many healthcare providers are still reluctant to discuss end-of-life topics proactively, selecting patients most benefiting from a palliative care approach remains essential. Therefore, Waller et al. proposed to divide the identification process in two steps 1) a pragmatic method of identifying patients with palliative care needs and 2) a more comprehensive assessment.[40] Regarding the first step, in our interviews with healthcare providers on user experiences with the ProPal-COPD tool, we found that the systematic screening of patients admitted with an acute exacerbation increased healthcare providers' awareness and encouraged them to initiate palliative care conversations (chapter 7). Providing healthcare providers with better insight into prognosis, may activate them to introduce end-of-life topics in a timely and proactively manner. In a next step, eventually, we can integrate such an approach during the whole disease trajectory.

A possibility is to alter the usual frequency of outpatient visits. Today, patients are scheduled in a fixed scheme with every 3 or 6 months a regular control visit with their pulmonologist or COPD nurse. Bove et al. assessed in Denmark an alternative structure where fixed appointments were replaced with a flexible model tailored to the patient's needs. This new structure included at least one ACP conversation per year and phone contact whenever needed.[41] A similar model worked well in patients with Parkinson's disease.[42] Testing this alternative care structure for patients with COPD in the Netherlands would be interesting. Moreover, it aligns with the Dutch guideline, which recommends that ACP should take place at least once a year.[43] Next to addressing ACP and the four palliative care dimensions, breathlessness services based on the Breathing-Thinking-Functioning model promise to alleviate breathlessness in severe COPD.[44] Such a service has been tested in the Netherlands and appeared feasible.[45] Furthermore, integration of a palliative care approach into pulmonary rehabilitation seems promising because the multidisciplinary nature allows for an integrated approach to all four palliative care dimensions.[46]

Interdisciplinary collaboration

In the Netherlands, palliative care is not considered a distinct specialism, but it is delivered by generalists (e.g., GPs, nurses, pulmonologists, cardiologists), who receive support from palliative care specialists when required.[7] This is even more relevant in organ failure such as COPD, since disease-directed care and palliative care overlap.[47] In our systematic review described in chapter 3, we found that components most valued by COPD patients were: patient and family education on breathlessness management, direct access to a professional for support and an ongoing relationship. These components are not palliative care specific and require expertise in pulmonary medicine. Therefore, in the COMPASSION study we focused on integrating palliative care into regular COPD care rather than creating a separate palliative care service to which patients should be referred. An advantage is that a longitudinal relationship often already exists with the pulmonologist or COPD nurse. Also, they have a higher caseload of patients with severe COPD than general practitioners, allowing to create expertise.

As COPD care involves primary as well as secondary care providers and there are regional differences when palliative care specialists are involved, the roles and responsibilities of healthcare providers involved in the care of patients with severe COPD remain unclear.[48] As long as palliative care is not a standard part of medical training and nurse education, palliative care specialists may play a bigger role first. But conversely, palliative care specialists primarily have experience in oncology and need to be trained in supporting patients with COPD[49]. Patients with COPD need a significantly different approach than patients with cancer. As half of the COPD patients have low literacy,[21] communication should be adapted to the patient's level of understanding. More importantly, end-of-life topics must be gently introduced, as COPD patients do not always associate their disease with death and dying.[50] Also, specific COPD problems such as fear of suffocation need to be addressed.

As patients with COPD mostly live at home, and outpatient visits can become too burdensome in later stages of the disease, it is important to have a smooth continuity between hospital and primary care. However, during the COMPASSION project, it became clear that collaboration between the hospital and primary care remained challenging, even though we actively tried to involve general practitioners. Due to a lack of time and availability, pulmonologists were not always able contact the patient's general practitioner by phone after a palliative care conversation had taken place. To facilitate transmural collaboration and information exchange, working agreements should be made and safeguarded in a protocol. Furthermore, COPD nurses in primary care may have a pivotal role in the management of patients with severe COPD at home and can function as a linking pin between the hospital and primary care.[51] They have the possibility to support patients at home in their own environment, and usually have more time than general practitioners. However, they are not available in all regions.

Factors for successful implementation

Implementation is a complex process, for which active and appropriate strategies are needed.[52, 53] Although there has been a national guideline on palliative care COPD since 2011 that has been fully revised in 2021,[43] research has shown that simply acquiring knowledge without actively engaging with it has minimal influence on healthcare providers' behavior.[54] The findings of this thesis will contribute to a better understanding of what factors are needed to effectively implement palliative care into regular COPD care.

Healthcare providers need to be trained to gain knowledge and skills to change behavior. Today, medical doctors and nurses in COPD care receive little education on palliative care and related communication.[55] Their training mainly focuses on pharmacological treatments of physical symptoms, denying the possibility that patients eventually die from their disease. Reflection on your own attitude towards death and how you cope with it as a healthcare provider, is not part of their training.[56] In Chapter 6, we showed that the COMPASSION training (comprising of communication training with roleplay, education on the identification of palliative patients, dyspnea management, and transmural care collaboration) increased self-efficacy of healthcare providers and enhanced job satisfaction as they could contribute more meaningfully to the patient's wellbeing. Furthermore, an interesting finding was that doing the conversations jointly with a pulmonologist and COPD nurse was preferred, because they could reinforce each other. Also, sharing experiences with healthcare providers of different intervention regions stimulated to continue implementation. To allow scaling up, we transformed the training into a blended learning program in a follow-up project, which can be freely accessed via www.palliatievezorgcopd.nl. Strategies on a national level may be needed to achieve behavior change across all COPD healthcare providers in the Netherlands, including those who are not motivated to voluntarily participate in a training ('late adopters'). Therefore, it is essential that palliative COPD care training, including non-pharmacological dyspnea management, multidimensional assessment and communication skills to discuss end-of-life topics, is integrated as a standard part of the training to become a nurse, doctor or pulmonologist. Also, knowledge on the management of non-oncological diseases like COPD should be integrated into specialist palliative care training.

To further stimulate behavior change, practical tools are needed, as was emphasized by the field. Throughout the COMPASSION project, alongside the scientific output, we developed many hands-on tools for use in practice, e.g. information leaflets and videos for patients, informal caregivers, and healthcare providers. The tools are offered in the online toolbox www.palliatievezorgcopd.nl and are enthusiastically received by many healthcare providers. The online toolbox has around 100 visitors per week (Google Analytics) and won the national palliative care impact prize in February 2023.

Next to behavior change of individual healthcare providers, it is of equal importance that organizational and financial prerequisites are fulfilled, in order to integrate palliative care in COPD in all regions of the Netherlands.[57] To achieve lasting successful change, a project-based approach with specific goals is important.[58] As became clear during the COMPASSION project where healthcare providers had difficulties to fill out an action plan, this process should preferably led by a dedicated implementation leader, since healthcare providers often lack knowledge and skills to lead a project in a systematic way.[59] The frequency and duration of outpatient visits may require reconsideration, in order to guarantee sufficient time for proactive palliative care conversations. For example by reserving a fixed spot in the weekly schedule, or by planning fewer but lengthier consultations. Transmural collaboration may be improved by a shared medical record and different financing structure and need to be studied further. However, these huge challenges apply to all chronic care and need a national approach. Lastly, a set of quality indicators for monitoring palliative care would serve as a catalyst for implementing high-quality palliative care in practice. In the Netherlands, ongoing efforts are being made to develop and establish such an indicator set.[60-62]

Although healthcare providers never mentioned financial resources as a barrier, time constraints was the second most important barrier to provide palliative care for pulmonologists (chapter 2), as ACP discussions usually take more time than a regular outpatient visit. Therefore, to ensure successful and durable implementation across all regions, the financing structure of palliative care, including ACP, must be properly regulated. Palliative care interventions might easily become cost effective if it prevents intensive care admissions, as our findings in chapter 5 suggest and is shown by the systematic review of Flierman et al.[63] In the USA, healthcare providers may bill for ACP discussions under CPT Code 99497 from 2016.[64] Fortunately, there are ongoing developments in the Netherlands too. Since 2022, medical specialists can declare discussions about treatment options, called 'Time to Talk', on condition that an individual care plan is created and reviewed by a consultant of a specialist palliative care team.[65] Also, the NZa is planning experiments with alternative funding systems in order to stimulate regional transmural collaboration, such as bundle financing. These experiments will start in 2024. Although we will need some more patience before the incentives will be effective, these are hopeful developments.

