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Integrating palliative home care early into standard care of end-stage COPD

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Table of content

Dankwoord

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General introduction

This dissertation departs from the need to explore early-integrated palliative home care into standard care for end-stage Chronic Obstructive Pulmonary Disease (COPD) in Belgium. Here, the *end-stage* reflects a state of (very) low lung function (GOLD III or IV[1]), often accompanied by a high physical and psychosocial symptom burden. This end-stage signalises the final years of life (although exact prognosis is impossible). It also leads to reduced health-outcomes[2] which are often unmet solely by a standard medical care approach[3]. Early-integrated palliative home care (meaning 'the early incorporation of specialised palliative home care' in this text) can provide an extra layer of support for this slow-evolving, chronic disease[4–6]. Still, end-stage COPD patients do not use this kind of palliative care often and if they do, only very close to death[7]. A global standard model for practice implementation is still lacking[4]. Here, I try to address these issues by 1) exploring palliative home care referral for COPD patients in Belgium; and by 2) developing and testing a model for early-integrated palliative home care into standard care. The overall goal of this model is to increase quality of life, health-related outcomes, care preferences and quality of care for end-stage COPD.

End-stage COPD: complex symptom burden

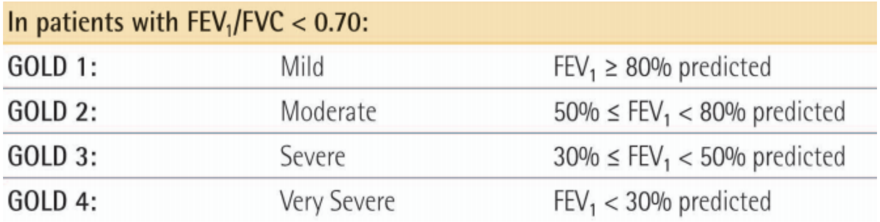
Over the past years, COPD, one of the major non-communicable diseases, has become one of the world's leading causes of morbidity and mortality while inducing a substantial economic and social burden[8]. In 2010, an estimated 384 million lived with the disease, with a global prevalence of 11.7% [95%(CI)8.4-15.0%].[9] Every year, around three million people die of COPD.[10] Although prevalence is directly related to tobacco smoking, other factors such as outdoor, occupational and indoor air pollution are also major risks[11]. Men (12.7%) develop COPD more often than women (8.3%) between the ages of 40 and 80 years.[12] Prevalence and burden are predicted to rise due to continued risk exposure and ageing[13]. This may cause deaths from COPD and related conditions to climb up to 4.5 million/year by 2030[13,14].

The Global Initiative for Chronic Obstructive Lung Disease (GOLD)[1], defines COPD as:

> *"A common, preventable and treatable disease, characterised by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases"*[1].

Chronic airflow limitation results from various combinations of small airways disease (e.g. obstructive bronchiolitis) and parenchymal destruction (emphysema). The two can vary and evolve at different rates over time. Persistent respiratory symptoms precede airflow limitation and may be complicated with often multiple acute exacerbations[15]. GOLD[1] has developed a classification of airflow limitation severity in COPD (Box 1) measured by spirometry (the most widely used and reproducible lung function test). As there is only a weak correlation between FEV1 and symptom burden or impairment of health status[16], formal symptomatic assessment is also required. The Modified *MRC dyspnea scale* (mMRC) for dyspnea and the *COPD Assessment Test* for COPD-physical symptom burden are said to be accurate measurement scales[1].

Box 1 Classification of airflow limitation according to GOLD[1]



In patients with $FEV_1/FVC < 0.70$:		
GOLD 1:	Mild	$FEV_1 \geq 80\%$ predicted
GOLD 2:	Moderate	$50\% \leq FEV_1 < 80\%$ predicted
GOLD 3:	Severe	$30\% \leq FEV_1 < 50\%$ predicted
GOLD 4:	Very Severe	$FEV_1 < 30\%$ predicted

Symptoms vary from chronic cough and phlegm (mucus) to continuous dyspnea[17]. In end-stage COPD, severe limitations in daily life activities, low mood, anxiety, sleeping disorders, and low energy levels become highly prevalent, reducing health-related quality of life in the final years before death[3]. Co-morbidities, which can elevate morbidity, often appear[18]. Cardiovascular diseases, osteoporosis, lung cancer, depression and diabetes are among the most common.[18]

The disease involves a progressive, inexorable functional decline with acute episodes of exacerbation[19]. As a result, prognosis of the disease and especially of its end stage is difficult. Hospitalisation for acute exacerbation is related with one-year death for only 22% of patients[20]. Other tools, such as ADO (age, dyspnea and forced expiratory volume in 1 sec), and BODE (body mass index, airflow obstruction, dyspnea and exercise capacity) seem better predictors of 6-month survival[21]. Until now, no solid predictor has been found and it is likely that there is none to date[22].

GOLD sees future challenges for pharmacological therapies (beyond the scope of this dissertation)[22] and for non-pharmacological treatment[22], of which three are most relevant: 1) *Prevention and management of external risks:* Pollution may continue to lead to new COPD cases[1]. Poverty and lower socioeconomic status (SES) is consistently related to this. Patients with lower SES risk twice as likely morbidity and mortality.[23] To reduce health inequalities, multidisciplinary collaboration for tailored prevention, management and palliation of COPD[24] are needed; 2) *Increasing patient education and self-management:* patients are said to be barely aware of COPD severity, prognosis and care options at the end of life.[25] Self-management activities on early recognition of exacerbation, decision-making, advance directive decisions can increase understanding and coping.[1] For example, negotiated action plans for worsening symptoms have led to fewer hospitalisations and improved health-related quality of life in COPD[26]; and 3) *Integrating multidisciplinary and comprehensive care programs:* managing COPD requires multiple health professionals working together closely[1] within people-centred and integrated health services including palliative care[27]. Integrated care should be tailored to the disease stage and the patient's level of health literacy[27]. Up until now, such end-stage COPD programs are scarce[28].

Palliative care for chronic-progressive diseases: a continuous evolving concept

COPD patients, like others with non-cancer diseases such as diabetes and cardiovascular diseases, are not often referred to palliative care services[7]. Nevertheless, patients with such diseases are numerous and clearly have unmet (palliative care) needs ranging from 26.8[29] to 40 million people/year[30]. 68% died of COPD in 2012[13]. The high symptom burden in end-stage COPD is causing distress that currently remains unaddressed by standard therapy alone[31]. Palliative care can offer relief of symptoms and stress for this chronic-progressive disease[32]. When early-integrated, its benefits seem twofold: 1) induce appropriate and less-costly care for an ageing population, and 2) positively affect quality of life and dying[32].

The World Health Organisation defined palliative care in 2002 as:

> *'An approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems of physical, psychosocial and spiritual.*
>
> - *provides relief from pain and other distressing symptoms;*
> - *affirms life and regards dying as a normal process;*
> - *intends neither to hasten or postpone death;*
> - *integrates the psychological and spiritual aspects of patient care;*
> - *offers a support system to help patients live as actively as possible until death;*
> - *offers a support system to help the family cope during the patients illness and in their own bereavement;*
> - *uses a team approach to address the needs of patients and their families, including bereavement counselling, if indicated;*
> - *will enhance quality of life, and may also positively influence the course of illness;*
> - *is applicable early in the course of illness, in conjunction with other therapies that are intended to prolong life, such as chemotherapy or radiation therapy, and includes those investigations needed to better understand and manage distressing clinical complications.'*[32]

Its foremost goal, improving quality of life, can be addressed by comprehensive symptom management, psychosocial support and disease insight. This should ideally happen from diagnosis of end-stage COPD[32] onwards, alongside standard therapies. To have a good understanding, quality of life can be defined as: '*An individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns'*.[33] Next, earlier planning of advance care, e.g. matching personal goals with care options and preferences[34], may result in more qualitative end-of-life care[34]. Finally, guidance towards death, followed by bereavement support[32], is important in the terminal phase. Provision can be done via 'generalist palliative care' by general practitioners and treating specialists or via 'specialist palliative care' by palliative care multidisciplinary teams. These teams received palliative care training and operate in hospital and (nursing) home settings.

The concept of palliative care and its application for chronic-progressive diseases such as cancer and COPD has evolved throughout the years and is still under debate. While literature has extensively discussed these evolution, I give a short overview of the most important steps here. In the 1960s[35], palliative care was tailored towards therapy-exhausted and terminal cancer[36]. PC was thus firstly seen as a 'Transition' model, with clear cut-offs between curative and palliative treatment. From 2000 on a 'Trajectory' model, introduced by Lynn and Adamson (Figure 1)[37], integrated curative and palliative care until close to death[38]. It was customised for chronic, slow-evolving diseases[37] as it would reflect their 'real life' course better[37]. This model has not gone unnoticed. In 2010, Boyd and Murray[39] clarified that the curative and palliative care integration is not linearly, but shifts continuously (see the dashed line in Figure 2)[37] while they also re-introduced terminal care as an important element[39].

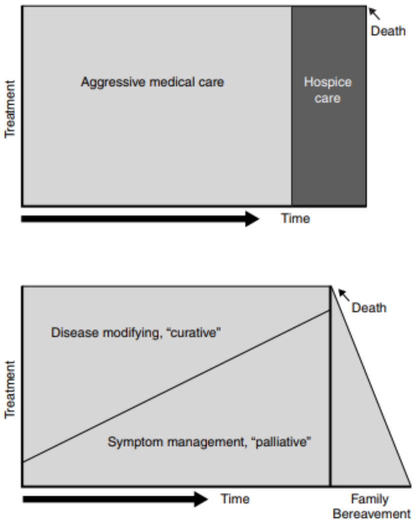


Figure 1 The older "Transition" model of care versus a "Trajectory" Model, adapted with permission by Lynn and Adamson (2000)[37].

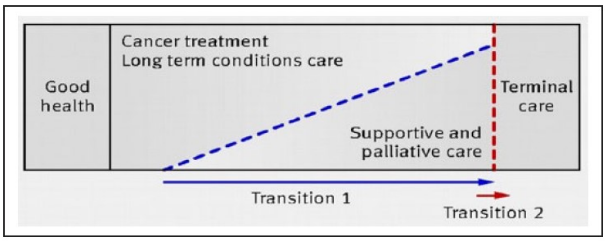


Figure 2 "Recognizing and managing key transitions in end-of-life care." Adapted with permission from Boyd and Murray (2010)[39].

Finally, the International Association for hospices and palliative care[40](IAHPC) proposed a new palliative care definition in 2018[I], emphasizing health-related suffering instead of life-limiting diseases as a referral criterion for palliative care:

> *'Palliative care is the active holistic care of individuals across all ages with serious health-related suffering due to severe illness, and especially of those near the end of life. It aims to improve the quality of life of patients, their families and their caregivers.'*

This led to wild debate in the field, whether 'health-related suffering due to severe illness' truly reflects the nature of palliative care, and if this broad concept will not lead to more confusion in practice[41]. Suffering itself is extremely difficult to define and a broad definition such as this does not aid practitioners and services in deciding how palliative care should be delivered and to whom. Furthermore, The proposed definition does not sufficiently reflect the complexity of palliative care, specifically in the overlap between specialist and generalist approaches to palliative care[41]. It also omits certain aspects of palliative care, such as rehabilitation, public health and compassionate community approaches. Due to all these concerns, no consensus has been reached over this new definition. As a result, it is clear that the final word on defining early-integrated palliative care and implications for practice has not been spoken.

Which early-integrated palliative care models are applicable for COPD?

The implementation of palliative care is often based on operational models of care. Models of care are standardised designs that provide frameworks for the organisation of care[42]. To date, a univocally accepted model for early integrated palliative care does not exist, even when confined to cancer or major chronic-progressive diseases[42]. This being said, there are calls to develop generic (applicable for all diseases) and disease-specific palliative care models[43]. Current generic models operationalise *integration of palliative care* in multiple ways, varying from a simple interaction between health professionals and a trained palliative care physician up to multi- or interdisciplinary

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[I] In this dissertation, the 2002 definition of Palliative care by the World Health Organisation is used and not the 2018 definition as this is still under discussion.

collaboration between PHC specialists, social workers, physicians and nurses[4]. A common denominator of these models is to address symptoms, psychosocial needs and to support informal caregivers[36].

For COPD, both respiratory care and pulmonary rehabilitation next to or within palliative care, have been used in integration models of care. In 2015, Vermylen et al[36] tailored a Trajectory model to end-stage COPD (Figure 3). Palliative treatment included symptom therapies (especially dyspnea), advance care planning and pulmonary rehabilitation techniques. Still, their model did not include well-defined integration aspects (in the sense of no interaction between standard and palliative care). In 2017, Maddock et al[4] proposed new models, based on results of refractory breathlessness interventions (Figure 4). While respiratory care (as a part of standard care) continues, symptom-triggered services, short-term integrated palliative care, advanced COPD clinics and integrated respiratory care services (pulmonary rehabilitation, early supported discharge, hospital at home) are provided. Still, COPD research has not extensively tested this model, impeding solid conclusion whether this is the preferred care pathway.

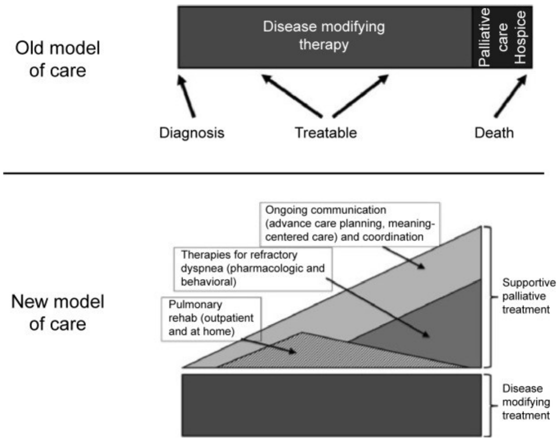

Figure 3 A proposed model of proactive palliative care in COPD, adapted with permission from Vermylen et al(2015)[36]

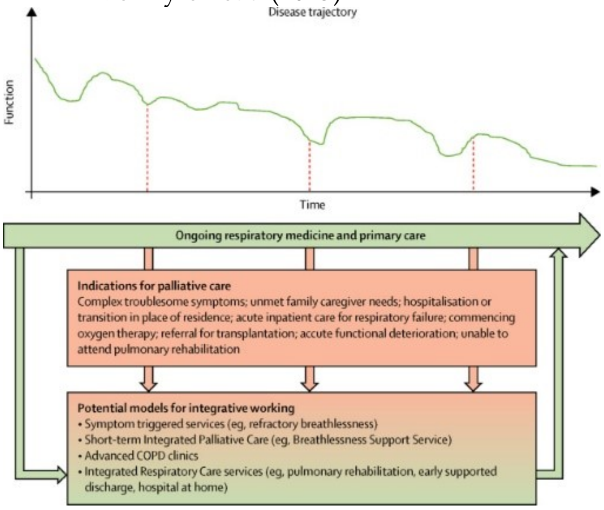

Figure 4 Models of integrative working with palliative care for people with COPD, adapted with permission from Maddocks et al(2017)[4]

Interventions testing early(-integrated) palliative care

With regard to cancer disease, Phase III interventions have explored early(-integrated) palliative care provided by specialised services at the hospital. In 2009, Bakitas et al[44] tested telephone-based support by advanced care nurses added to usual care for advanced cancer. The 2010 landmark study by Temel et al[45] provided early multidisciplinary specialised palliative care alongside standard medical care for lung cancer. Both trials increased health-related quality of life and mood for cancer patients with one-year prognosis. In 2014, Zimmerman et al[46]'s cluster-RCT on early specialised palliative care failed to find benefits at the primary endpoint for cancer (6-24 months clinical prognosis) although the results supported the used model. A 2018 Belgian nurse-led study by Vanbutsele et al[47] increased health-related quality of life in all types of cancer (diagnosis of cancer).

Regarding COPD , the study of Higginson et al[5] showed that the integration of breathlessness and palliative care services and a breathlessness pack for patients with refractory breathlessness and advanced disease (including COPD) improved mastery of breath. This is a quality of life domain in the Chronic Respiratory Questionnaire. In 2016, a similar study by Farquhar et al[48] found comparable results. In 2014, Duenk et al[49] tested monthly proactive hospital-based palliative care visits, which did not result in increased quality of life[50]. In 2015, Buckingham et al[51] found that a self-management intervention using an action plan and telephone-based follow-up by nurses heralded benefits in addressing holistic care needs throughout the disease trajectory of COPD.

Interventions with clear evidence for COPD are thus scarce and practice often struggles with a number of barriers. These barriers are also relevant in explaining why palliative care is often not provided for COPD and if so, only in the terminal phase. First, *the unpredictable COPD illness trajectory*[4] inhibits prognosis and insight into patterns of decline. This seems to restrict and delay palliative care because health professionals do not know when to consider and implement it[52]. Second, *communication barriers prevent palliative care conversations*. Health professionals have expressed fear of destroying patients' hopes[53]. They assume that COPD patients have low understanding of prognosis[25], the severity of the disease[54] and future care options[55]. In contrast, other research found that COPD patients fear a premature death, are worried about their future[56] and want to talk about end-of-life care[57] but do not want to bother staff with their concerns[58].

Third, *health system characteristics do not facilitate palliative care referral.* Few countries have a sufficient number of palliative care specialists to meet current, let alone anticipated future needs.[59] As a result, palliative care seems to be limited mainly to cancer[60]. Palliative care is also often not reimbursed before the terminal stage for both health professionals and patients[61]. Finally, education and training for health professionals in screening patients and palliative care skills is currently underdeveloped, especially in non-cancer (such as respiratory) fields[36]. It is relevant to further dissect whether low referral is also true in the Belgian case and which reasons are mentioned as explanations.

Palliative home care: the preferred care pathway?

Healthcare systems are shifting towards home care to limit costs and assure quality of life[62]. End-stage COPD patients also prefer home care and a home death[63,64], even though they currently die more often in hospitals than at home[65]. This amplifies the need for palliative home care, if the situation allows it. Palliative home care is associated with an increased likelihood of patients dying at home[66]. A 2013 review by Gomes et al[67] on 23 palliative home care intervention-studies also showed a reduction of symptom burden, although mainly for cancer. When early-integrated, it may avoid hospital admissions and escalation of end-of-life related costs[6].

Experimental design evidence for early-integrated palliative *home care* in COPD care is scarce. At the beginning of this dissertation/investigation, only the COPD IMPACT feasibility study of Horton et al[68] of 2013 was available. A palliative home care intervention for COPD patients and their informal caregivers provided leaflets for self-management, educational material for symptom control, a comprehensive palliative home care consultation, a common medical chart at the patient's home for coordinated care and ongoing case management. This was welcomed by patients and health professionals, but did not alter health-related quality of life, death at home, caregiver burden or symptom severity.

In 2016, Damps-Konstansa[64] proved in a small, unpowered study that COPD patients accept integrated care and support at home. In 2019, Weber et al[69] published the results of a 2014 trial of monthly palliative home care visits by specialised nurses who used a structured protocol addressing multiple symptoms and support (no integration components). They did not show intervention-control group differences[70]. Clear-cut evidence for successful models, benefits on health-related quality of life, symptom burden and quality of care in COPD are thus in short supply and should be further explored in this dissertation.

Palliative home care in Belgium

In Belgium, specialised palliative home care is a regionally organised, separate, second-line care service. The multidisciplinary support teams consist of a palliative home care physician, a psychologist and a number of nurses. In total, 27 such networks (of which there are 15 in Flanders) operate in Belgium. The services are requested by the patient's general practitioner. Depending on individual context, this is mostly in consultation with the patient, informal carers, community nurses or in some cases by palliative care nurses in the hospital or specialists involved. The specialised palliative home care nurses are at the centre of the offered support. They provide support towards the patient and informal carers for psychological, social, physical and spiritual needs (holistic approach). They also collaborate with the general practitioner involved. The palliative home care physician is more involved in the weekly team meetings and the psychologist provides psychological support to patients and informal carers, if necessary. Most teams do not use standardised documents or scales to assess the symptoms and needs of the patients. Instead, they upload reports into a general electronic patient file, which is not systematically shared with other health professionals. Contact with the latter is mainly by telephone.

Before referring patients to palliative home care, the general practitioner can request a 'palliative status', which is a form for palliative home care eligibility providing reimbursement of costs related to the palliative phase. This includes free consultations with general practitioners, physiotherapists and community nurses. Furthermore, a palliative status also enables a palliative home care allowance (*Forfait palliatieve zorg*) of €647 to compensate for extra costs related to their care, for example, materials and non-reimbursed medications, with the possibility of making a second claim[71]. Until recently, the reimbursement system for palliative home care in Flanders was restricted by law to patients with three months life expectancy[72]. This law was altered in November 2018 to a life expectancy of six to twelve months (assessed by a negative answer to the 'surprise question': Would I [health professional] be surprised if my patient dies within six to twelve months?) and accompanying criteria focused on care needs and low functioning.

Objectives of this dissertation

Following the advice of several institutions[1,73,74] and evidence for palliative care in cancer and non-cancer populations, the rationale of this dissertation is to explore early-integrated palliative home care in standard care for end-stage COPD in Belgium. With palliative home care, I mean the specialised multidisciplinary palliative home care teams in Belgium. Specific focus is on 1) reasons/implications for access to palliative care; 2) the views, feasibility and acceptability of early-integrated palliative home care for patients and involved health professionals, and 3) preliminary indications of the effectiveness on health-related quality of life and quality of care. In sum, this dissertation has five aims to answer specific research questions:

Aim **one** explored reasons for and implications on access to specialist palliative care services and their relationship with medical resource use, with the following research questions:

- What is the use and timing of palliative home care services for COPD versus lung cancer patients in Flanders? [using quantitative multivariate analysis on Flemish End-of-Life Decision data, 2013]
- What is the effect of use and timing of palliative home care teams for COPD on medical resource use in the Belgian patient's last thirty days of life? [using quantitative multivariate analysis on Belgian InterMutualistic Agency data between 2010 and 2015]

Aim **two** was to obtain knowledge about the current context and research on early integrated palliative home care for COPD in Flanders, with the corresponding research questions:

- What are the barriers and facilitators for early integration of palliative home care for end-stage COPD according to general practitioners and community nurses? [using a qualitative method of focus group conversations]
- What are the successful components of interventions on palliative home care and COPD? [using an explorative literature search method of palliative care interventions and protocols]
- What are the views of experts in COPD and/or palliative care on early-integrated palliative home care for end-stage COPD? [using a qualitative method of semi-structured expert consultations]

Aim **three** described the development of and protocol for a pilot study for early-integrated palliative home care for end-stage COPD patients in Belgian standard care.

Aim **four** assessed a pilot intervention of early-integrated palliative home care team for end-stage COPD patients [using the guidelines of the Medical Research Council Phase O-II], with the following research questions:

- What is the feasibility of early-integrated palliative home care for end-stage COPD patients and their health professionals?
- What is the acceptability of early-integrated palliative home care for end-stage COPD patients and their health professionals?
- What is the preliminary effectiveness of early-integrated palliative home care on quality of life and quality of care for end-stage COPD patients?

Aim **five** reflected on the perspective for respiratory services regarding palliative home care for end-stage COPD.

Methodology

To answer the aims and corresponding research questions of this dissertation, three different data collections are used.

A mortality follow-back study among physicians

To answer research question 1 of aim 1, I show numbers on access to and timing of palliative care services for Flemish COPD patients compared to lung cancer patients in Chapter 1. The methods used are quantitative analysis on the Flemish population data from the End-of-Life Decision (ELD) survey conducted in the first half of 2013[7]. Data of the death certificate study was used for this quantitative mortality follow-back design, looking backwards from death[7].

The study design has been repeatedly applied and validated in earlier studies to evaluate end-of-life care and decision making[75,76]. The Flemish Agency for Care and Health selected a random stratified sample of all death certificates of people aged one year or older from 1 January until 30 June 30th 2013. The sample was drawn on a weekly basis as new death certificates came in. Stratification was proportionate for month of death and province of death. We also applied disproportionate stratification based on the cause of death and the corresponding likelihood that an end-of-life decision (ELD) had been made, as determined by actual frequencies in previous surveys (larger sampling fractions were taken for deaths where an ELD was more likely e.g. those from cancer). This was done to yield more death cases where an ELD had occurred, and therefore more statistical information. The sample represented 12% of all deaths in Flanders in 2013.

A lawyer was involved in the mailing procedure as a trusted third party between responding physicians, researchers and the Flemish Agency for Care and Health to guarantee full anonymity i.e. that completed questionnaires could never be linked to a particular patient or physician. The mailing and anonymity procedures were approved by the Ethical Review Board of the University Hospital of Vrije Universiteit Brussel, the Belgian National Disciplinary Board of Physicians, and the Federal Privacy Commission.

InterMutualistic Agency-population data

In Chapter 2, Belgian population data on the link between use and timing of palliative home care and resource use in the last month of life for COPD is presented to answer research question 2 of aim 1. The methods used are quantitative analysis of the Belgian population retrospective data from the InterMutualistic Agency (IMA) between 1 January 2010 and 31 December 2015[77]. A total of seven administrative and health claims databases were linked to create one common full population database[77]. Data consisted of health claims data retrieved from the IMA and socio-demographic, socioeconomic and death certificate data from Statistics Belgium. In short, the IMA database contains all reimbursed healthcare consumption and pharmaceutical dispensing data for all Belgian citizens.[78] Statistics Belgium manages the national demographic database, which is derived from the population registry[79] and data from Census 2011[80]. Finally, a fiscal database (i.e. net taxable household income), also managed by Statistics Belgium, was linked to allow additional socio-economic insights. A detailed description of the databases, the data linkage process and content is described in detail elsewhere.[77]

Medical Research Council Framework for complex interventions

In Part 2 (Chapter 3-5), the Medical Research Council Framework was used for developing and testing the intervention to answer aim 2-4. Published in 2000[81], it has since been used for a variety of treatments, services and public health interventions[82]. It is recommended for palliative care programs[83], and has been tested for several trials[84,85]. It follows five Phases in an iterative manner (Figure 5), of which in this dissertation Phase 0-II was used.[85]

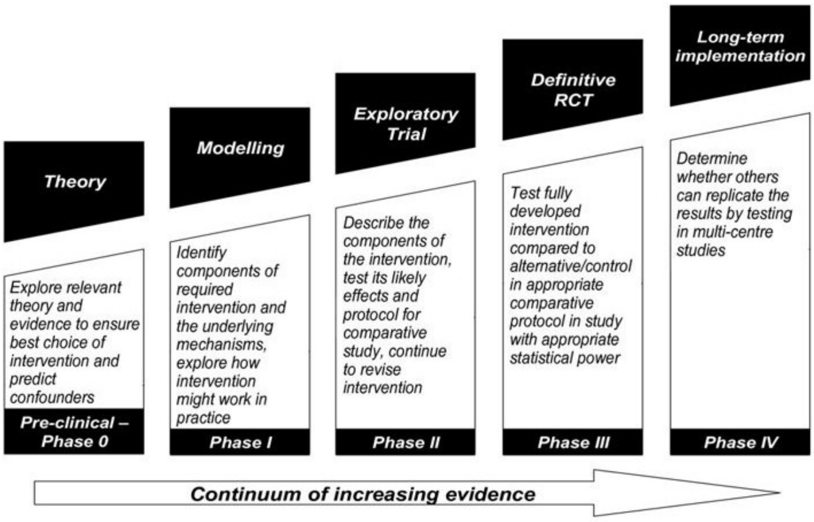

Figure 5 The Medical Research Council Framework for complex interventions[85]

We used three methods to obtain data for the development of the key components of the intervention (Phase 0). Key components - the core of the intervention - are intended to be or have been demonstrated through research to be positively associated with the outcomes that address identified needs[84,86]. We also obtained data on possible inclusion criteria for participants.

The first method was an exploration of the relevant literature between April 2015 and November 2016. This search identified published trial results and the protocol papers of uncompleted trials on palliative care and/or symptom management for COPD. The used methodology was an explorative literature search. No appraisal tool was used as the design was exploratory and not systematic.

The second method, undertaken between May and September 2016, was to consult experts for their views on possible components and inclusion criteria based on their experiences and ideas about the future of palliative home care; 27 national and international experts from clinical and/or research settings were selected for their research and/or clinical expertise in palliative care and/or COPD as a criterion. An extra criterion was stipulated for Belgian experts, i.e. their knowledge of the Flemish healthcare context concerning care for COPD, as this was information we could not gather from the literature search and from international experts.

Thirdly, we conducted focus groups between September 2015 and September 2016 to gain more insight into palliative home care practices, current standard care, barriers to be overcome and facilitators to promote timely integration of palliative home care for people with end-stage COPD in Flanders, Belgium. In this way, we tried to complement the results of the literature search and expert consultations with information from the healthcare professionals' context in which the intervention will be implemented.