Recommendations

The discussion of the main findings and methodological considerations yielded multiple recommendations regarding the integration of a proactive palliative care approach into regular COPD care. These recommendations will now be summarized, divided into recommendations for clinical practice, education, policy and future research.

Recommendations for clinical practice

- Patients with COPD should be systematically screened on palliative care needs, by using an easy, quick method. Although a perfect tool does not yet exist, the indicators of the ProPal-COPD tool including the Surprise Question could be used.

- All healthcare providers are encouraged to have a look at the online toolbox www.palliatievezorgcopd.nl, where they can freely select from a wide range of readily available tools that best suit their needs and preferences.
- In COPD, using a two-track approach in palliative care conversations ('hope for the best, prepare for the worst') helps to initiate end-of-life topics in an earlier stage of the disease.
- Respiratory care should be organized in such a way that it ensures sufficient time for palliative care conversations, e.g. by reserving a fixed spot in the weekly schedule.
- Establish working agreements about interdisciplinary and transmural collaboration and reach consensus when to involve specialist palliative care and how all involved healthcare providers will be informed.
- COPD nurses in primary care can play a pivotal role in palliative care in COPD as care coordinator and linking pin between primary and secondary care, and should become available across all regions in the Netherlands.
- To guarantee successful and sustainable implementation, install a small implementation team that works with clearly defined goals, meets regularly, and is led by an engaged implementation leader. A blended learning program have been developed and provides guidance and practical tips.

Recommendations for education

- Non-pharmacological dyspnea management, multidimensional assessment, and communication skills to discuss end-of-life topics should be integrated as a standard part of the training to become a nurse, medical doctor, or pulmonologist.
- Part of the training should be to understand the healthcare provider's own barriers, biases, and attitude towards death and dying, as the difficulty in talking about death often reflects one's discomfort.
- Next to the management of oncological diseases, palliative care specialists should be trained in COPD management and learn how to communicate appropriately with patients with COPD.

Recommendations for policy

- Define a set of quality indicators that are easy to extract from the medical records to monitor the quality of palliative care.
- Make regulations for an appropriate financial structure of palliative care, allowing interdisciplinary and transmural collaboration.
- For the development and nationwide implementation of complex interventions, funding should be available for implementation projects over a period exceeding four years, considering the comprehensive nature of the process and to guarantee continuity of expertise.

8

Future research

- Our study emphasized the importance to test the intervention's and study procedures' feasibility and incorporate an implementation period, before formal evaluation of the clinical effectiveness takes place.
- When preparing an effectiveness study, define the focus of the intervention based on the five goals of Fleuren et al.[25] and select an outcome measure appropriate for the intervention, while considering the low literacy and energy levels of patients with COPD.
- To reach consensus on when specialist palliative care should be involved in patients with severe COPD, a study using a Delphi design should be conducted.
- Future research is needed on how informal caregiver needs can be addressed.
- Assess the feasibility of an alternative care structure that replaces fixed control visits with a flexible model tailored to patient needs, including an annual ACP ("Look Back and Ahead") conversation and access to phone contact.

Final conclusion

Patients with advanced COPD and their informal caregivers suffer from a high symptom burden that has been insufficiently addressed in the past. Healthcare providers and policymakers are becoming increasingly aware that palliative care for this patient group genuinely needs to be proactively and structurally provided. The findings of this thesis contribute to the understanding what is needed to integrate a palliative care approach into COPD care. The tools and blended learning program developed during and after the PhD-project directly support healthcare providers in their day-to-day clinical practice. However, we are not there yet. Future research is needed to create evidence on the clinical effectiveness to support guidelines, and to explore how informal caregiver needs can be addressed. Furthermore, prerequisites need to be met, such as changes in the care organization providing more time for palliative care conversations, and financial structures that allow interdisciplinary and transmural collaboration.

8

References

1. Habraken JM, van der Wal WM, Ter Riet G, et al. Health-related quality of life and functional status in end-stage COPD: a longitudinal study. *Eur Respir J* 2011; 37: 280-288. 2010/06/10. DOI: 10.1183/09031936.00149309.
2. Lozano R, Naghavi M, Foreman K, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012; 380: 2095-2128. 2012/12/19. DOI: 10.1016/s0140-6736(12)61728-0.
3. 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. 2016/11/29. DOI: 10.1001/jama.2016.16840.
4. Siouta N, van Beek K, Preston N, et al. Towards integration of palliative care in patients with chronic heart failure and chronic obstructive pulmonary disease: a systematic literature review of European guidelines and pathways. *BMC Palliat Care* 2016; 15: 18. 2016/02/14. DOI: 10.1186/s12904-016-0089-4.
5. Dalgaard KM, Bergenholtz H, Nielsen ME, et al. Early integration of palliative care in hospitals: A systematic review on methods, barriers, and outcome. *Palliat Support Care* 2014; 12: 495-513. DOI: S1478951513001338 [pii];10.1017/S1478951513001338 [doi].
6. Curran GM, Bauer M, Mittman B, et al. Effectiveness-implementation hybrid designs: combining elements of clinical effectiveness and implementation research to enhance public health impact. *Med Care* 2012; 50: 217-226. 2012/02/09. DOI: 10.1097/MLR.0b013e3182408812.
7. IKNL/Palliactief. Netherlands Quality Framework for Palliative Care. 2017.
8. Moore GF, Audrey S, Barker M, et al. Process evaluation of complex interventions: Medical Research Council guidance. *BMJ (Clinical research ed)* 2015; 350: h1258. 2015/03/21. DOI: 10.1136/bmj.h1258.
9. Levati S, Campbell P, Frost R, et al. Optimisation of complex health interventions prior to a randomised controlled trial: a scoping review of strategies used. *Pilot and Feasibility Studies* 2016; 2: 17. DOI: 10.1186/s40814-016-0058-y.
10. Sepúlveda C, Marlin A, Yoshida T, et al. Palliative Care: the World Health Organization's global perspective. *J Pain Symptom Manage* 2002; 24: 91-96. DOI: 10.1016/s0885-3924(02)00440-2.
11. 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. DOI: 10.1089/jpm.2006.9.111 [doi].
12. 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. DOI: S2213-2600(14)70226-7 [pii];10.1016/S2213-2600(14)70226-7 [doi].
13. 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. DOI: 10.2147/COPD.S141974 [doi];copd-12-2795 [pii].
14. 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. DOI: 10.1001/archinte.164.1.83 [doi];164/1/83 [pii].
15. Rocker GM and Verma JY. 'INSPIRED' COPD Outreach Program: doing the right things right. *Clinical and investigative medicine Medecine clinique et experimentale* 2014; 37: E311-319. 2014/10/06.
16. 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. *Journal of Hospice & Palliative Nursing* 2014; 16: 514-520.
17. 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. 2019/10/13. DOI: 10.1016/j.jpainsymman.2019.09.012.
18. 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. 2018/09/27. DOI: 10.1089/jpm.2018.0321.
19. 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. DOI: 10.1159/000495312.
20. 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. DOI: 10.1089/jpm.2012.0285 [doi].
21. Heijmans M, Brabers A and Rademakers J. *Hoe gezondheidsvaardig is Nederland? Factsheet Gezondheidsvaardigheden–Cijfers 2019*. 2019. Utrecht: Nivel.
22. Lyons KD, Bakitas M, Hegel MT, et al. Reliability and validity of the Functional Assessment of Chronic Illness Therapy-Palliative care (FACIT-Pal) scale. *J Pain Symptom Manage* 2009; 37: 23-32. 2008/05/28. DOI: 10.1016/j.jpainsymman.2007.12.015.
23. 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. DOI: 10.1186/s13063-016-1304-6 [doi];10.1186/s13063-016-1304-6 [pii].
24. Dodd SR, Payne SA, Preston NJ, et al. Understanding the Outcomes of Supplementary Support Services in Palliative Care for Older People. A Scoping Review and Mapping Exercise. *J Pain Symptom Manage* 2020 2020/03/24. DOI: 10.1016/j.jpainsymman.2020.03.010.

25. Fleuren N, Depla M, Janssen DJA, et al. Underlying goals of advance care planning (ACP): a qualitative analysis of the literature. *BMC Palliat Care* 2020; 19: 27. 2020/03/08. DOI: 10.1186/s12904-020-0535-1.
26. Tilburgs B, Koopmans R, Vernooij-Dassen M, et al. Educating Dutch General Practitioners in Dementia Advance Care Planning: A Cluster Randomized Controlled Trial. *J Am Med Dir Assoc* 2020; 21: 837-842.e834. 2019/11/25. DOI: 10.1016/j.jamda.2019.09.010.
27. Weiner SJ, Kelly B, Ashley N, et al. Content coding for contextualization of care: evaluating physician performance at patient-centered decision making. *Med Decis Making* 2014; 34: 97-106. 20130619. DOI: 10.1177/0272989x13493146.
28. Engelberg R, Downey L and Curtis JR. Psychometric characteristics of a quality of communication questionnaire assessing communication about end-of-life care. *J Palliat Med* 2006; 9: 1086-1098. DOI: 10.1089/jpm.2006.9.1086.
29. Houben CHM, Spruit MA, Luyten H, et al. Cluster-randomised trial of a nurse-led advance care planning session in patients with COPD and their loved ones. *Thorax* 2019; 74: 328-336. 20190119. DOI: 10.1136/thoraxjnl-2018-211943.
30. Nakken N, Janssen DJ, van den Bogaart EH, et al. Informal caregivers of patients with COPD: Home Sweet Home? *European respiratory review : an official journal of the European Respiratory Society* 2015; 24: 498-504. 2015/09/02. DOI: 10.1183/16000617.00010114.
31. Iyer AS, Dionne-Odom JN, Ford SM, et al. A Formative Evaluation of Patient and Family Caregiver Perspectives on Early Palliative Care in Chronic Obstructive Pulmonary Disease across Disease Severity. *Annals of the American Thoracic Society* 2019; 16: 1024-1033. DOI: 10.1513/AnnalsATS.201902-112OC.
32. Reinke LF, Engelberg RA, Shannon SE, et al. Transitions regarding palliative and end-of-life care in severe chronic obstructive pulmonary disease or advanced cancer: themes identified by patients, families, and clinicians. *J Palliat Med* 2008; 11: 601-609. 2008/05/06. DOI: 10.1089/jpm.2007.0236.
33. 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…". *Journal of Pain and Symptom Management* 2003; 26: 1010-1015.
34. 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. DOI: npjpcrm201520 [pii];10.1038/npjpcrm.2015.20 [doi].
35. Casale G, Magnani C, Fanelli R, et al. Supportive and palliative care indicators tool (SPICT™): content validity, feasibility and pre-test of the Italian version. *BMC Palliative Care* 2020; 19: 79. DOI: 10.1186/s12904-020-00584-3.
36. Thoonsen B, Engels Y, van RE, et al. Early identification of palliative care patients in general practice: development of RADboud indicators for PAlliative Care Needs (RADPAC). *Br J Gen Pract* 2012; 62: e625-e631. DOI: 10.3399/bjgp12X654597 [doi].

37. Bellou V, Belbasis L, Konstantinidis AK, et al. Prognostic models for outcome prediction in patients with chronic obstructive pulmonary disease: systematic review and critical appraisal. *BMJ (Clinical research ed)* 2019; 367: l5358. 20191004. DOI: 10.1136/bmj.l5358.
38. Duenk RG, Verhagen C, Bronkhorst EM, et al. Development of the ProPal-COPD tool to identify patients with COPD for proactive palliative care. *Int J Chron Obstruct Pulmon Dis* 2017; 12: 2121-2128. DOI: 10.2147/COPD.S140037 [doi];copd-12-2121 [pii].
39. Janssen DJ, Ament SM, Boyne J, et al. Characteristics for a tool for timely identification of palliative needs in heart failure: The views of Dutch patients, their families and healthcare professionals. *European journal of cardiovascular nursing : journal of the Working Group on Cardiovascular Nursing of the European Society of Cardiology* 2020: 1474515120918962. 2020/05/07. DOI: 10.1177/1474515120918962.
40. Waller A, Hobden B, Fakes K, et al. A Systematic Review of the Development and Implementation of Needs-Based Palliative Care Tools in Heart Failure and Chronic Respiratory Disease. *Front Cardiovasc Med* 2022; 9: 878428. 20220413. DOI: 10.3389/fcvm.2022.878428.
41. 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. 2019/03/04. DOI: 10.1186/s12904-019-0410-0.
42. Bloem BR, Darweesh SKL and Meinders MJ. Palliative Programs for Persons With Parkinsonism-The Next Frontier. *JAMA Neurol* 2020; 77: 548-550. DOI: 10.1001/jamaneurol.2019.4697.
43. IKNL/LAN. *National guideline Palliative care in COPD, version 2.0*. 2021. Utrecht, The Netherlands.
44. Spathis A, Booth S, Moffat C, et al. The Breathing, Thinking, Functioning clinical model: a proposal to facilitate evidence-based breathlessness management in chronic respiratory disease. *NPJ Prim Care Respir Med* 2017; 27: 27. 2017/04/23. DOI: 10.1038/s41533-017-0024-z.
45. Mooren K, Wester D, Kerstjens H, et al. Filling the Gap: A Feasibility Study of a COPD-Specific Breathlessness Service. *Copd* 2022; 19: 324-329. DOI: 10.1080/15412555.2022.2099821.
46. 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. *Chronic respiratory disease* 2014; 11: 111-119. 2014/04/15. DOI: 10.1177/1479972314529674.
47. Harrington SE, Rogers E and Davis M. Palliative care and chronic obstructive pulmonary disease: where the lines meet. *Curr Opin Pulm Med* 2017; 23: 154-160. DOI: 10.1097/mcp.0000000000000358.
48. Oishi A and Murtagh FE. The challenges of uncertainty and interprofessional collaboration in palliative care for non-cancer patients in the community: a systematic review of views from patients, carers and health-care professionals. *Palliat Med* 2014; 28: 1081-1098. DOI: 0269216314531999 [pii];10.1177/0269216314531999 [doi].
49. PZNL. *Palliatieve zorg in Nederlandse ziekenhuizen 2022. (available from www.palliaweb.nl).*