In Phase I, the intervention was modelled. Outcomes were stipulated to be improvement in quality of life for people with end-stage COPD and improvements in quality of care. The research team developed a first draft of a complex intervention testing early-integrated palliative home care for end-stage COPD. The draft was based on the results of Phase 0, by selecting the most commonly used and mentioned inclusion criteria and intervention components, while also taking into account the research setting, the Flemish context, possibilities of replicating the intervention and feasibility and acceptability issues. This draft was refined by one expert panel and two individual expert opinions to further select the best courses of action in order to enhance implementation of the intervention in clinical practice. These Flemish experts identified possible implementation barriers which could occur and searched for solutions to adjust the components in order to overcome them.

In Phase 2, the intervention was tested with an underpowered pilot study[86] using the methodology of a non-blinded randomised controlled trial in the Ghent-Eeklo region of Flanders, Belgium. We tested feasibility, acceptability and preliminary effectiveness using post-intervention interview with participating intervention patients, palliative home care nurses, general practitioners and pulmonologists. Next, we six-weekly assessed following outcomes: *health-related quality of life*, measured with the Dutch 36 item Short Form Health Survey (SF-36 SF) version 2, validated for COPD[87,88], with a physical and mental composite score (score-ranging: 0-100 [maximum health-related quality of life]); *Anxiety and mood,* measured with the Hospital Anxiety and Depression Scale (HADS)[89,90], with anxiety and depression subscale (validated for small COPD population[91,92]) symptoms (score-range: 0-21 [maximum distress]); *COPD-related symptom burden* measured with the COPD Assessment Test (CAT) (score-range: 0-40 [maximum symptom burden]); *The amount of exacerbations, primary care interventions, hospitalisations and living will decisions*, measured with patient-reported health records; *Perceived quality of care,* measured with the Dutch Patient Assessment of Chronic Illness Care (PACIC), validated for COPD[93], (score-range 0-5 [maximum quality of care]) and *Place of death* (hospital, home, nursing home) as reported by the involved healthcare professionals.

Outlining

This dissertation consists of three parts.

Part one (Chapter 1-2) provides insight into the current state of palliative care referral for COPD in Belgium. Chapter 1 explores use and timing of palliative care services in Flanders in relation to lung cancer, and provides insights in reasons of non-referral. In Chapter 2, palliative home care service use and timing in Belgium is explored and associations with medical resource use in the final month of life are found. Suggestions for policy measures and health system changes are given in both chapters.

The second part presents the theoretical framework, accompanying studies, results of and reflections on the pilot intervention. The methods used are the Medical Resource Council framework for Phase II interventions. Chapter 3 presents a qualitative study with general practitioners and community nurses on barriers and facilitators for early-integrated palliative home care. I conclude the chapter with insights into the Flemish context for the intervention. Chapter 4 shows the theoretical and development phase of the intervention. The theory phase handles the results of an explorative literature search and expert consultations. The development phase integrates these results with the qualitative study into an intervention consisting of five components. I continue this part with chapter 5 that provides the results of and reflections on the pilot intervention on feasibility, acceptability and preliminary effectiveness. The sixth and final chapter provides four recommendations for clinical practice for respiratory services based on the previous studies and other literature.

I conclude the dissertation with a general discussion, first providing a summary of the results of the research papers and the research's methodological considerations. I reflect on the implications of this research and offer suggestions for future research. Finally, I provide recommendations for policy makers and clinical practice, based on the results of all studies from parts one and two and end this dissertation with a general conclusion.

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PART 1

POPULATION RESEARCH

CHAPTER 1

Comparing the use and timing of palliative care services in chronic obstructive pulmonary disease (COPD) and lung cancer: a population-based survey[ii]

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Abstract

Background: Palliative care (PC) improves quality of life for people with COPD and lung cancer. Although they have similar PC needs, studies on PC focus mainly on lung cancer. This study describes treatment goals in the last week of life, use and timing of PC services and reasons for non-referral in COPD and lung cancer.

Methods: We performed a survey on use and timing of PC services among physicians certifying a representative sample of deaths in 2013 (n=6871) in Belgium. We selected deaths from COPD (n=251) and lung cancer (n=192).

Results: For COPD, the proportion of deaths labelled as sudden/unexpected was higher (p<0.001) than for lung cancer, treatment goals in the last weeks of life less often aimed at comfort/palliation (p<0.001) and patients less often referred to PC services (37.3% to 73.5%) (p<0.001). The median timing of referral for COPD was six days prior to death (interquartile range (IQR): 3-14) and 17 days for lung cancer (IQR: 7-54) (p<0.001). Physicians whose patients had not been referred cited PC not being meaningful in 36% of COPD and 18% of lung cancer (p=0.059) cases.

Interpretation: While PC services are used mainly as terminal care in both diseases, our study shows less and later PC service use for COPD. This is likely to be due to its unpredictable illness trajectory and to lack of understanding of its need. This may be overcome by demonstrating the benefits of PC for COPD and its value in the pre-terminal phase for both diseases.

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Background

According to the World Health Organization (WHO)[1]*'palliative care is an approach that improves the quality of life of patients and their families facing problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual'*. Palliative care (PC) is a proven approach to improving quality of life and care in advanced illness and dying for people with COPD[2] and lung cancer[3]; the WHO definition implies that it is useful before the terminal phase. Studies have found that early-integrated PC is beneficial for lung cancer,[4,5] in particular the landmark study by Temel et al[6], and for COPD[7]. However, little is known about whether and when people with COPD and lung cancer in non-experimental settings receive PC.

People with severe COPD and lung cancer experience similar symptoms such as pain, insomnia, fatigue, low mood and dyspnea[8–13] more often reported in COPD[10]. A study by Gore et al[14] on quality of life in people with severe COPD and lung cancer found worse physical, social, and emotional functioning for COPD than for non-small cell lung cancer. Anxiety or depression occurred far more with COPD (90%) than with lung cancer (52%).[14] These symptoms clearly signal PC needs[14] and require treatment focused on symptom management and psychosocial support for more than just the terminal phase.[15] Research on the use of PC services could provide further information about whether they are utilised in both diseases. Because some people might not need specialized PC but could be supported by treatments focused on comfort care integrated into standard care it is also necessary to study the extent to which these different services are provided.

Studies show the low use of PC for COPD compared with lung cancer[3,16] which leaves people with unmet needs and a reduced quality of life[14]. Difficulties in predicting disease trajectories and poor prognostic factors may explain why people with COPD are referred less often to PC[17]. Unclear prognosis in COPD is often stated as an important reason for shortcomings in PC and referral to PC services[18,19], though this has not been explicitly studied so far. A more detailed examination of this and other possible reasons for the lack of referrals for COPD compared with lung cancer would be a valuable contribution to this debate.

Previous studies on timing and use of PC services, and treatment goals at the end of life for people with COPD and lung cancer, are mostly limited to specific settings[16,20] or small sample sizes[14,20]. Robust population-based studies that compare treatment goals and the use and timing of PC for COPD and lung cancer are lacking. A population-level perspective is important to understand whether and when people with COPD and lung cancer receive PC, and to identify the characteristics of PC access, and inequality in access, through the health care system.

This population-based study uses a representative sample to compare the use of PC services for people dying from COPD with those dying from lung cancer in Flanders, Belgium. Specific research questions are: (1) what are the treatment goals in the last week of life for people dying with COPD and lung cancer? (2) how often are PC services involved with people dying from COPD and lung cancer? (3) what is the average timing of referral to PC services before death of people suffering from COPD and lung cancer? and (4) what are the reasons given by attending physicians for not referring people dying from COPD and lung cancer to PC services?

Methods

Study design

We conducted a nationwide death certificate survey in the first half of 2013 based on a large and representative sample of deaths (n=6,871) in Flanders, Belgium. The study design has been repeatedly applied and validated in earlier studies to evaluate end-of-life care and decision making[21,22]. The Flemish Agency for Care and Health selected a random stratified sample of all death certificates of people aged one year or older from 1 January until 30 June 30th 2013. The sample was drawn on a weekly basis as new death certificates came in. Stratification was proportionate for month of death and province of death. We also applied disproportionate stratification based on the cause of death and the corresponding likelihood that an end-of-life decision (ELD) had been made, as determined by actual frequencies in previous surveys (larger sampling fractions were taken for deaths where an ELD was more likely e.g. those from cancer). This was done to yield more death cases where an ELD had occurred, and therefore more statistical information. The sample represented 12% of all deaths in Flanders in 2013.

Every physician certifying a death certificate in the sample was sent a four-page questionnaire by mail. Non-respondents received up to three reminders and, after data collection, a one-page questionnaire asking for their reasons for not participating.

Study population

For this study, we selected deaths from COPD and lung cancer. The COPD group includes cases where COPD was reported as the underlying or as an intermediate or associated cause of death (ICD-10 codes J40-44) where cancer (ICD-10 code C) was not an underlying cause. This allowed us to give a more representative view of people living with and dying from COPD[15]. For lung cancer, we took deaths for which only lung cancer was the underlying cause (ICD-10 codes C33-C34). People younger than 18 were not considered in the analysis as in Belgium the PC systems for children and adults are organised differently.

Measurements

The validated questionnaire first inquired whether death had occurred ‘suddenly and totally unexpectedly’. If the answer was no, and referral to PC would not have been precluded, the physician was asked to answer a number of questions regarding the care received by the patient:

Treatment goal at the end of life: was treatment during the last week of life mainly focused on 'cure or life-prolongation' or 'comfort/palliation'.

Use of PC services and timing of referral: had one or more of the four existing types of PC services in Belgium been applied i.e. multidisciplinary palliative home care teams (multidisciplinary teams skilled in PC that support the caregivers at home), mobile hospital-based PC teams (multidisciplinary teams that guide PC in different hospital wards), inpatient PC units (separate wards in the hospital devoted to PC) and a reference person (usually a nurse, trained in and responsible for PC in a nursing home). The physician was also asked to indicate the timing of the referral, i.e. the number of days between the first referral and death.

Reasons for not using PC services: when no PC services were used, physicians were asked for the reasons, potentially more than one for each patient. The possible reasons were selected based on relevant literature about factors hindering the use of PC services[23–28] and on existing qualitative research[29]: PC was not or was insufficiently meaningful; PC was not available; the care had already adequately met the patient's palliative and supportive needs; there was insufficient time to engage a PC service; not to deprive the patient and/or the family of hope; the person who was dying did not want it; family did not want it; other reasons.

Coded demographic and clinical patient characteristics were obtained from the death certificates and were anonymously linked to questionnaire data by the third party: age, sex, place of death, living situation and underlying or intermediate cause of death coded in three-digit ICD-10 codes.

Data analysis

Data were weighted for disproportionate sampling and for differences due to non-response between the response sample and all deaths in terms of province of death and place of death. For all other characteristics, no difference was found. After this complex weighting procedure, there were no significant differences between the response sample and all deaths for the combination of age, sex, marital status, province of death, cause of death and place of death.

Pearson chi square test analyses were calculated for bivariate associations. We also performed multivariable logistic regression to explore characteristics independently associated with treatment goal, use of PC services, and reasons for not using them. The non-parametric Kruskal-Wallis test and multivariable ordinal logistic regression were used to test for differences in timing of referral. All analyses were conducted with SPPS 24.0 software using the complex samples function in order to account for the complex survey design. All presented results are weighted. Ultimately, confirmatory post hoc sensitivity bivariate and multivariable analysis was performed on the results to assess their robustness where deemed necessary.

Anonymity and ethical considerations

A lawyer was involved in the mailing procedure as a trusted third party between responding physicians, researchers and the Flemish Agency for Care and Health to guarantee full anonymity i.e. that completed questionnaires could never be linked to a particular patient or physician. The mailing and anonymity procedures were approved by the Ethical Review Board of the University Hospital of Vrije Universiteit Brussel, the Belgian National Disciplinary Board of Physicians, and the Federal Privacy Commission.

Results

Population characteristics [Table 1]

A total of 251 deaths (6.7%) from COPD and 192 from lung cancer (5.1%) were drawn for analyses from the response sample with a response rate of 60.6% (3751/6188). The people with COPD differed significantly from those with lung cancer in terms of distribution for sex, age, place of death, living situation and proportion of deaths labelled as sudden and totally unexpected by the physician ($p<0.001$).

Treatment goal in the last week of life

Of all non-sudden deaths for COPD ($n=155$) and lung cancer ($n=154$), the treatment goal in the last week of life was less often aimed at comfort/palliation for COPD (59.1%) than for lung cancer (92.1%) ($p<0.001$). These bivariate results are corroborated by multivariable tests, where we controlled for sex, age and living situation (OR: 9.901, 95%CI [4.739-20.408]) ($p<0.001$) [Table 2]. Post hoc sensitivity bivariate and multivariable analysis also showed that whether PC services were initiated or not, treatment aimed at comfort/palliation in the last week of life was always less for COPD than lung cancer (when referred to PC services: COPD (80.7%) versus lung cancer (97.3%); when not referred to PC services: COPD (45.7%) versus lung cancer (79.5%)) ($p<0.001$) [not in Table].

Rate and timing of use of PC services [Table 3]

Of all non-sudden deaths, referral to any of the available PC services happened less for COPD (37.3%) than for lung cancer (73.5%) ($p<0.001$): less PC support at home for COPD (7.2%) (lung cancer 35.5%), fewer hospital based PC services for COPD (18.8%) (lung cancer 32.2%), fewer referrals to PC unit for COPD (2.6%) (lung cancer 12.6%), but more referrals to a PC reference person in a nursing home for COPD (11.7%) (lung cancer 3.3%) ($p<0.001$). After controlling for sex, age and living situation the chances of a referral to a PC service were six times higher for lung cancer than for COPD (OR: 5.682, 95% CI [3.258-9.901]) ($p<0.001$).

The median timing of the first PC service provided in cases of COPD was six days before death (interquartile range (IQR): 3-14) (16 days for lung cancer IQR: 7-54) (p<0.001). Multivariable tests controlling for sex, age and living situation in non-sudden deaths show that the first PC provision took place on average 28 days earlier for lung cancer than for COPD in relation to the moment of death (unstandardized B = 28.248, 95%CI [3.449-53.395]) (p<0.025). Bivariate results of use of PC services on all deaths can be seen in appendix [Table 5].