50. Knauft E, Nielsen EL, Engelberg RA, et al. Barriers and facilitators to end-of-life care communication for patients with COPD. *Chest* 2005; 127: 2188-2196. 2005/06/11. DOI: 10.1378/chest.127.6.2188.
51. Disler R, Cui Y, Luckett T, et al. Respiratory Nurses Have Positive Attitudes But Lack Confidence in Advance Care Planning for Chronic Obstructive Pulmonary Disease: Online Survey. *J Hosp Palliat Nurs* 2021; 23: 442-454. DOI: 10.1097/njh.0000000000000778.
52. Cabana MD, Rand Cs Fau - Powe NR, Powe Nr Fau - Wu AW, et al. Why don't physicians follow clinical practice guidelines? A framework for improvement. *JAMA* 1999; 282.
53. Powell BJ, Beidas RS, Lewis CC, et al. Methods to Improve the Selection and Tailoring of Implementation Strategies. *The journal of behavioral health services & research* 2017; 44: 177-194. 2015/08/21. DOI: 10.1007/s11414-015-9475-6.
54. Davis DA, Thomson MA, Oxman AD, et al. Changing physician performance. A systematic review of the effect of continuing medical education strategies. *Jama* 1995; 274: 700-705. DOI: 10.1001/jama.274.9.700.
55. de Bruin J, Verhoef MJ, Slaets JPJ, et al. End-of-life care in the Dutch medical curricula.
56. Galiana L, Oliver A, De Simone G, et al. A Brief Measure for the Assessment of Competence in Coping With Death: The Coping With Death Scale Short Version. *J Pain Symptom Manage* 2019; 57: 209-215. 20181115. DOI: 10.1016/j.jpainsymman.2018.11.003.
57. Wensing M and Grol R. Knowledge translation in health: how implementation science could contribute more. *BMC Medicine* 2019; 17: 88. DOI: 10.1186/s12916-019-1322-9.
58. Hagger MS and Luszczynska A. Implementation intention and action planning interventions in health contexts: state of the research and proposals for the way forward. *Applied psychology Health and well-being* 2014; 6: 1-47. 2014/03/05. DOI: 10.1111/aphw.12017.
59. Solberg LI, Brekke Ml Fau - Kottke TE, Kottke Te Fau - Steel RP, et al. Continuous quality improvement in primary care: what's happening?
60. Pasman HR, Brandt HE, Deliens L, et al. Quality indicators for palliative care: a systematic review. *J Pain Symptom Manage* 2009; 38: 145-156. DOI: 10.1016/j.jpainsymman.2008.07.008.
61. Brandt HE, Francke AL, Pasman HRW, et al. *Indicatoren voor Palliatieve Zorg. Ontwikkeling en toetsing van een set kwaliteitsindicatoren voor de palliatieve zorgverlening*. 2009. NIVEL.
62. Van Schoten S, Schouten B, de Jong L, et al. *Kwaliteitsindicatoren en zorggerelateerde schade aan het levenseinde Een retrospectief dossieronderzoek bij patiënten overleden in Nederlandse ziekenhuizen*. 2023. NIVEL.
63. Flierman I, Gieteling E, Van Rijn M, et al. Effectiveness of transmural team-based palliative care in prevention of hospitalizations in patients at the end of life: A systematic review and meta-analysis. *Palliat Med* 2023; 37: 75-87. 20221221. DOI: 10.1177/02692163221135616.
64. Center for Medicare and Medicaid Services. Frequently Asked Questions about Billing the Physician Fee Schedule for Advance Care Planning Services, https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/PhysicianFeeSched/Downloads/FAQ-Advance-Care-Planning.pdf (July 2016).

65. Nederlandse zorgautoriteit. Prestatiebeschrijvingbeschikking facultatieve prestatie Time to talk: bespreken wensen en grenzen in de palliatieve fase - TB/REG-21685-01, https://puc.overheid.nl/nza/doc/PUC_660378_22/1/ (2021).

Chapter 9

Summary

Chronic Obstructive Pulmonary Disease (COPD) is an incurable, progressive lung disease and is the third leading cause of death globally. Patients suffering from COPD experience debilitating symptoms such as breathlessness, fatigue, anxiety, and depression, resulting in a reduced quality of life. Patients with severe COPD may benefit from a palliative care approach to improve the quality of life and reduce symptom burden. However, palliative care is poorly implemented due to various reasons, including the disease's unpredictable trajectory, patient and family's limited understanding of COPD and palliative care, and healthcare providers' lack of communication skills or time constraints. Therefore, the COMPASSION project, initiated by the Lung Alliance Netherlands, Leiden University Medical Center, and Radboudumc, aimed to improve the implementation of palliative care provision for patients with COPD and their informal caregivers.

First, in **Chapter 2,** we explored the current level of palliative care provision for patients with COPD in the Netherlands. We developed a survey based on previous studies and national guidelines and invited pulmonologists and general practitioners to complete the survey between April and August 2019. Data were analyzed using descriptive statistics. Most physicians reported discussing palliative care topics with COPD patients, and opioid prescription for dyspnea was common. This appeared to have increased compared with numbers from previous research. However, the study also showed that palliative care for patients with COPD remained mainly unstructured, with only a minority of general practices or hospitals having formalized agreements or protocols. Often, discussions took place in an acute care setting. However, there was a positive trend towards improvement, with half of the pulmonologists and one-tenth of general practitioners intending to establish protocols in the future. The most critical barrier for palliative care discussions appeared to be difficulty predicting the disease course. Collaboration between healthcare providers was generally satisfactory, but information exchange between primary and secondary care was identified as an area for improvement. The study highlights the need for clear guidance on the timing of palliative care discussions, specialist palliative care referrals, and improved care continuity.

In **Chapter 3**, we searched the international literature to systematically review the evidence available on palliative care interventions in patients with COPD. Across seven databases, we screened for eligible studies published between January 1990 and June 2020. We identified 31 articles reporting on 20 palliative care interventions, varying from short-term interventions focused on breathlessness to longitudinal coordinated care models. Although qualitative results indicated that the acceptance was high among patients and informal caregivers (with 'having someone to call for support' and 'education about breathlessness' as the most valued characteristics), quantitative results on effectiveness were mixed and inconclusive. We concluded that little high-quality evidence was available since few interventions had been evaluated using a controlled study design. Also, adequate process evaluations using standardized methodologies were still lacking.

To fill this knowledge gap, we designed a hybrid type 2 effectiveness-implementation study in which the integration of palliative care into regular COPD care was studied, the COMPASSION trial. A hybrid type 2 design was chosen because it allows studying both the clinical effectiveness of an intervention and its implementation process simultaneously, with equal importance. In **Chapter 4**, the study protocol of the COMPASSION trial was comprehensively described. We developed an integrated palliative care intervention based on existing guidelines, a literature review, and input from patient and professional organizations. The intervention consisted of 1) identification of palliative patients with COPD admitted to the hospital for an acute exacerbation using the ProPal-COPD tool, 2) palliative care conversations comprising a multidimensional assessment, symptom management, and advance care planning, 3) coordination and continuity of care, and 4) aftercare for the informal caregiver when a patient died. An implementation strategy was developed to facilitate the uptake of the intervention: an online toolbox with practical information and existing tools, two interactive training sessions including roleplay for healthcare providers, a regional action plan, and implementation guidance during monitoring meetings. In the Netherlands, eight hospital regions (pulmonary care departments collaborating with affiliated general practitioners, home care organizations, and palliative care consultation teams) were recruited and randomized into the intervention group or control group. Healthcare providers of the four intervention regions received the implementation strategy, and healthcare providers of the four control regions continued to provide care as usual. Various clinical patient outcomes were measured using questionnaires and medical record data. Additionally, informal caregiver burden and healthcare professionals' self-efficacy to provide palliative care were measured by questionnaires. The implementation process was evaluated using mixed methods. The results of the COMPASSION trial are described in Chapters 5 and 6.