Reasons for not using PC services [Table 4]

Of all non-sudden deaths, 96 people (62%) with COPD and 40 (26%) with lung cancer were not referred to PC services. Reasons for not referring did not differ significantly between the two. The main reasons indicated by physicians were that PC needs were already sufficiently addressed by regular care in COPD (39.8%) and lung cancer (55.3%). PC services were not or not sufficiently meaningful in COPD (36%) and lung cancer (18.4%), there was not enough time to initiate it (23% in COPD and 23.4% in lung cancer). Multivariable tests indicated that ‘PC needs were already sufficiently addressed by regular care.’ This was more likely to be a reason for non-referral in lung cancer than in COPD (OR: 2,439, 95%CI [1.046-5.682]) (p<0.039).

Discussion

This population-based mortality follow-back survey in Flanders, Belgium shows that both treatment aimed at comfort and palliation in the last week of life and referral to PC services were less likely, and took place closer to death, for people with COPD than for those with lung cancer. However, the timing of referral to PC services was late in both groups. The reasons most cited by physicians for not referring to PC services were that PC needs were already met by standard care for both diseases and that, mainly for COPD, PC services were not sufficiently meaningful.

As well as people with COPD being more often reported as dying suddenly and unexpectedly than those with lung cancer, even in cases of non-sudden and expected deaths, their treatment in the last week of life was often less aimed at comfort and palliation (59.1%) than for lung cancer (92.1%). Also, referral to PC services happened on average 28 days later, and far less frequently, for COPD (37.3%) than for lung cancer (73.5%) for all PC services, except for PC in a nursing home, possibly because more people with COPD were living in nursing homes. Overall, the discrepancy found is in line with previous research[3,14,16] though the differences in use of PC services between diseases were smaller in our study. The study of Gore et al[14], for example, did not find people with COPD who had received specialized PC for social support, though they found that 30% of people with lung cancer had. An American retrospective cohort study on health care utilization in the last six months of life reported that people with COPD were more likely to have had a primary care visit and been admitted to an intensive care unit but less likely to receive palliative medications than those with lung cancer.[16]

Physicians may also be more aware of the advantages of PC services for people with cancer, which would confirm existing evidence that PC is still largely associated with cancer[8]. However, COPD and lung cancer are both diseases for which PC needs are often signalled[15], though more so with COPD14. Given the volume of literature pointing this out[14,30], our findings that PC needs tend to be adequately addressed less often for COPD than for lung cancer, and are more often viewed as not meaningful, is striking. It raises the question of whether physicians do not recognize PC needs in COPD or view PC services as not useful for COPD.

The near-universal focus on life-prolongation, even into the last week of life, could be due to physicians perceiving COPD as a chronic disease requiring ongoing therapeutic care, even in the final phase of life, and only intervening reactively in response to acute exacerbations rather than proactively based on a developed care plan[16]. This could impede the integration of holistic comfort-focused palliative care for COPD, perhaps further exacerbated by the outdated view that it is merely terminal care[31]. On the other hand, as qualitative research[32] has found, people with COPD themselves often do not fully understand the severity of their disease and their prognosis, and therefore may tend to prefer aggressive interventions[33]. Our results show that, according to physicians, patients rejected PC in only 5.7% of cases which could mean either that people with COPD are more involved in taking decisions about their treatment than is commonly supposed[34] or that physicians simply do not discuss PC with their COPD patients[35].

The difficulties of predicting illness progression and closeness to death may also explain these results. In lung cancer, a long period of fairly good functioning is followed by a rapid decline and a relatively predictable death. COPD is characterized by a gradual but steady decline accompanied by exacerbations which can lead to an unexpected death[8,36,37]. COPD progresses at a variable rate; research shows that difficulties in prognosis impact on communication about PC and what dying might entail[19,38] which might complicate referral to PC services[39] more in COPD than in lung cancer.

Though the differences between uses of PC services in the two conditions are striking, one similarity is worth noting, i.e. that for both groups the timing of referral was very close to death (median of six days for COPD and 16 for lung cancer). This indicates that PC services are still seen mainly as terminal care at the very end of life, despite increasing calls for earlier integration for life-limiting diseases[1,15] and evidence-based studies showing important benefits for lung cancer[4] and for COPD[7].

This study responds to the scarcity of population-based studies on treatment goals in the last week of life, on PC use and timing in COPD and lung cancer and on the reasons for not using PC. The retrospective method - using a large and representative sample of death certificates - is well suited to population studies on the use of PC services as it is the only way to obtain population-based estimates of PC service use. Population level studies also make it possible to generalise insights across the entire population studied[20,40,41].

However, the responding physicians may not have been able to reconstruct the full care trajectory before death, as there may have been other treating physicians in other settings. There was also a certain delay (maximum three months) between the death and the questionnaire, leading potentially to memory/recall bias. To mitigate this, physicians were instructed to consult the patient's medical file. It is also possible that some answers were not covered by the pre-defined response categories, such as reasons for not referring to PC services, although the options given were based on previous studies and a literature review discussing barriers and reasons for not referring to PC services.

This population-based research on the use and timing of PC services shows that they are still used mainly as terminal care services in lung cancer and, even more so, in COPD. This suggests an urgent need for models that integrate PC earlier into COPD care trajectories and for studies demonstrating the benefits and meaningfulness of PC in a pre-terminal phase in COPD. Most current and past studies focus on early and integrated PC in cancer. Drawing attention to the similarities between COPD and lung cancer in symptomatology can enhance understanding of the advantageous effect of PC on quality of life and care for COPD. We also suggest better education and training for PC teams about specific palliative care needs for COPD. Multidisciplinary deliberation in the presence of the pulmonologist, GP, the person with COPD and the family carers might facilitate the integration of a palliative approach into regular therapeutic care and could be useful if there are differences of opinion between the professionals and the caregivers/patient. Finally, to move towards earlier PC use in both COPD and lung cancer it is essential to challenge the perception of PC as a form of terminal care only. Legislation that perpetuates this by linking PC to a short life expectancy, as is the case in Belgium and several other European countries[42], can be considered as an impediment to this and may need to be revised.

Tables

Table 1 Characteristics of people dying with COPD and lung cancer (weighted %)

	COPD	*Lung cancer*	*p-value†*
Weighted number (weighted % of all deaths)	251 (6.7%)	192 (5.1%)	
Sex			.007
Male	59.0	71.4	
Age at death			<.001
18-64y	8.4	30.1	
65-84y	33.5	46.1	
≥ 85y	58.2	23.8	
Place of death			<.001
Hospital	55.8	52.8	
Home	19.9	37.8	
Nursing home	22.3	7.8	
Other	2.0	1.6	
Living situation			<.001
Alone	25.6	22.6	
In household with others	49.6	69.5	
Institution	24.8	7.9	
Death sudden and totally unexpected*	38.2	19.8	<.001
Attending physicians			.690
Family physician	*39.8*	*44.0*	
Specialist	*53.0*	*50.8*	
Other	*6.0*	*4.7*	

Percentages are column percentages. Missing values: <1% for both groups on all variables.

*As indicated by the physician. In such cases, no further questions were asked and we assumed that PC services had not been involved at the end of life.

†Pearson $\chi 2$ test testing for differences between the two illnesses: COPD and lung cancer.

Table 2 Treatment goal in the last week of life (% of non-sudden deaths)

	COPD	*Lung Cancer*	**Bivariate p-value***	**Multivariable analysis**
	N=155	N=154		*OR (95%CI)§*
Treatment goal in last week of life			<.001	
Cure/life-prolongation	40.9	7.9		
Comfort/palliation	59.1	92.1		9.901 (4.739-20.408), p<.001 §

Missing values for treatment goal: 2.9%, opiate use: 1.6%, time of onset opiate use: 5.02%

*Pearson χ^2 test testing for differences in treatment goal and opiate use between the two illnesses.

§ Odds ratios with 95% confidence intervals from complex samples multivariable logistic regression with cause of death (COPD = reference category), living situation, sex and age as independent variables. Calculations for non-sudden deaths only.

Table 3 Use and timing of palliative care services (% of non-sudden deaths)

	COPD	***Lung Cancer***			
	N=155 %	*N=154* %	*Bivariate p-value*	*OR (95%CI)§*	*Multivariate p-value*
Any type	37.3	73.5	<.001†	5.682(3.258-9.901)	(p<0.001)
Palliative care support at home	7.2	35.5	<.001†	6.757(3.135-14.493)	(p<0.001)
Hospital-based palliative care service (excl. Palliative care unit)	18.8	32.2	<.009†	1.946(1.080-3.509)	(p<0.027)
Palliative care unit	12.6	12.6	<.001†	5.988(1.908-18.868)	(p<0.002)
Palliative care reference person in a nursing home	11.7	3.3	<.008†	0.639(0.189-2.165)	(p<0.472)
	Days prior to death	*Days prior to death*	*Bivariate p-value*	*B (95%CI)¥*	*B (95%CI)¥*
*Timing of palliative care service **					
Median [P25-75]	6 [3-14]	16 [7-54]	<.001‡	28.248 (3.449-53.395)	(p<0.025)
Mean (min-max)	13.30(1-90)	40.22 (1-666)			

Abbreviations: OR= Odds Ratio; CI= Confidence Interval; P25-75= percentile 25 to 75; B = unstandardized coefficient.

Percentages are column percentages. Percentages may not add up to total percentage of referrals because more than one palliative care service was used in some cases. Missing values for PC referral: 4/149.

†Pearson χ^2 test testing for differences in referral between the two illness groups.

§Odds ratios with 95% confidence intervals from complex samples multivariable logistic regression with dependent palliative care referral (no referral vs referral) as dependent variable, and cause of death, living situation, sex and age as independent variables with COPD = reference category.

*Calculations only for patients with a referral to palliative care services (only available for non-sudden deaths). Missing values for time of onset: Lung cancer 15/114; COPD 6/58

‡Kruskal-Wallis test testing for differences in time of onset between the two illness groups.

¥Unstandardized B coefficient with 95% confidence intervals from complex samples multivariable linear regression with dependent timing of referral (ie days prior to death) as dependent variable, and cause of death, living situation, sex and age as independent variables with COPD = reference category.

Table 4 Reasons given by physicians for not using palliative care services (PCS) (% of deaths without referral to PC services)

	COPD	*Lung cancer*		*OR(95%CI) §*	*p-value*
Not using PCS *(% of non-sudden deaths)*	N=96 (62.7%)	N=40 (26.5%)	bivariate p-value		
Palliative care needs addressed	39.8	55.3	.122	2.439 (1.046-5.682)	(p<0.039)
Not meaningful	36.4	18.4	.059	0.385 (0.143-1.035)	(p<0.059)
Not enough time	22.7	23.4	>.999	0.899 (0.345-2.347)	(p<0.828)
Patient did not want	5.7	15.8	.086	3.155 (0.820-12.195)	(p<0.095)
Family did not want	4.4	10.3	.243	3.226 (0.683-15.152)	(p<0.139)
PCS not available	3.4	0	.553	/	
Not take away hope	1.1	2.6	.522	1.209 (0.064-22.727)	(p<0.899)
Other	1.1	0	>.999	/	

Abbreviations: PCS=palliative care services; OR= Odds Ratio; CI=Confidence Interval; N/A: not applicable because no cases.

Percentages are column percentages. Percentages may add up to more than 100 because more than one reason could be indicated.

Missing values for reason not using palliative care n= 10/136 (7.3%); 2/40 LC – 8/96 COPD.

*Bivariate Pearson chi^{2} test testing for differences in reasons of not using PCS between the two illnesses.

†Complex samples multivariate logistic regression analyses with individual reasons for non-referral as dependent variable (indicated vs not indicated) and cause of death, place of death, sex and age as independent variables.

Bold denotes significant at p< .05.

§Odds ratios with 95% confidence intervals from complex samples multivariable logistic regression with dependent palliative care referral (no referral vs referral) as dependent variable, and cause of death, living situation, sex and age as independent variables with COPD = reference category. Calculations only for decedents not referred to PC services).

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Appendix 1 Use and timing of palliative care services (% of all deaths)

	COPD	*Lung Cancer*	
	N=251 %	N=192 %	Bivariate p-value
Any type	22.9	58.4	<.001†
Palliative care support at home	4.4	28.4	<.001†
Hospital-based palliative care service (excl. Palliative care unit)	11.6	25.8	<.001†
Palliative care unit	1.6	10.1	<.001†
Palliative care reference person in a nursing home	7.2	2.6	<.001†

Abbreviations: OR= Odds Ratio; CI= Confidence Interval; P25-75= percentile 25 to 75; B = unstandardized coefficient.

Percentages are column percentages. Percentages may not add up to total percentage of referrals because more than one palliative care service was used in some cases. Missing values for PC referral: 4/444.

†Pearson χ^2 test testing for differences in referral between the two illness groups.

CHAPTER 2

Does use and timing of palliative home care have an effect on medical resource use in the last thirty days before death in COPD? A full-population retrospective study[iii]

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[iii] Submitted

Abstract

Background: COPD patients often use extensive medical resources, e.g. frequent hospitalisations, when they are close to death. Palliative home care (PHC) could affect end-of-life medical resource use. However, population studies studying this possible effect for COPD are lacking.

Aim: To study the effect of use and timing of PHC on medical resource use in the last 30 days before death (DBD) for COPD.

Methods: Retrospective study of all Belgian decedents in 2010-2015 who died with COPD. Odds ratios (OR) for medical resources in the last 30 DBD were calculated between using versus not using PHC, and between four PHC timing categories (>360; 360-181; 180-91; 90-31 DBD) versus not using PHC. Confounders were socio-demographic, care intensity and disease severity variables.

Results: Of the 58,527 decedents with COPD, 644 patients (1.1%) received PHC before 30 DBD. Using PHC (versus not using) decreased the OR for hospitalisation (0.35), intensive care unit admission (0.16), specialist contacts (0.58), invasive ventilation (IV) (0.13), medical imaging including chest radiograph (0.34), sedatives (0.48) and hospital death (0.14). It increased the OR for home care (3.27), general practitioner contact (4.65), palliative care unit admission (2.61), non-IV (2.65), gastric tube (2.15), oxygen (2.22), opioids (4.04) and morphine (5.29) ($p<0.001$). The results of all timing categories were similar but using PHC 90-31 DBD (versus not using) decreased or increased the OR most for these resources except for nursing home death, which had the highest increase when using PHC >360 DBD ($p<0.001$).