In **Chapter 5**, we examined the effects of palliative care on the clinical outcomes of patients with COPD. A cluster randomized controlled trial was performed across the eight hospital regions. Patients admitted to the hospital with an exacerbation of COPD and a positive ProPal-COPD score were included in the study between May 2019 and August 2020. Quality of life was the primary outcome measure and measured using the FACIT-Pal questionnaire, a 46-item questionnaire consisting of four subscales on physical, social/family, emotional, and functional well-being, and a fifth palliative care subscale. Secondary outcomes were spiritual well-being, anxiety and depression, the number of emergency department visits, the number of unplanned hospital admissions, the number of intensive care unit admissions, and the place of death. Questionnaires were administered at baseline and three and six months after inclusion. Medical record data were assessed twelve months after inclusion. Data were analyzed using generalized linear mixed modeling. In total, 222 patients were included. Quality of life and other secondary outcomes did not differ between patients of the intervention group and those of the control group. However, intensive care unit admissions were lower in the intervention group. Factors hampering the effectiveness evaluation included insufficient power due to the COVID-19 pandemic, not all patients of the intervention group receiving the intervention, and several patients not returning questionnaires.

In **Chapter 6**, the implementation strategy and process were comprehensively evaluated using process data, questionnaires, medical records, and interview data. The training including roleplay was positively evaluated and improved healthcare provider's self-efficacy in providing palliative care, measured by the End-Of-Life Professional Caregiver Survey (EPCS). Less than half of the 98 patients identified received one or more palliative care conversations at the outpatient clinic, on average six weeks after inclusion, and held mainly by the pulmonologist and COPD nurse together. The intervention was highly valued because it gave patients and relatives more peace and clarity and higher provider job satisfaction. The most important barriers to implementation were insufficient time for palliative care conversations, low priority to implementation due to the COVID-19 pandemic, and lack of a communication tool for transmural collaboration. Facilitators were systematic screening of patients, adapting to the patient's readiness, conducting palliative care conversations with a pulmonologist and COPD nurse, and meeting regularly with a small team led by a dedicated project leader. The study highlights the importance of communication training and setting up a small project team led by a dedicated implementation leader. Also, it emphasizes that future research is needed to optimize transmural collaboration and reach consensus on when to involve specialist palliative care.

As identification of the palliative phase was considered a main barrier to palliative care provision, the ProPal-COPD tool was previously developed by Duenk et al. to facilitate healthcare providers to identify palliative patients with COPD during hospital admission for an exacerbation of COPD. The prediction model was based on the Surprise Question and six clinical indicators: MRC dyspnea score, CCQ score, lung function, BMI, specific comorbidities, and previous hospitalizations. Death within one year was used as a proxy for palliative care needs and the tool seemed promising with a high sensitivity. In **Chapter** 7, the ProPal-COPD tool was externally validated and we assessed user experiences of healthcare providers using interview data. We showed that the tool did not predict 1-year mortality with high accuracy, but in the qualitative evaluation, we found that systematically screening patients using its indicators helped healthcare providers to become aware of the palliative phase and to timely initiate appropriate care in COPD patients with palliative care needs.

To conclude, in **Chapter 8**, the main research findings are summarized and critically discussed in light of the methodologies used and previous literature. The chapter also reflects on the implications of the results of this thesis on clinical practice and future research. First, methodological challenges must be considered when designing a hybrid effectiveness-implementation study. I recommend testing the feasibility and study procedures before the trial and providing a more extended implementation period before collecting clinical effectiveness data. Second, a specific outcome measure aligned with the goal and timing of the intervention should be chosen. Indeed, our qualitative data showed that palliative care leads to more clarity and peace of mind in patients with COPD, but the questionnaires did not capture this. It is questionable whether existing questionnaires are appropriate to assess the quality of life in patients with severe COPD and whether a broad outcome such as quality of life is an appropriate measure to assess palliative care intervention effects in this patient group at all. Third, this thesis contributes to the ongoing discussion of when palliative care should be initiated. Although a clear tipping point may not exist within the COPD trajectory, we found that systematic screening of patients is essential to overcome the healthcare provider's reluctance to discuss end-of-life topics. Fourth, I address the uncertainty of the roles and responsibilities of healthcare providers involved in caring for patients with severe COPD and the challenges to provide continuous care. Fifth, I discuss what is needed to successfully implement palliative care into COPD care. Achieving this requires behavior change in individual healthcare providers and organizational changes with appropriate financial structures. Finally, I conclude with recommendations for clinical practice, education, policy, and future research.

Nederlandse samenvatting

Chronic Obstructive Pulmonary Disease (COPD) is een ongeneeslijke, progressieve longziekte en wereldwijd de op twee na belangrijkste doodsoorzaak. Patiënten met COPD ervaren vaak invaliderende symptomen zoals kortademigheid, vermoeidheid, angst en depressie, wat resulteert in een verminderde kwaliteit van leven. Patiënten met ernstige COPD kunnen baat hebben bij een palliatieve zorgbenadering om de kwaliteit van leven te verbeteren en de symptoomlast te verminderen. Echter, palliatieve zorg wordt vaak niet ingezet om verschillende redenen, waaronder het onvoorspelbare verloop van de ziekte, de beperkte kennis van patiënten en familie over wat COPD en palliatieve zorg inhoudt en het gebrek aan communicatievaardigheden of tijdgebrek bij zorgverleners. Daarom was het doel van het COMPASSION-project, geïnitieerd door de Long Alliantie Nederland, het Leids Universitair Medisch Centrum en het Radboudumc, om de implementatie van palliatieve zorg voor patiënten met COPD en hun mantelzorgers te verbeteren.

Allereerst onderzochten we in **hoofdstuk 2** de huidige mate van palliatieve zorgverlening voor patiënten met COPD in Nederland. We ontwikkelden een vragenlijst op basis van eerdere studies en landelijke richtlijnen en nodigden longartsen en huisartsen uit om de vragenlijst in te vullen tussen april en augustus 2019. De gegevens werden geanalyseerd met behulp van beschrijvende statistiek. De meeste artsen gaven aan palliatieve zorgonderwerpen te bespreken met COPD-patiënten en opioïden voor te schrijven voor kortademigheid. Dit leek toegenomen vergeleken met cijfers uit eerder onderzoek. Uit het onderzoek bleek echter ook dat palliatieve zorg voor patiënten met COPD voornamelijk ongestructureerd was en dat slechts een minderheid van de huisartsenpraktijken of ziekenhuizen geformaliseerde afspraken of protocollen had. Vaak vonden de gesprekken plaats in een acute zorgsetting. Er was echter een positieve trend zichtbaar: de helft van de longartsen en een tiende van de huisartsen was van plan om in de toekomst protocollen op te stellen. De meest belangrijke belemmering voor het voeren van palliatieve zorggesprekken bleek het moeilijk kunnen voorspellen van het ziektebeloop. De samenwerking tussen zorgverleners was over het algemeen naar tevredenheid, maar informatie-uitwisseling tussen de eerstelijnszorg en tweedelijnszorg werd gezien als verbeterpunt. Het onderzoek benadrukt de behoefte aan duidelijke richtlijnen over de timing van palliatieve zorggesprekken, verwijzingen naar specialistische palliatieve zorg en betere continuïteit van de zorg.

In **hoofdstuk 3** doorzochten we de internationale literatuur om op systematische wijze het bestaande wetenschappelijk onderzoek naar palliatieve zorginterventies bij patiënten met COPD te beoordelen. In zeven databases hebben we gezocht naar relevante studies die gepubliceerd zijn tussen januari 1990 en juni 2020. We vonden 31 artikelen die rapporteerden over 20 palliatieve zorginterventies, variërend van kortdurende interventies gericht op kortademigheid tot langdurige interventies met zorgcoördinatie. Hoewel kwalitatieve resultaten aantoonden dat de mate van acceptatie hoog was onder patiënten en mantelzorgers (met 'iemand hebben die je kan bellen voor ondersteuning' en 'voorlichting over kortademigheid' als meest waardevolle aspecten), waren de kwantitatieve resultaten over de effectiviteit gemengd en niet eenduidig. We concludeerden dat er nog maar weinig bewijs van hoge kwaliteit beschikbaar was, omdat slechts enkele interventies waren geëvalueerd in een gecontroleerde onderzoeksopzet. Ook ontbraken nog goede procesevaluaties.

Om deze kenniskloof te dichten, ontwierpen we een hybride type 2 effectiviteits-implementatiestudie waarin de inbedding van palliatieve zorg in de reguliere COPD-zorg werd bestudeerd, het COMPASSION-onderzoek. Er werd gekozen voor een hybride type 2 design omdat hiermee gelijktijdig de klinische effectiviteit van een interventie en het implementatieproces bestudeerd kunnen worden. In **hoofdstuk 4** werd het studieprotocol van het COMPASSION-onderzoek uitgebreid beschreven. We ontwikkelden een interventie voor geïntegreerde palliatieve zorg op basis van bestaande richtlijnen, literatuuronderzoek en input van patiënten- en professionele organisaties. De interventie bestond uit 1) identificatie van palliatieve patiënten met COPD die in het ziekenhuis werden opgenomen voor een longaanval met behulp van de ProPal-COPD tool, 2) palliatieve zorggesprekken bestaande uit een multidimensionaal assessment, symptoommanagement en advance care planning, 3) coördinatie en continuïteit van zorg, en 4) nazorg voor de mantelzorger wanneer een patiënt overleed. Er werd een implementatiestrategie ontwikkeld om de invoering van de interventie te faciliteren: een online toolbox met praktische informatie en bestaande hulpmiddelen, twee interactieve trainingssessies inclusief communicatietraining met rollenspellen voor zorgverleners, een regionaal actieplan en implementatiebegeleiding tijdens monitoringbijeenkomsten. Er werden in Nederland acht ziekenhuisregio's (longafdelingen met huisartsen, thuiszorgorganisaties en consultatieteams palliatieve zorg) geworven en gerandomiseerd naar de interventiegroep of de controlegroep. Zorgverleners in de vier interventieregio's ontvingen de implementatiestrategie en zorgverleners in de vier controleregio's bleven hun gebruikelijke zorg verlenen. Verschillende klinische patiëntuitkomsten werden gemeten met behulp van vragenlijsten en gegevens uit het medisch dossier. Daarnaast werden ook mantelzorgerbelasting en de *self-efficacy* van zorgverleners om palliatieve zorg te verlenen gemeten aan de hand van vragenlijsten. Het implementatieproces werd geëvalueerd met behulp van kwalitatieve en kwantitatieve onderzoeksmethodes (*mixed methods*). De resultaten van het COMPASSION-onderzoek worden beschreven in hoofdstuk 5 en 6.

In **hoofdstuk 5** onderzochten we het effect van palliatieve zorg op klinische patiëntuitkomsten. Een cluster gerandomiseerde gecontroleerde trial werd uitgevoerd in de acht ziekenhuisregio's. Patiënten die werden opgenomen in het ziekenhuis met een longaanval en een positieve ProPal-COPD score werden geïncludeerd in de studie tussen mei 2019 en augustus 2020. Kwaliteit van leven was de primaire uitkomstmaat en werd gemeten met behulp van de FACIT-Pal vragenlijst, een 46-item vragenlijst bestaande uit vier subschalen over fysiek, sociaal/familiaal, emotioneel en functioneel welzijn, en een vijfde palliatieve zorg subschaal. Secundaire uitkomsten waren spiritueel welzijn, angst en depressie, het aantal spoedeisende hulpbezoeken, het aantal ongeplande ziekenhuisopnames en intensive care opnames en de plaats van overlijden. Vragenlijsten werden afgenomen bij inclusie en drie en zes maanden later. Twaalf maanden na inclusie werd het medisch dossier bekeken. De gegevens werden geanalyseerd met behulp van *generalized linear mixed modeling*. In totaal werden 222 patiënten geïncludeerd. De kwaliteit van leven en andere secundaire uitkomsten verschilden niet tussen patiënten van de interventiegroep en die van de controlegroep. Het aantal opnames op de intensive care was wel statistisch significant lager in de interventiegroep. Factoren die de effectiviteitsevaluatie belemmerden waren onder andere onvoldoende power vanwege de COVID-19 pandemie en het feit dat niet alle patiënten van de interventiegroep de interventie hadden gekregen en meerdere patiënten geen vragenlijsten terugstuurden.

In **hoofdstuk 6** werden de implementatiestrategie en het implementatieproces grondig geëvalueerd aan de hand van procesdata, vragenlijsten, medische dossiers en interviews. De training inclusief rollenspel werd positief geëvalueerd en verbeterde de *self-efficacy* van zorgverleners om palliatieve zorg te verlenen, gemeten met de End-Of-Life Professional Caregiver Survey (EPCS). Minder dan de helft van de 98 geïdentificeerde patiënten kreeg één of meer palliatieve zorggesprekken op de polikliniek, gemiddeld zes weken na inclusie, en ze werden voornamelijk gevoerd door een longarts en longverpleegkundige samen. De interventie werd zeer gewaardeerd, omdat het patiënten en mantelzorgers meer rust en duidelijkheid gaf en het werkplezier van de zorgverlener vergrootte. De belangrijkste belemmerende factoren voor implementatie waren onvoldoende tijd voor palliatieve zorggesprekken, lage prioriteit voor implementatie vanwege de COVID-19 pandemie en het ontbreken van een communicatiemiddel voor transmurale samenwerking. Bevorderende factoren waren het systematisch screenen van patiënten, aanpassen aan de *readiness* van de patiënt, het voeren van palliatieve zorggesprekken met een longarts en longverpleegkundige of verpleegkundig specialist samen en het regelmatig bijeenkomen met een klein team onder leiding van een enthousiaste projectleider. Het onderzoek benadrukt het belang van communicatietraining en het opzetten van een klein projectteam onder leiding van een toegewijde implementatieleider. Ook onderstreept het dat toekomstig onderzoek nodig is om de transmurale samenwerking te optimaliseren en consensus te bereiken over wanneer specialistische palliatieve zorgverleners betrokken moeten worden.

Omdat het identificeren van de palliatieve fase werd beschouwd als een van de belangrijkste belemmeringen voor het verlenen van palliatieve zorg, was eerder al de ProPal-COPD tool ontwikkeld door Duenk et al. om zorgverleners te helpen palliatieve patiënten met COPD te identificeren tijdens een ziekenhuisopname voor een COPD-exacerbatie (longaanval). Het predictiemodel was gebaseerd op de Surprise Question en zes klinische indicatoren: MRC-dyspneuscore, CCQ-score, longfunctie, BMI, specifieke comorbiditeiten en eerdere ziekenhuisopnames. Daarbij werd overlijden binnen een jaar gebruikt als proxy voor palliatieve zorgbehoeften en de tool leek veelbelovend met een hoge sensitiviteit. In **hoofdstuk 7** werd de ProPal-COPD tool extern gevalideerd en onderzochten we door middel van interviews de gebruikerservaringen van zorgverleners die de tool in de praktijk hadden gebruikt. We toonden aan dat de tool niet met grote nauwkeurigheid de sterfte binnen een jaar voorspelde, maar in de kwalitatieve evaluatie vonden we dat het systematisch screenen van patiënten met behulp van de indicatoren zorgverleners bewuster maakte van de palliatieve fase en hen hielp om tijdig passende zorg te starten bij COPD-patiënten met palliatieve zorgbehoeften.