Conclusion: PHC use is associated with less extensive medical resource use in the last 30 DBD for COPD. Health policy and services should focus on increasing PHC access, while research should further explore the effects of early initiation of PHC for COPD.
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Background

Chronic Obstructive Pulmonary Disease (COPD) is one of the leading causes of death with global prevalence estimated to further rise in the near future[1]. There are a number of studies signalizing extensive medical resource use that might be inappropriate close to death for COPD, such as diagnostic testing, frequent acute hospitalisations in the final month of life[2] and life-prolonging care instead of comfort care in the last week before an expected death[3]. Earlier research has shown that end-stage COPD patients prefer to be cared for at home[4] and suffer from symptoms such as low mood, breathlessness, sleeping problems and anxiety.[5] These symptoms reflect their palliative care needs[5]. As a result, palliative care provision at home is needed if the patient's situation allows it.

The World Health Organisation[6] advocates a timely initiation of palliative home care (PHC). This type of support might better align medical resource use with patient care preferences, as the patient-centred approach takes into account individual care needs and wishes in a timely manner[7]. A 2016 U.S.-based study exploring the effects of PHC on healthcare use for COPD patients reported less hospital use and lower costs[8]. Other results showed that PHC reduces hospital death[9,10], improves patients' quality of life[11–13] and decreases the burden of symptoms[14]. However, despite these promising study results and pleas from health organizations, a small minority of COPD patients receive PHC[3,5,15] and if so, only very close to death[2].

A number of studies have reported on the link between palliative care and lower medical resource use for COPD such as hospitalisations[8,16]. However, population-level evidence is lacking on this topic for COPD, although it could give us more insight into the provision of appropriate end-of-life care in the whole COPD population. Here, we report the results of a population-wide retrospective study that describes the effect of use and timing of PHC, provided by multidisciplinary teams in Belgium (see Box 1), on medical resource use in the last month of life for COPD. Two research questions are addressed: 1) How does medical resource use and intensity in the last month of life differ between those COPD patients who received PHC and those who did not? 2) How does medical resource use and intensity in the last month of life differ between those COPD patients who received PHC for the first time >360, 360-181, 180-91, 90-31 days before death and those who did not?

Box 1 Palliative home care teams in Belgium

Organisation

Belgium has region-bound palliative home care (PHC), which is a separate secondary care service provided by a multidisciplinary team consisting of a PHC physician, PHC nurses and a psychologist. In total, 27 networks (of which 15 in Flanders) are operating in Belgium. PHC is requested by the patient's general practitioner (GP), depending on individual context, this is mostly in consultation with the patient, informal carers, involved community nurses, palliative care nurses in the hospital, or specialists. The main focus of PHC teams are their home visits by the PHC nurses to support the patient and informal carers for psychological, social, physical and spiritual needs (holistic approach). PHC nurses also collaborate with the involved GP if necessary. The PHC physician and the PHC psychologist are involved in weekly meetings and in psychological support for patients and informal carers. Although variation exists, most PHC team do not use standardised documents or scales to assess the symptoms and needs of the patients. Rather, they report in a general electronic patient file, which is not systematically shared with other health professionals. Contact with the latter is mainly by telephone.

Palliative status

Before referring patients to PHC, the responsible GP can request an optional 'palliative status', which is a form for PHC eligibility providing reimbursement of costs related to the palliative phase. The reimbursement system for PHC in Flanders is by law restricted to patients with three months life expectancy, with the possibility of making a second claim[70]. This has recently been altered to six months in 2018. If a palliative status is not requested, PHC can still be provided.

Methods

Study design and setting

We performed a retrospective full population analysis of people dying with COPD between 1 January 2010 and 31 December 2015 in Belgium, using linked data from administrative databases.

Data sources

A total of seven administrative and health claims databases were linked to create one common full population database[18]. Data consisted of health claims data retrieved from the InterMutualistic Agency (IMA) and socio-demographic, socioeconomic and death certificate data from Statistics Belgium. In short, the IMA database contains all reimbursed healthcare consumption and pharmaceutical dispensing data for all Belgian citizens.[19]

Statistics Belgium manages the national demographic database, which is derived from the population registry[20] and data from Census 2011[21]. Finally, a fiscal database (i.e. net taxable household income), also managed by Statistics Belgium, was linked to allow additional socio-economic insights. A detailed description of the databases, the data linkage process and content is described in detail elsewhere.[18]

Study population

The study population consisted of a selection of persons who died with COPD and died of COPD or cardiovascular diseases. We first selected all those who died with COPD. Then we extracted two groups based on their underlying cause of death noted on the death certificate in Belgium between 2010 and 2015: 1) those who died of COPD (International Classification of Diseases, 10th Revision, codes (ICD10-code: J41-44) and 2) those who died of cardiovascular diseases (ICD10-code I00-I99). We only included these causes of death because previous population-based research in Belgium has shown similar referral to PHC for both[22]. If we had included those dying from lung cancer, referral numbers to PHC would be biased due to the strong association between PHC and cancer[3]. Cardiovascular diseases are also the second most common cause of death and comorbidity for COPD patients, after COPD itself[23].

Variables & Measures

Outcomes: medical healthcare use

First, medical healthcare resources were selected from previous studies exploring frequent medical resource use in the final stages of life for COPD[2,22,24]. Next, the final selection was decided after discussion with a multidisciplinary group of researchers (pulmonologist, sociologists, general practitioners). We grouped them into 1) (hospital and primary) care interventions and admissions: hospitalisation, emergency room, intensive care unit, palliative care unit, one-day-care, home care and contacts with general practitioner (GP), specialist and physiotherapist; 2) medical procedures typical for COPD patients and end-of-life care: invasive ventilation, non-invasive ventilation, urinary tract catheter, cardiopulmonary resuscitation, medical imaging, chest radiograph, spirometry; 3) medication for COPD and comfort: oxygen, COPD medication, opioids, sedatives, morphine; and 4) place of death: in hospital, at home, in a nursing home.

In the IMA healthcare and pharmaceutical databases, health care activities and medication data are coded respectively as nomenclature codes for reimbursement purposes and Anatomical Therapeutic Chemical Classification (ATC) codes. In order to answer our research questions, specific nomenclature numbers were interpreted and aggregated into meaningful care interventions/admissions, procedures and medication categories.

Exposure: Palliative Home Care use

The exposure, using PHC, was defined as receiving a minimum of one home visit from a multidisciplinary PHC team. This was operationalised with a categorical variable of timing in days before death and was defined for analysis purposes based upon the dates related to a code for the reimbursement of costs related to PHC. This did not give us insight in the frequency of PHC visits, as we could not derive this from the data.

To compare medical resource use between those who did and did not receive PHC for the first time in the two years before death, the selected data had to meet two conditions. Firstly, the exposure variable (PHC) had to occur before the outcome variable (medical resource use). Therefore we only selected those patients who received PHC for the first time one month before death or earlier, while looking at medical resource use in the last month of life. Those who used PHC in the last month of life were only included for place of death (i.e. last day of life). Secondly, confounding factors were minimized. We controlled for as many covariates as possible that could potentially affect the results. Socio-economic covariates were: age, gender, household type, educational level attained, income, comorbidities, year of death, urbanisation level of the municipality of residence. Care intensity and disease severity covariates were: number of home care visits from a community nurse with a palliative character in the last 360 days of life (this is not the same as PHC visits), mean length of stay after admission to an intensive care unit, number of hospital, one-day-care and emergency room admissions, number of chest radiographs and invasive ventilations, and number of contacts with a GP, physiotherapist and specialist. Participant characteristics included sex, age at death, urbanisation level of the municipality of residence, educational level attained, household type, Charlson comorbidity index and taxable income (see Appendix 1 for information on which covariates were used for which medical resource use variable).

Besides describing the effect of PHC use on specific resource use, we analysed the timing of first PHC use. For this, we distinguished four timing categories: (1) having received PHC for the first time more than 360 days before death, (2) between 360 and 181 days, (3) between 180 and 91 days, and (4) between 90 and 31 days. This distinction was based on 1) the eligibility criteria for reimbursement of PHC-related costs in Belgium as determined by law between 2010-2015, which stated a maximum life expectancy of 90 days; 2) for analysis purposes: to calculate odds ratios and maximum likelihood ratios of medical resource use between each timing category and those who did not use PHC.

Statistical analysis

We conducted multivariable analysis controlling for many covariates. The aim here was to approximate the advantages of randomization and the prospective setting of a trial, as executing a trial for this study purpose would be impossible for ethical and practical reasons. To investigate potential differences, we compared patient characteristics and resource use in COPD patients who used PHC earlier than thirty days before death and those who did not, by performing chi square tests for categorical variables and Wilcoxon rank sum tests for continuous variables. Resource data were analysed using a general linear model for continuous variables and logistic regression for binary variables, with using PHC v. not using PHC as independent variables and controlling simultaneously for various covariates (see measures for details of covariates). We set the significance level at $p \leq .05$. We calculated odds ratio estimates for dichotomous outcomes and maximum likelihood estimates for continuous outcomes of each given type of medical resource use in the last thirty days of life for those who used PHC compared to those who did not use PHC. To analyse the impact of timing of PHC we offset each timing category against those who did not use PHC. All analyses were made using SAS version 9.3.

In accordance with Belgian law, approvals for access to the various databases and the database integrating all databases were obtained from two separate national sectoral committees for privacy protection: the 'Sectoral Committee of Social Security and Health, Section Health' and the 'Statistical Supervisory Committee'. Both are subcommittees of the Belgian Commission for the Protection of Privacy. Additionally, the ethics committee of the Ghent University Hospital granted its approval (B670201422382).

Results

Between 2010 and 2015, 642,901 people died in Belgium. Of those, 634,445 (98.7) were insured by one of the eight health insurance funds and therefore had data on reimbursement of health care and medication data.

Population characteristics [Table 1]

Of all 642,901 deaths between 2010-2015, 58,527 (9.1%) died with COPD and died of COPD or of cardiovascular diseases. Of those 58,527 people, 1751 (3.0%) used PHC, with 644 doing so before the last month of life. The majority of these 644 people were men (59.8%), 75-84 (38.5%) years old, who had received primary education (30.3%) and lived with their partner (49.2%). Significant differences with those who did not use PHC were dying of COPD (57.6% versus 41.4%) (p<0.001). No particular differences in the number of comorbidities or urbanization and income levels were observed (Table 1). Appendix 1 shows the population characteristics for the PHC timing categories.

Medical resource use in the last month of life for using palliative home care [Table 2]

1. Care interventions and admissions: those who used PHC versus those who did not were hospitalised less often (24.7% versus 47.9%) and for shorter periods (2.6 versus 5.3 days). They were less often admitted to the intensive care unit (3.7% versus 19.2%) and one-day care (0.9% versus 2.1%), and had specialist contact less often (9.2% versus 16.9%). More of them were admitted to the palliative care unit (7.6% versus 1.4%), received home care (73.1% versus 32.2%) and had contact with their GP (91.1% versus 75.4%) or physiotherapist (55.6% versus 50.5%). Contact with the GP was also more frequent (5.7 versus 2.4) (p<0.001).
2. Procedures: those who used PHC versus those who did not received invasive ventilation (1.2% versus 8.6%), cardiopulmonary resuscitation (0.3% versus 2.0%) and medical imaging including chest radiographs (27.0% versus 60.0%) less often. They received non-invasive ventilation more often (61.2% versus 24.0%) (p<0.001).
3. Medication: those who used PHC versus those who did not were administered sedatives less often (12.6% versus 20.0%), but oxygen (14.0% versus 6.0%), opioids (66.8% versus 33.1%) and morphine (43.3% versus 13.2%) more often (p<0.001).
4. Place of death: fewer of those who used PHC died in hospital versus those who did not (15.6% versus 55.0%), but more died at home (60.8% versus 25.9%) or in a nursing home (23.6% versus 19.1%) (p<0.001).

Multivariable tests controlling simultaneously for the different identified confounders (see Appendix 1) confirmed these results, except for one-day-care (not enough cases) and physiotherapist contact (not significant). Differences for length of stay of intensive care unit, number of specialist and physiotherapist contact, gastric tube, urinary tract catheter, spirometry and COPD drugs were very small or not existent (Table 2 & Appendix 1).

Medical resource use for timing of palliative home care (Figure 1)

Figure 1 shows the results of multivariable tests controlling simultaneously for the identified confounders between four timing categories of PHC versus no PHC for medical resource use in the last month of life.

Figure 1.A shows that each timing category of PHC versus no PHC increased the odds for

1. Care interventions and admissions: GP contact, home care, palliative care unit
2. Procedures: non-invasive ventilation
3. Medication: oxygen, opioids and morphine
4. Place of death: home and nursing home death

Figure 1.B. shows that each timing category of PHC versus no PHC decreased the odds for

1. Care interventions and admissions: hospital, intensive care unit, and emergency room
2. Procedures: invasive ventilation and medical imaging including chest radiograph
3. Medication: sedatives
4. Place of death: hospital death

Of all timing categories, using PHC for the first time 90-31 days before death (versus no PHC) showed the largest increase in home care, non-invasive ventilation, opioids and morphine ($p<0.001$) from Figure 1.A. It also showed the largest decrease in each of those resource use variables from Figure 1.B except for nursing home deaths ($p<0.001$). Detailed results can be found in Appendix 3.

Discussion

Summary of the results

This population-level study using administrative data of 58,527 COPD deceased between 2010 and 2015 shows that receiving palliative home care (PHC) changes medical resource use in the last month of life for people with COPD. Those receiving PHC (versus no PHC) were admitted to the hospital, emergency room and intensive care unit less often, received medical imaging (including chest radiographs), invasive ventilation and sedatives less often, and fewer of them died in hospital. More of them received home care, non-invasive ventilation, opioids and morphine, had general practitioner contact, and died at home or in a nursing home. These results were similar for all four PHC timing categories (versus no PHC), although the differences for the majority of medical resources were largest for those who used PHC between 90 and 31 days before death.

Interpretation of the results

A first striking result of our study was that PHC users had less extensive medical resource use than no PHC users. Hospitalisation occurred less often, which confirms the study results of a 2016 hospital-based palliative care program for COPD on lower hospitalisation[8]. The odds ratio in our study for PHC users was 4.77 times higher for dying at home. This is even higher than the odds ratio (2.21) found in a Cochrane review of 23 PHC trials for people with advanced illness (including COPD) by Gomes et al[25]. It is similar to the odds ratio (4.08) in a 2019 population study of PHC for chronically ill people by Maetens et al[13]. Our study also revealed that GP contact was high for both PHC users and non-users (91.1% and 75.4%), but differed in the frequency of contact (mean 5.7 versus 2.4). In comparison, Maetens et al[13] reported a mean number of GP contacts of 3.1 versus 0.8 in the final 14 days of life for chronically ill people.

Our results can also be related to the recent study by De Schreye et al[26] who developed and validated quality indicators, i.e. 'well-defined and measurable aspects of care'[27], to measure appropriate and inappropriate end-of-life care in COPD. Our results show that using PHC increases the chance of using more appropriate healthcare resources such as GP contacts, opioids, oxygen, home death or nursing home death[26]. GOLD guidelines also state that for the final stages of life, opioids can relieve breathlessness and that oxygen may offer some benefit even if the patient is not hypoxaemic[28]. Likewise, our results indicated that PHC can decrease inappropriate resource use, such as excessive admissions and medical imaging.

The results also showed very low and late PHC use for COPD patients. Of all 58,527 COPD patients who died of COPD or cardiovascular diseases between 2010 and 2015, only 1751 (3.0%) made use of PHC. Of those 1751 cases, the majority (1107) received PHC even in the final month of life. The population study by Maetens et al[13] reported that of 82,621 decedents, 13.5% used PHC. However those included cancer patients, which probably explains the higher referral rate[29]. Our results were also lower than the 7.2% of COPD deceased that made use of PHC in a study based on the population of the Flanders region in Belgium using 2013 data[3]. The causes could be the unpredictable disease trajectory of COPD and a lack of knowledge among COPD patients about the severity of COPD and possibilities for PHC[30]. Some health professionals also believe PHC is not meaningful or too time-consuming for COPD patients[3]. Although referral to PHC is low, it does affect extensive medical resource use positively and is associated with less inappropriate- and more appropriate care. Therefore health policy should take into account the beneficial effects of PHC on appropriate end-of-life care when designing care plans for COPD patients. Policy measures should try to increase access to PHC for COPD by incorporating knowledge and skills regarding PHC into educational programs more effectively[31] and creating public awareness campaigns about PHC and COPD for COPD patients[32].

The results on timing revealed that, of all timing categories, using PHC for the first time 90-31 days before death differed the most from not using PHC in terms of fewer hospital admissions, less medical imaging including chest radiographs, more prescriptions for opioids and morphine and more contact with GPs. This was somewhat surprisingly, given the large body of intervention studies[16,33–36] and recommendations[6,31,37,38] for early integration of palliative care (albeit mostly in cancer populations). We can suggest some explanations for this beneficial effect of late PHC initiation.

First, those using PHC for the first time 90-31 days before death may be in worse health than those using PHC for the first time more than 360 days before death. Multivariable analysis controlled for certain aspects of care intensity and severity of disease in the final two years of life, such as hospital and ICU admissions and research has, for instance, indicated that being hospitalized for an acute exacerbation is considered a good predictor of poor health or even impeding death for COPD[39]. However, the multivariable analyses might not have been able to capture all illness-related differences that can influence outcomes. It may be that the earlier initiation of palliative care indicates more uncertainty about prognosis which leads to different care use.

Second, there are possible differences in PHC intensity that are not accounted for in our analysis. As the data only provided information about the first referral to PHC, earlier PHC users might have received fewer PHC visits than late users or might even have stopped PHC visits altogether[37]. These patients could have returned to merely life-prolonging care. Finally, certain influences such as the care preferences of health professionals or their views on the meaningfulness of PHC[3] and preferences of family members and patients themselves[30] were impossible to assess. Further research should take those in account for a better analysis of medical resource use. Despite these findings, our study still shows that, regardless of the timing of first PHC use, it affects medical resource use in the same direction.

Strengths and limitations

This was, to our knowledge, the first retrospective population study of the effect of use and timing of PHC on medical resource use in the last month of life for COPD patients. We were able to use full population data from Belgians who died between 2010 and 2015. Because seven databases were linked, we could analyse medical resource use while also taking socio-demographical confounders into account. This led to a large quantity of results on care interventions, admissions, procedures and medication use. This is relevant information for designing health policy concerning access or lack of access to palliative care services in the COPD population. We also acknowledge several limitations of our study.

First, the retrospective design of the study may miss the distinction between illness when defined retrospectively and prospectively. As such, we may be assuming that all medical resources were used by patients clearly in the final stage of illness, while this might not be completely true[40]. Next, because we used administrative databases, we could not examine specific patient, informal caregiver or health professional preferences that might have influenced medical decisions and patterns of medical service use.

Moreover, decisions on end-of-life resource use in the last month of life for COPD patients might also be influenced by the severity of the disease or the number of exacerbations. However, due to a lack of specific diagnostic information available on medical files, we could not account for such confounders. Nevertheless, a retrospective design allowed us to measure real-life performance in end-of-life care for COPD patients[41]. We also simulated the conditions (controlling for confounders, exposure to PHC before receiving medical resource use) for a randomised controlled trial in the best possible way.

A third limitation was the lack of data on services not covered by insurers, such as mobile hospital palliative care teams[18]. It was also impossible to gather information on PHC intensity (frequency of visits). The data only provided information about the first PHC visit. We tried to solve this by controlling for the number of community nurse home visits of a palliative nature, which could be an indicator for the frequency of PHC visits. Lastly, to identify those who died with COPD, we used a validated algorithm as well as the intermediate and associated causes of death indicated on the death certificates. However, using the algorithm, it was impossible to determine the specific level of the disease from our data, since only dispensing data and not prescription data were available. Although there is no standard validated algorithm, the use of pharmacy data to identify COPD patients in administrative databases was found adequate in previous studies[42].

Conclusion

PHC use is strongly associated with less extensive medical resource use in the last 30 days before death for COPD. Patients received home care, non-invasive ventilation, opioids and morphine more often, had more contact with their GP and more of them died at home or in a nursing home. These results were similar when PHC was given any time between 720 and 30 days before death. However, the largest differences were for the majority of medical resources seen when using PHC 90-31 days before death. The results suggest that health policy and services should focus on increasing PHC access for COPD, while research should further explore the timing effects of early palliative home care for COPD.

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Conflict of interest

The authors declare no conflict of interest.

Tables

Table 1 Characteristics of patients who did and did not use palliative home care

	No Palliative Home Care[¥]	*Palliative home care > 30 DBD*[$]	*Palliative Home Care*[µ]
n (%)**	56776(97.0)	644(1.1)	1751(3.0)
Sex. n (%)*			
Male	33965(59.8)	385(59.8)	1060(60.4)
Female	22811(40.2)	259(40.2)	691(39.5)
Age. n (%)*			
18-64y	5548(9.8)	75(11.6)	130(7.4)
65-74y	9897(17.4)	127(19.7)	280(16.0)
75-84y	20963(36.9)	248(38.5)	644(36.8)
85-94y	18581(32.7)	179(27.8)	629(35.9)
≥ 95y	1744(3.1)	14(2.2)	66(3.8)
Educational level, n (%)*[&]			
None	4276(7.5)	54(8.4)	154(8.8)
Primary	17295(30.5)	195(30.3)	528(30,2)
Lower secondary	10430(18.4)	144(22.4)	376(21.5)
Upper secondary	5925(10.4)	79(12.3)	205(11.7)
Higher	2988(5.3)	48(7.5)	128(7.3)
Household type, n (%)*			
Single person	17939(31.6)	161(25.0)	411(23.5)
Living together, with no children in household	21207(37.4)	317(49.2)	813(46.4)
Living together, with children in household	4086(7.2)	50(7.8)	133(7.6)
One-parent family	2874(5.1)	45(7.0)	107(6.1)
Other household types	1320(2.3)	13(2.0)	32(1.8)
Collective (nursing home. psychiatric hospital)	9299(16.4)	58(9.0)	255(14.6)
Urbanisation, n (%)*			
Very high	17157(30.2)	196(30.4)	490(28.0)
High	15818(27.9)	185(28.7)	484(27.6)
Average	15508(27.3)	158(24.5)	462(26.4)
Low	7015(12.4)	93(14.4)	268(15.3)
Rural	833(1.5)	9(1.4)	33(1.9)
Cause of death, n(%)*			
COPD	23497(41.4)	371(57.6)	904(51.7)
Cardiovascular disease	33279(58.6)	273(42.4)	845(48.3)
Charlson Comorbidity Index, n (%)*			
0	48790(85.9)	559(86.8)	1441(82.3)
1	6847(12.1)	52(8.1)	211(12.1)
2	2083(3.7)	26(4.0)	78(4.5)
≥ 3	353(0.6)	7(1.1)	21(1.2)
Income, n (%)*[£]			
Lowest 40%	6107(10.8)	78(12.1)	185(10.5)
41-60%	31916(56.2)	367(57.0)	989(56.5)
Highest 39%	18702(32.9)	199(30.9)	577(32.9)

Abbreviations: PHC: palliative home care; DBD: days before death

**Percentage of total population with COPD (n=58527)

*Column percentages

[$] 644 patients received palliative home care earlier than 30 days before death

[µ] All patients receiving palliative home care

[&] 28.0% missing values for no palliative home care and 21.0% for palliative home care

[£] Income percentages represent the proportion of the total population's income

Table 2 Medical resource use utilization in the last 30 days of life for patients who did and did not use palliative home care

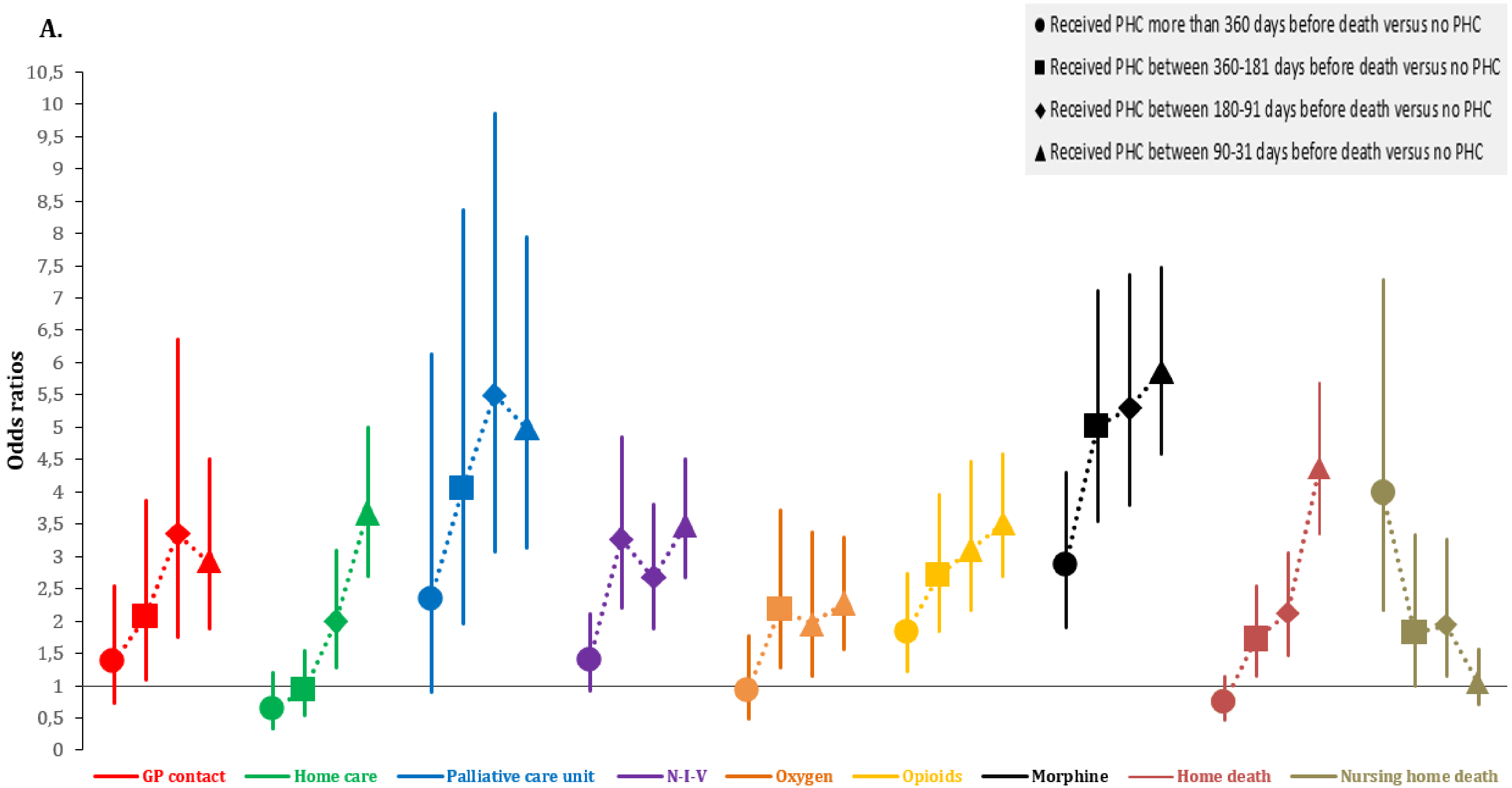
Medical resource use	*Bivariate results*		*Multivariate results*	
	No PHC#	**PHC >30 DBD#**	**PHC >30 DBD# vs no PHC**	
			Or[a](CI 95%)	**Lr[b]**
Total n	56776	644	56776	644
Admissions and care interventions				
Hospital admission, n(%)	27169(47.9)	159(24.7)	0.35(0.32-0.40)	
Hospital days, mean (CI 95%)	5.3(5.2-5.4)	2.6(2.3-2.9)		-2.60¥
ICU admission,n(%)	10884(19.2)	24(3.7)	0.16(0.12-0.20)	
LOS ICU, mean (CI 95%)	1.0(0.9-1.0)	0.1(0.1-0.2)		-0.76¥
Palliative care unit admission, n(%)	780(1.4)	49(7.6)	2.61(2.01-3.39)	
LOS Palliative care unit, mean (CI 95%)	0.1(0.1-0.1)	0.3(0.2-0.4)		0.22¥
ODC admission ,n(%)	1208(2.1)	6(0.9)	Not enough cases	
ER-admission, n(%)	22360(39.4)	126(19.6)	0.43(0.38-0.48)	
Home care, n(%)	18294(32.2)	471(73.1)	3.27(2.91-3.66)	
GP contact, n(%)	42818(75.4)	587(91.1)	4.65(3.77-5.74)	
Number of contacts, mean (CI 95%)	2.4(2.4-2.4)	5.7(5.5-5.9)		2.85¥
Specialist contact, n(%)	9566(16.9)	59(9.2)	0.58(0.50-0.69)	
Number of contacts, mean (CI 95%)	0.2(0.2-0.2)	0.1(0.1-0.2)		-0.08¥
Physiotherapist contact, n(%)	28643(50.5)	358(55.6)	0.94(0.85-1.04)	
Number of contacts, mean (CI 95%)	5.7(5.6-5.8)	5.5(5.1-5.8)		-1.14¥
Procedures				
Invasive ventilation, n(%)	4864(8.6)	8(1.2)	0.13(0.08-0.21)	
Non-invasive ventilation, n(%)	13795(24.0)	394(61.2)	2.65(2.39-2.93)	
Gastric tube, n(%)	116(0.2)	3(0.5)	2.15(1.11-4.16)	
Urinary tract catheter, n(%)	202(0.4)	3(0.5)	1.02(0.44-2.34)	
CPR,n(%)	1031(2.0)	2(0.3)	0.09(0.02-0.36)	
Medical imaging, n(%)	34010(60.0)	174(27.0)	0.34(0.31-0.38)	
Chest radiograph, n(%)	31757(56.0)	162(25.2)	0.34(0.31-0.38)	
Number Chest radiograph, mean, (CI 95%)	2.6(2.5-2.6)	0.7(0.6-0.8)		-1.56¥
Spirometry, n(%)	66(0.1)	0(0.0)	Not enough cases	
Medication				
Oxygen, n(%)	3473(6.1)	90(14.0)	2.22(1.89-2.61)	
Opioids, n(%)	18775(33.1)	430(66.8)	4.04(3.63-4.49)	
Sedatives, n(%)	11357(20.0)	81(12.6)	0.48(0.41-0.57)	
Morphine, n(%)	7465(13.2)	279(43.3)	5.29(4.78-5.86)	
COPD drugs, n(%)	35319(62.2)	411(63.8)	0.97(0.87-1.07)	
Place of death	56776	1751		
Hospital death, n(%)	31225(55.0)	274(15.6)	0.14(0.13-0.16)	
Home death, n(%)	14731(25.9)	1064(60.8)	4.77(4.29-5.30)	
Death in nursing home or residence, n(%)	10820(19.1)	413(23.6)	1.72(1.50-1.96)	