Tot slot worden in **hoofdstuk 8** de belangrijkste onderzoeksresultaten samengevat en kritisch besproken in relatie tot de gebruikte methodes en voorgaande wetenschappelijke literatuur. Het hoofdstuk reflecteert ook op wat de resultaten van dit proefschrift betekenen voor de klinische praktijk en toekomstig onderzoek. Ten eerste moet er rekening worden gehouden met de methodologische uitdagingen bij het opzetten van een hybride effectiviteits-implementatiestudie. Ik raad aan om de haalbaarheid en studieprocedures te testen voorafgaand aan het onderzoek en om een langere implementatieperiode in te lassen voordat klinische data worden verzameld. Ten tweede moet er een specifieke uitkomstmaat worden gekozen die is afgestemd op het doel en de timing van de interventie. Onze kwalitatieve gegevens toonden namelijk aan dat palliatieve zorg leidt tot meer rust en duidelijkheid bij patiënten met COPD, maar dit werd niet weerspiegeld door de vragenlijsten. Het is de vraag of bestaande vragenlijsten geschikt zijn om de kwaliteit van leven te beoordelen bij patiënten met ernstige COPD en of een brede uitkomstmaat zoals kwaliteit van leven überhaupt geschikt is om de effecten van palliatieve zorginterventies in deze patiëntengroep te beoordelen. Ten derde draagt dit proefschrift bij aan de voortdurende discussie over wanneer palliatieve zorg moet worden gestart bij COPD. Hoewel er misschien geen duidelijk omslagpunt bestaat binnen het ziektebeloop van COPD, ontdekten we dat het systematisch screenen van patiënten essentieel is om de terughoudendheid van zorgverleners te overwinnen om onderwerpen rondom het levenseinde te bespreken. Ten vierde ga ik in op de onzekerheid over de rollen en verantwoordelijkheden van zorgverleners die betrokken zijn bij de zorg voor patiënten met ernstige COPD en de uitdagingen om continuïteit van zorg te bieden. Ten vijfde bespreek ik wat er nodig is om palliatieve zorg succesvol te implementeren in de reguliere COPD-zorg. Om dit te bereiken is gedragsverandering bij individuele zorgverleners nodig en organisatorische wijzigingen met passende financiering. Ter afsluiting doe ik aanbevelingen voor de klinische praktijk, onderwijs, beleid en toekomstig onderzoek.

Dankwoord

Waarover ik zes jaar geleden alleen maar kon dromen, is eindelijk werkelijkheid geworden: mijn proefschrift is af! Ondanks alle hobbels en worstelingen die samengaan met het doen van promotieonderzoek, zeker bij een omvangrijk project, was het onderwerp voor mij tot het einde toe een sterke drijfveer om door te gaan. Ik ben trots dat we de zorg voor mensen met COPD in hun laatste fase een stukje beter hebben kunnen maken. Veel dank aan iedereen die hier onderweg aan heeft bijgedragen.

Alle professionals die deelnamen aan werkgroepen en aan de COMPASSION-studie: zonder jullie enthousiasme en inzet had ik dit proefschrift niet kunnen schrijven. Kris Mooren, dank voor je waardevolle bijdrage aan de COMPASSION-training. Ook dank aan alle patiënten en mantelzorgers die de tijd en moeite namen om vragenlijsten in te vullen en hun ervaringen wilden delen in interviews.

Mijn copromotor en promotoren. Lieve Rianne, dank voor jouw steun en je geloof in mij. Je was altijd bereid om met je sterk inhoudelijke blik mee te denken over de puzzels van het project en waardevolle feedback te geven op mijn stukken. Beste Niels, dank voor je ultrasnelle reacties op de mail en het vertrouwen dat je me gaf het onderzoek op mijn eigen manier uit te voeren. Lieve Yvonne, dank voor je warme begeleiding en je waardevolle expertise in palliatieve zorgonderzoek. Beste Huib, dank voor je scherpe blik, heldere analyses en kritische vragen. Blij dat je als vierde begeleider wilde aansluiten bij mijn promotieteam.

LAN-collega's, dank voor het thuisgevoel bij de LAN. Lieve Els, zonder jou was dit proefschrift er misschien wel niet gekomen. Veel dank voor je bevlogenheid en voor onze eindeloze gesprekken, inspirerende brainstormsessies, gezellige reizen door het hele land, je goede adviezen en het samen zoeken naar perfecte formuleringen. Beste Emiel, dank voor het op de kaart zetten van dit belangrijke onderwerp!

Roukayya, dank voor de samenwerking bij het rapport over wensen en behoeften, Bart en Daisy voor jullie hulp bij de systematic review en Ewald voor je hulp bij statistische analyses. Jeroen van DBTA, dank voor het vormgeven van de trainingssessie met trainer-acteurs. Brian, Noortje en Nelleke van het OZC, dank voor jullie kennis en onmisbare hulp bij het verzamelen van de studiedata. Dank aan alle masterstudenten die ik begeleidde: Julia, Mirjam, Ezgi, Liore, Enisa, Dorien, Sonja en Noortje.

Mijn mede-promovendi, leden van het Green Team en de promovendicommissie, dank voor alle leuke meetings, borrels, lunches en online gatherings in coronatijd. Collega-onderzoekers van het Radboudumc en de Leidse Lablunch, dank voor het delen van ervaringen met palliatieve zorgonderzoek en de gezelligheid bij palliatieve zorgcongressen.

Lieve paranimfen, fijn dat jullie straks naast me staan! Lieve Annemieke, ik heb genoten van alle avonturen die we samen in Amsterdam hebben beleefd en ik hoop dat er nog vele gaan volgen. Lieve Willemijn, door jouw relativerende blik en onze gezellige borrels en lunches waren de laatste loodjes lichter.

Dank aan al mijn lieve vrienden en familie. Anne-lena, Hanna, Foppie, Rianne, Marjolijn, Wieke, Veera, Yvette, Myrthe, Yaxi, Jessica, Ernst en Maaike: van onze goede gesprekken word ik altijd blij. Jonathan, Hilko, Jos, Annemieke, Gemma en Willemijn: ik kijk uit naar alle volgende festivals, concerten en culturele uitjes. Mimidaeanen: op nog vele inspirerende boeken. Znoozcampers: samen sporten leegde mijn hoofd. Rosaline, Jarith, Bart, Mary, Iris en Marjon: samen muziek maken met jullie was heerlijke afleiding!

Lieve Herman en Corrie, Wouter en Nouscha, de leukste en liefste schoonfamilie die ik me kan wensen. Dank voor jullie steun.

Lieve Gineke, Marjonne en Alexander, Raymond en Mandy, wat een tijd hebben we achter de rug met het overlijden van Julia en papa. Dank voor de verbondenheid en de humor die er onverminderd was.

Lieve papa, ik mis onze lange fijne telefoongesprekken over het leven en de wereldproblematiek. Jij was voor velen een voorbeeld hoe je de naderende dood volledig kan accepteren, door simpelweg te zijn met wat er is.

Lieve zus, wat ben ik blij dat ik jouw zusje ben. Dank dat ik altijd bij je terecht kan voor een knuffel, bemoedigende woorden of hulp als ik ergens over twijfel.

Lieve Hans, dank voor jouw verhalen, kennis en ongezouten mening. In onze gesprekken stimuleerde jij me kritisch na te denken en precies te formuleren.

Lieve mama, contact maken met de ander terwijl je in verbinding blijft met jezelf kan jij als geen ander. Dank dat je er altijd voor me bent en voor je interesse in alles wat ik doe.

Lieve Vic, nooit gedacht dat twee mensen zó goed bij elkaar kunnen passen. Dank je wel voor je onvoorwaardelijke liefde en steun. Ik hoop nog heel lang van het leven te kunnen genieten met jou en straks met zijn drietjes.

Curriculum Vitae

Johanna Broese was born on the 2nd of November 1990 in Harlingen and grew up in Groningen. After finishing her secondary school at the Willem Lodewijk Gymnasium in 2008, she studied medicine at the Rijksuniversiteit Groningen. She was active in various committees and on the board of the student orchestra Mira. During her master's, Johanna did medical internships at the University Medical Center Groningen, Isala Klinieken in Zwolle, Sint Lucas Andreas Ziekenhuis in Amsterdam, Gesundheitsamt Breisgau-Hochschwarzwald in Freiburg (Germany), and Policlínico 19 de Abril in Havana (Cuba). She was inspired by the Cuban primary care system and promoted exchange between the Cuban and Dutch medical world as a member of an interuniversity group. During her scientific internship at the Academic Medical Center in Amsterdam, her interest in elderly care was sparked. After graduating in 2015, she worked as a medical doctor at the geriatric department in Medisch Centrum Alkmaar.

In 2017, Johanna started her PhD research on palliative care in COPD at the Public Health and Primary Care (PHEG) department of the Leiden University Medical Center, which was a national project in cooperation with the Long Alliantie Nederland and Radboudumc. During her PhD, she was actively involved in teaching medical and psychology students. Additionally, she was the coordinator of the PHEG Green Team and a member of the PhD-students committee. At the moment, Johanna is working as a medical doctor in the nursing home Oudshoorn in Alphen aan den Rijn. In 2024, she will start her training to become an elderly care physician.

Bibliography

Scientific publications

- **Broese JMC**, van der Kleij R, Kerstjens HAM, Verschuur EML, Engels Y and Chavannes NH. A cluster randomized controlled trial on a multifaceted implementation strategy to promote integrated palliative care in COPD: study protocol of the COMPASSION study. BMC Palliat Care 2020; 19: 155. 2020/10/12. DOI: 10.1186/s12904-020-00657-3.
- **Broese JM**, de Heij AH, Janssen DJ, Skora JA, Kerstjens HAM, Chavannes NH, Engels Y and van der Kleij R. Effectiveness and implementation of palliative care interventions for patients with chronic obstructive pulmonary disease: A systematic review. *Palliat Med* 2021; 35: 486-502. 20201218. DOI: 10.1177/0269216320981294.
- **Broese JMC**, van der Kleij R, Verschuur EML, Kerstjens HAM, Engels Y and Chavannes NH. Provision of Palliative Care in Patients with COPD: A Survey Among Pulmonologists and General Practitioners. *Int J Chron Obstruct Pulmon Dis* 2021; 16: 783-794. 2021/04/06. DOI: 10.2147/COPD.S293241.
- **Broese JMC**, van der Kleij R, Verschuur EML, Kerstjens HAM, Engels Y and Chavannes NH. Implementation of a palliative care intervention for patients with COPD - a mixed methods process evaluation of the COMPASSION study. BMC Palliat Care 2022; 21: 219. 20221207. DOI: 10.1186/s12904-022-01110-3.
- **Broese JMC**, van der Kleij R, Verschuur EML, Kerstjens HAM, Bronkhorst EM, Chavannes NH and Engels, Y. External Validation and User Experiences of the ProPal-COPD Tool to Identify the Palliative Phase in COPD. Int J Chron Obstruct Pulmon Dis 2022; 17: 3129-3138. 20221222. DOI: 10.2147/COPD.S387716.
- **Broese J**, van der Kleij RM, Verschuur EM, Kerstjens HAM, Bronkhorst EM, Engels Y and Chavannes NH. The effect of an integrated palliative care intervention on quality of life and acute healthcare use in patients with COPD: Results of the COMPASSION cluster randomized controlled trial. Palliat Med 2023; 37: 844-855. 20230331. DOI: 10.1177/02692163231165106.

Other publications

- Oueslati R, Broese JMC & Touwen DP. Palliatieve zorg en COPD. Een kwalitatief onderzoek naar de wensen en behoeften van patiënten en naasten, en de visies van zorgverleners. LAN/LUMC: Amersfoort, 2019.
- Broese J & Verschuur E. Meer compassie voor patiënten met vergevorderd COPD door implementatie van palliatieve zorg; het Compassion project. Inspiratie 2020; 1.
- Broese J & Verschuur E. Palliatieve zorg met compassie voor patiënten met COPD. CAHAG bulletin 2021; 3.

Presentations at (inter)national conferences

- Implementatie van integrale palliatieve zorg voor patiënten met COPD, Vlaams-Nederlandse wetenschapsdagen Palliatieve zorg 2017, Amsterdam, the Netherlands *(poster presentation)*.
- Proactieve palliatieve zorg voor patiënten met COPD. Longdagen 2018, Ermelo, the Netherlands *(oral presentation)*.
- Integrale palliatieve zorginterventies voor patiënten met COPD: een systematische review. Nationaal Congres Palliatieve Zorg 2018, Lunteren, the Netherlands *(poster presentation)*.
- Implementatie van integrale palliatieve zorg voor patiënten met COPD; CAHAG conferentie 2019, Zeist, the Netherlands *(oral presentation; **Best Abstract Award**)*.
- Integrated palliative care interventions for patients with COPD: a systematic review. World Congress of the European Association for Palliative Care 2019, Berlin, Germany *(poster presentation; **poster award**)*.
- Inhoud en organisatie van palliatieve zorg bij COPD: Een landelijk vragenlijstonderzoek onder longartsen en huisartsen. Vlaams-Nederlandse wetenschapsdagen Palliatieve zorg 2019, Antwerpen, Belgium *(oral presentation)*.
- COPD Palliative and supportive care implementation (COMPASSION): an evaluation of a multidisciplinary experienced based training program. World Research Congress of the European Association for Palliative Care 2020, online *(poster presentation; **poster award**)*.
- Providing palliative care in patients with COPD: a national survey among Dutch pulmonologists and GPs. World Research Congress of the European Association for Palliative Care 2020, online *(oral presentation)*.
- The COMPASSION project. Value Based Health Care Dragons Grant and Endorsement 2021, online *(pitch; **nominated for the VBHC prize**)*.
- Experiences with implementing integrated palliative care for patients with COPD: a qualitative study. World Congress of the European Association for Palliative Care 2021, online *(poster presentation; **poster award**)*.
- Implementatie van integrale palliatieve zorg voor patiënten met COPD – een kwalitatieve studie naar ervaringen van patiënten, mantelzorgers en zorgverleners. Vlaams-Nederlandse wetenschapsdagen Palliatieve zorg 2021, Tiel, the Netherlands *(oral presentation)*.
- Tools voor passende palliatieve zorg bij COPD. Nationaal Congres Palliatieve Zorg 2022, Tiel, the Netherlands *(workshop)*.
- Hoe integreer je palliatieve zorg in de reguliere COPD-zorg? Een mixed-method evaluatie van het COMPASSION onderzoek. Nationaal Congres Palliatieve Zorg 2022, Tiel, the Netherlands *(poster presentation)*.
- The effect of palliative care on quality of life and acute healthcare use in patients with COPD. Dutch Lung Congress 2022, Utrecht, the Netherlands *(poster presentation)*.
- The effect of integrated palliative care on quality of life and acute healthcare use in patients with COPD: Results of the COMPASSION study. European Respiratory Society 2022, Barcelona, Spain *(oral presentation)*.

- Effectiveness of integrated palliative care on quality of life and acute healthcare use in patients with COPD – outcomes of the COMPASSION study. World Conference of the International Primary Care Respiratory Group 2022, online *(poster presentation)*.
- Palliative care and advance care planning in COPD. Belgian Pneumology Days 2022, Brussels, Belgium *(invited oral presentation)*.
- Toolbox 'Passende palliatieve zorg bij COPD'. Amsterdam Symposium Palliatieve zorg 2023, Amsterdam, the Netherlands *(pitch; **Jaarprijs Palliatieve Zorg Impact**)*.

Products & materials

- All information leaflets, animations, videos, webinars, tutorials and manuals developed within the COMPASSION project can be found in the online toolbox at www.palliatievezorgcopd.nl
- The e-learning 'Palliatieve zorg bij COPD: Wat is het en hoe breng je het in de praktijk?' can be found at https://www.bsl.nl/shop/palliatieve-zorg-bij-copd-80743e