Abbreviations: PHC: palliative home care; DBD: Days before death; LOS: length of stay (in days); ICU: intensive care unit; ODC: one day care; GP: general practitioner; CPR: cardiopulmonary resuscitation; n.a.: not applicable. N.s.: not significant

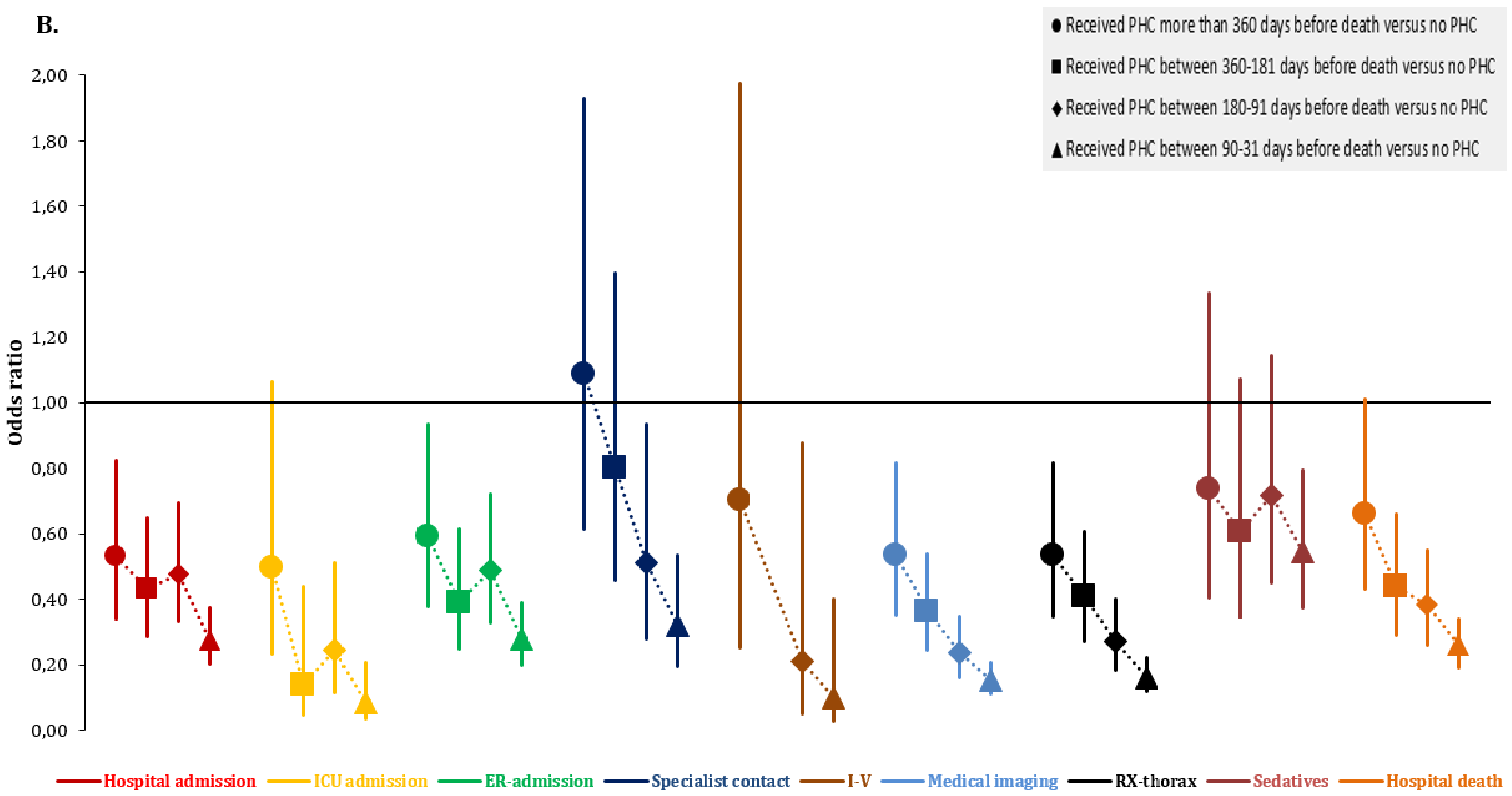
[#]Column percentages

[A]odds Ratios and [b]likelihood Ratios were obtained by logistic regression with reference category: no palliative home care, controlled for age, household type, attained educational level, urbanization, year of death, amount of comorbidity, amount of home care visits with a palliative character from a community nurse in the last 360 days of life and care intensity parameters in the last 365 days of life (Appendix 1). ¥P <.05 versus no palliative home care.

Figure 1 Medical resource utilization in the last thirty days of life and timing of palliative home care



Abbreviations: PHC: palliative home care; GP: general practitioner; N-I-V: non-invasive ventilation. Symbols reflect an odds ratio, and the lines represent the range. Figure 1.A. shows positive odds of palliative home care timing categories versus not using palliative home care; Covariates: see Appendix 1.



Abbreviations: PHC: palliative home care; ICU: intensive care unit; ER: emergency room; I-V: invasive ventilation. Symbols reflect an odds ratio, and the lines represent the range. Figure 1.B. shows negative odds of palliative home care timing categories versus not using palliative home care. Covariates: see Appendix 1.

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Appendix 1 List of covariates for each medical resource use

Medical resource use	*Demographic variables* and number of visits with a palliative character from a community nurse 365-30 days before death*	***Between 720 and 30 days before death***								
		Mean length of stay ICU admission	Number of ICU admissions	Number of hospitalisations	Number of ER admissions	Number of GP contacts	Number of physiotherapist contacts	Number of specialist contacts	Number of Chest radiograph	Number of invasive ventilation
Hospital admission	X	X	X		X	X	X	X	X	X
Hospital days, mean	X	X	X		X	X	X	X	X	X
ICU admission	X			X	X	X	X	X	X	X
LOS ICU	X			X	X	X	X	X	X	X
Palliative care unit admission	X	X	X	X	X	X	X	X	X	X
LOS Palliative care unit	X	X	X	X	X	X	X	X	X	X
ODC	X	X	X	X	X	X	X	X	X	X
ER admission	X	X	X	X		X	X	X	X	X
Home care	X	X	X	X	X	X	X	X	X	X
GP contact	X	X	X	X	X		X	X	X	X
Number of GP contacts	X	X	X	X	X		X	X	X	X
Specialist contact	X	X	X	X	X	X	X		X	X
Number of specialist contacts	X	X	X	X	X	X	X		X	X
Physiotherapist contact	X	X	X	X	X	X		X	X	X
Number of physiotherapist	X	X	X	X	X	X		X	X	X
Invasive ventilation	X	X	X	X	X	X	X	X	X	
Non-invasive ventilation	X	X	X	X	X	X	X	X	X	X
Gastric tube	X	X	X	X	X	X	X	X	X	X
Urinary tract catheter	X	X	X	X	X	X	X	X	X	X
CPR	X	X	X	X	X	X	X	X	X	X
Medical imaging	X	X	X	X	X	X	X	X	X	X
Chest radiograph	X	X	X	X	X	X	X	X		X
Number Chest radiograph	X	X	X	X	X	X	X	X		X
Spirometry	X	X	X	X	X	X	X	X	X	X
Oxygen	X	X	X	X	X	X	X	X	X	X
Opioids	X	X	X	X	X	X	X	X	X	X
Sedatives	X	X	X	X	X	X	X	X	X	X
Morphine	X	X	X	X	X	X	X	X	X	X
COPD drugs	X	X	X	X	X	X	X	X	X	X
Hospital death	X	X	X	X	X	X	X	X	X	X
Home death	X	X	X	X	X	X	X	X	X	X
Death in nursing home	X	X	X	X	X	X	X	X	X	X

*Age, gender, household type, attained educational level, income, comorbidities, year of death, urbanisation level of the municipality of residence.

Abbreviations: ICU: intensive care until; ER: Emergency Room, GP: general practitioner; ODC: one-day-care; CPR: coronary pulmonary resuscitation

Appendix 2.a Demographic characteristics for use of palliative home care

DEMOGRAPHIC RESULTS FOR PALLIATIVE HOME CARE USE

	Total study population	No Palliative Home Care[¥]	Palliative home care >30DBD	Palliative Home Care[#]
n (´% of n)	58527(100.0)	56776(.0)	644	1751(3.0)
Sex. n (%)*				
Male	35025(59.8)	33965(59.8)	385(59.8)	1060(3.0)
Female	23502(40.2)	22811(40.2)	259(40.2)	691(2.9)
Age. n (%)*				
18-64y	5678(9.7)	5548(9.8)	75(11.6)	130(2.3)
65-74y	10177(17.4)	9897(17.4)	127(19.7)	280(2.4)
75-84y	21607(36.9)	20963(36.9)	248(38.5)	644(2.5)
85-94y	19210(32.8)	18581(32.7)	179(27.8)	629(2.6)
≥ 95y	1810(3.1)	1744(3.1)	14(2.2)	66(2.7)
Educational level. n (%)*				
None	4430(7.6)	4276(7.5)	54(8.4)	154(3.5)
Primary	17823(30.5)	17295(30.5)	195(30.3)	528(3.0)
Lower secondary	10806(18.5)	10430(18.4)	144(22.4)	376(3.5)
Upper secondary	6130(10.5)	5925(10.4)	79(12.3)	205(3.3)
Higher	3116(5.3)	2988(5.3)	48(7.5)	128(4.1)
Household type. n (%)*				
Single person	18350(31.4)	17939(31.6)	161(25.0)	411(2.2)
Living together, with no children in household	22020(37.7)	21207(37.4)	317(49.2)	813(3.7)
Living together, with children in household	4219(7.2)	4086(7.2)	50(7.8)	133(3.2)
One-parent family	2981(5.1)	2874(5.1)	45(7.0)	107(3.6)
Other household types	1352(2.3)	1320(2.3)	13(2.0)	32(2.4)
Collective (nursing home. psychiatric hospital)	9554(16.3)	9299(16.4)	58(9.0)	255(2.7)
Urbanisation*				
Very high	17647(30.2)	17157(30.2)	196(30.4)	490(2.8)
High	16302(27.9)	15818(27.9)	185(28.7)	484(3.0)
Average	15970(27.3)	15508(27.3)	158(24.5)	462(2.9)
Low	7283(12.4)	7015(12.4)	93(14.4)	268(3.7)
Rural	866(1.5)	833(1.5)	9(1.4)	33(3.8)
Cause of death, n(%)				
COPD	24401(41.7)	23497(41.4)	371(57.6)	904(51.7)
Cardiovascular diseases	34124(58.3)	33279(58.6)	273(42.4)	845(48.3)
Previous hospitalisations				
Mean LOS hospitalisations in the past 2 years until 30 DBD	38.1(38.2-39.1)	38.9(38.5-39.2)	51.6(45.5-58.3)	46.8(44.7-48.8)
Hospitalisations in the past 2 years until 30 DBD, mean (s.d.)	2.6(2.7)	2.7(2.8)	4.2(3.6)	3.6(3.1)
Charlson Comorbidity Index. n (%)*				
0	48934(83.61)	48790(85.9)	559(86.8)	1441(2.9)
1	7058(12.06)	6847(12.1)	52(8.1)	211(3.0)
2	2161(3.69)	2083(3.7)	26(4.0)	78(3.6)
≥ 3	374(0.6)	353(0.6)	7(1.1)	21(5.6)
Income*				
Lowest 40%	6292(10.7)	6107(10.8)	78(12.1)	185(5.9)
41-60%	32905(53.3)	31916(56.2)	367(57.0)	989(3.0)
Highest 39%	19279(33.0)	18702(32.9)	199(30.9)	577(6.2)

*Column percentages. [¥]Column percentages of population receiving palliative home care; [#]Row percentages of total study population; Abbreviations: LOS: length of stay; DBD: days before death; n.a.: not-applicable; s.d.: standard deviation

Appendix 2.b Demographic characteristics for timing of palliative home care

DEMOGRAPHIC RESULTS FOR TIMING CATEGORIES OF PALLIATIVE HOME CARE

	Timing receiving palliative home care in days before death				
	>360	360-181	180-91	90-31	30-1
n (´% of n)	110(6,3)	129(7.4)	143(8.2)	262(15.0)	1107(11.0)
Sex. n (%)*					
Male	71(6.7)	68(6.4)	91(8.6)	155(14.6)	676(63.7)
Female	39(5.6)	61(8.8)	52(7.5)	107(15.5)	432(62.5)
Age. n (%)*					
18-64y	13(10.0)	18(13.8)	19(14.6)	25(19.2)	55(42.3)
65-74y	17(6.1)	28(10.0)	26(9.3)	56(20)	153(54.6)
75-84y	44(6.8)	40(6.2)	56(8.7)	108(16.8)	396(61.6)
85-94y	33(5.2)	37(5.9)	38(6)	71(11.3)	450(71.6)
≥ 95y	2(3)	6(9.1)	4(6.1)	2(3)	52(78.8)
Educational level. n (%)*					
None	9(5.8)	19(12.3)	7(4.5)	19(12.3)	100(64.9)
Primary	23(4.4)	42(8)	49(9.3)	81(15.3)	333(63.1)
Lower secondary	22(5.9)	26(6.9)	32(8.5)	64(17)	232(61.7)
Upper secondary	11(5.4)	12(5.9)	25(12.2)	31(15.1)	126(61.5)
Higher	14(21.3)	9(65.7)	7(13.7)	18(51.1)	80(62.5)
Household type. n (%)*					
Single person	30(7.3)	36(8.8)	34(8.3)	61(14.8)	250(60.8)
Living together, with no children in household	50(6.2)	60(7.4)	77(9.5)	130(16.0)	496(61.0)
Living together, with children in household	9(6.8)	9(6.8)	11(8.3)	21(15.8)	83(62.4)
One-parent family	7(6.5)	10(9.3)	8(7.5)	20(18.7)	62(57.9)
Other household types	2(6.3)	1(3.1)	1(3.1)	9(28.1)	19(59.4)
Collective (nursing home. psychiatric hospital)	12(4.7)	13(5.1)	12(4.7)	21(8.2)	197(77.2)
Urbanisation*					
Very high	32(6.5)	41(8.4)	38(7.8)	85(17.3)	294(60)
High	39(8.1)	37(7.6)	39(8.1)	70(14.5)	299(61.8)
Average	20(4.3)	28(6.1)	43(9.3)	67(14.5)	304(65.8)
Low	17(6.3)	21(7.8)	18(6.7)	37(13.8)	175(65.3)
Rural	1(3.0)	2(6.1)	4(12.1)	2(6.1)	24(72.7)
Cause of death, n(%)					
COPD	61(55.5)	83(64.3)	77(53.9)	150(57.3)	535(43.3)
Cardiovascular diseases	49(44.5)	46(35.7)	66(46.2)	112(42.8)	572(51.7)
Previous hospitalisations					
Mean LOS hospitalisations in the past 2 years until 30 DBD, mean (range)	48.8 (41.4-56.2)	46.0 (39.2-52.8)	57.5 (48.9-66.1)	52.4 (46.9-57.9)	n.a.
Hospitalisations in the past 2 years until 30 DBD, mean (s.d.)	3.9(2.8)	3.9(3.2)	4.4(3.4)	4.4(3.6)	n.a.
Charlson Comorbidity Index. n (%)*					
0	91(6.3)	112(7.8)	126(8.7)	230(16)	882(61.2)
1	14(6.6)	10(4.7)	10(4.7)	18(8.5)	159(75.4)
2	4(4.8)	5(9.5)	5(9.5)	12(9.5)	52(66.8)
≥ 3	1(4.8)	2(9.5)	2(9.5)	2(9.5)	14(66.7)
Income*					
Lowest 40%	9(12.4)	19(22.0)	19(18.6)	31(32.9)	107(57.8)
41-60%	62(6.3)	69(7.0)	84(8.5)	152(15.4)	622(62.9)
Highest 39%	39(13.3)	41(13.2)	40(13.5)	79(27.5)	378(65.5)

Abbreviations: LOS: length of stay; DBD: days before death; n.a.: not-applicable; s.d.: standard deviation; *Column percen

Appendix 3.a Medical resource use for palliative home care use and timing (bivariate results)

Medical resources

	No PHC#	PHC >30 DBD #	Timing of receiving PHC for the first time in days before death				
			>360#	360-181#	180-91#	90-31#	30-1#
Total n	**56776**	**644**	**110**	**129**	**143**	**262**	**1107**
Admissions and care interventions							
Hospital admission, n(%)	27169(47.9)	159(24.7)	29(26.4)	32(24.8)	43(30.1)	55(21.0)	n.a.
LOS hospital days, mean (CI 95%)	5.3 (5.2-5.4)	2.6 (2.3-2.9)	3.6 (2.4-4.8)	2.5 (3.6-2.4)	1.2 (2.5-3.6)	1.9 (1.2-2.5)	n.a.
ICU admission, n(%)	10884(19.2)	24(3.7)	8(7.3)	3(2.3)	8(5.6)	5(1.9)	n.a.
LOS ICU, mean (CI 95%)	1.0(0.9-1.0)	0.1 (0.1-0.2)	0.2 (0.0-0.3)	0.2 (0.2-0.0)	0.0 (0.2-0.2)	0.1 (0.0-0.2)	n.a.
Palliative care unit admission, n(%)	780(1.4)	49(7.6)	5(4.6)	9(7.0)	14(9.8)	21(8.0)	n.a.
LOS Palliative care unit, mean (CI 95%)	0.1 (0.1-0.1)	0.3 (0.2-0.4)	0.9 (0.3-1.5)	1.1 (0.9-0.3)	0.4 (1.1-0.9)	0.8 (0.4-1.1)	n.a.
ODC admission ,n(%)	1208(2.1)	6(0.9)	1(0.9)	2(1.6)	1(0.7)	2(0.8)	n.a.
ER admission, n(%)	22360(39.4)	126(19.6)	26(23.6)	24(18.6)	34(23.8)	42(16.0)	n.a.
Home care, n(%)	18294(32.2)	471(73.1)	74(67.3)	92(71.3)	105(73.4)	200(76.3)	n.a.
GP contact, n(%)	42818(75.4)	587(91.1)	98(89.1)	118(91.5)	132(92.3)	239(91.2)	n.a.
Number of GP contacts, mean (CI 95%)	2.4 (2.4-2.4)	5.7 (5.5-5.9)	4.8 (4.1-5.4)	6.3 (4.8-4.1)	5.1 (6.3-4.8)	5.7 (5.1-6.3)	n.a.
Specialist contact, n(%)	9566(16.9)	59(9.2)	15(13.6)	15(11.6)	12(8.4)	17(6.5)	n.a.
Number of specialist contacts, mean (CI 95%)	0.2 (0.2-0.2)	0.1 (0.1-0.2)	0.1 (0.0-0.2)	0.1 (0.1-0.0)	0.0 (0.1-0.1)	0.1 (0.0-0.1)	n.a.
Physiotherapist contact, n(%)	28643(50.5)	358(55.6)	57(51.8)	81(62.8)	81(56.6)	139(53.1)	n.a.
Number of physiotherapist, mean (CI 95%)	5.7 (5.6-5.8)	5.5 (5.1-5.8)	7.6 (5.9-9.2)	7.4 (7.6-5.9)	5.3 (7.4-7.6)	6.3 (5.3-7.4)	n.a.
Procedures							
Invasive ventilation, n(%)	4864(8.6)	8(1.2)	4(3.6)	0(0.0)	2(1.4)	2(0.8)	n.a.
Non-invasive ventilation, n(%)	13795(24.0)	394(61.2)	58(52.7)	87(67.4)	86(60.1)	163(62.2)	n.a.
Gastric tube, n(%)	116(0.2)	3(0.5)	0(0.0)	1(0.8)	2(1.4)	0(0.0)	n.a.
Urinary tract catheter, n(%)	202(0.4)	3(0.5)	1(0.9)	1(0.8)	1(0.7)	0(0.0)	n.a.
CPR, n(%)	1031(2.0)	2(0.3)	1(0.9)	0(0.0)	0(0.0)	1(0.4)	n.a.
Medical imaging, n(%)	34010(60.0)	174(27.0)	38(34.6)	38(29.5)	41(28.7)	57(21.8)	n.a.
Chest radiograph, n(%)	31757(56.0)	162(25.2)	35(31.8)	37(28.7)	39(27.3)	51(19.5)	n.a.
Number Chest radiograph, mean, (CI 95%)	2.6 (2.5-2.6)	0.7 (0.6-0.8)	0.7 (0.4-1.0)	0.5 (0.7-0.4)	0.2 (0.5-0.7)	0.4 (0.2-0.5)	n.a.
Spirometry, n(%)	66(0.1)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	n.a.
Medication							
Oxygen, n(%)	3473(6.1)	90(14.0)	13(11.8)	21(16.3)	18(12.6)	38(14.5)	n.a.
Opioids, n(%)	18775(33.1)	430(66.8)	65(59.1)	87(67.4)	98(68.5)	180(68.7)	n.a.
Sedatives, n(%)	11357(20.0)	81(12.6)	13(11.8)	14(10.9)	22(15.4)	32(12.2)	n.a.
Morphine, n(%)	7465(13.2)	279(43.3)	33(30.0)	57(44.2)	65(45.5)	124(47.3)	n.a.
COPD drugs, n(%)	35319(62.2)	411(63.8)	76(69.1)	82(63.6)	95(66.4)	158(60.3)	n.a.
Place of death		**1751**					
Hospital death	31225(55.0)	274(15.6)	38(34.5)	37(28.7)	47(32.9)	68(26.0)	84(7.6)
Home death	14731(25.9)	1064(60.8)	48(43.6)	72(55.8)	72(50.3)	158(60.3)	714(64.5)
Death in nursing home of residence	10820(19.1)	413(23.6)	24((21.8)	20(15.5)	24(16.8)	36(13.7)	309(27.9)

Abbreviations: PHC: palliative home care; DBD: Days before death; ICU: intensive care unit; ODC: one day care; GP: general practitioner; CPR: cardiopulmonary resuscitation; n.a.: not applicable. n.s.: not significant #column percentages

Appendix 3.b Medical resource use for palliative home care use and timing (multivariate results)

	PHC vs no PHC		*>360 vs no PHC*		*360-181 vs no PHC*		*180-91 vs no PHC*		*90-31 vs no PHC*	
	OR ^{a}(CI 95%)	**LR ^{b}**	**OR^{a} (CI 95%)**	**LR ^{b}**	**OR^{a} (CI 95%)**	**LR ^{b}**	**OR ^{a}(CI 95%)**	**LR^{b}**	**OR ^{a}(CI 95%)**	**LR^{b}**
Admissions and care interventions										
Hospital admission	0.35(0.32-0.40)		0.53(0.34-0.82)		0.43(0.28-0.65)		0.48(0.33-0.69)		0.28(0.20-0.37)	
LOS hospital, mean		-2.60¥		-1.46¥		-2.08¥		-1.63¥		-3.46¥
ICU admission	0.16(0.12-0.20)		0.50(0.23-1.06)		0.14(0.04-0.44)		0.24(0.12-0.51)		0.08(0.04-0.21)	
LOS ICU, mean		-0.76¥		-0.20		-0.60¥		-0.78¥		-0.83¥
Palliative care unit admission	2.61(2.01-3.39)		2.34(0.89-6.14)		4.05(1.96-8.36)		5.50(3.07-9.86)		4.99(3.14-7.95)	
LOS Palliative care unit, mean		0.22¥		0.18		0.82¥		0.75¥		0.63¥
ODC admission	not enough cases		not enough cases		not enough cases		not enough cases		not enough cases	
ER admission	0.43(0.38-0.48)		0.59(0.38-0.93)		0.39(0.25-0.61)		0.49(0.33-0.72)		0.28(0.20-0.39)	
Home care	3.27(2.91-3.66)		0.64(0.34-1.20)		0.91(0.54-1.55)		1.99(1.28-3.09)		3.68(2.70-5.01)	
GP contact	4.65(3.77-5.74)		1.36(0.72-2.55)		2.05(1.09-3.87)		3.34(1.76-6.36)		2.91(1.89-4.51)	
Number of GP contacts, mean		2.85¥		0.09		1.65¥		1.58¥		2.83¥
Specialist contact	0.58(0.50-0.69)		1.09(0.61-1.93)		0.80(0.46-1.40)		0.51(0.28-0.93)		0.32(0.20-0.53)	
Number of specialist contacts, mean		-0.08¥		0.06		-0.05		-0.07		-0.12¥
Physiotherapist contact	0.94(0.85-1.04)		0.68(0.45-1.01)		1.19(0.82-1.74)		0.86(0.61-1.21)		0.84(0.65-1.08)	
Number of physiotherapists, mean		-1.14¥		-1.80¥		0.30		-0.60		-0.91
Procedures										
Invasive ventilation	0.13(0.08-0.21)		0.70(0.25-1.97)		not enough cases		0.21(0.05-0.88)		0.10(0.03-0.40)	
Non-invasive ventilation	2.65(2.39-2.93)		1.38(0.91-2.10)		3.27(2.20-4.85)		2.67(1.87-3.81)		3.47(2.67-4.51)	
Gastric tube	2.15(1.11-4.16)		not enough cases		not enough cases		not enough cases		not enough cases	
Urinary tract catheter	1.02(0.44-2.34)		3.70(0.47-28.87)		3.14(0.40-24.47)		2.25(0.30-17.05)		not enough cases	
CPR	0.09(0.02-0.36)		1.18(0.16-8.73)		not enough cases		not enough cases		0.28(0.04-2.05)	
Medical imaging	0.34(0.31-0.38)		0.53(0.35-0.81)		0.36(0.24-0.54)		0.24(0.16-0.35)		0.15(0.11-0.21)	
Chest radiograph	0.34(0.31-0.38)		0.53(0.35-0.82)		0.41(0.27-0.61)		0.27(0.18-0.40)		0.16(0.12-0.22)	
Number Chest radiograph, mean		-1.56¥		-0.73		-1.22¥		-1.74¥		-2.01
Spirometry	not enough cases		not enough cases		not enough cases		not enough cases		not enough cases	
Medication										
Oxygen	2.22(1.89-2.61)		0.92(0.48-1.76)		2.17(1.27-3.71)		1.96(1.14-3.37)		2.27(1.56-3.30)	
Opioids	4.04(3.63-4.49)		1.83(1.22-2.73)		2.70(1.84-3.96)		3.11(2.16-4.46)		3.50(2.68-4.58)	
Sedatives	0.48(0.41-0.57)		0.74(0.41-1.34)		0.61(0.34-1.07)		0.72(0.45-1.15)		0.54(0.37-0.79)	
Morphine	5.29(4.78-5.86)		2.86(1.90-4.31)		5.02(3.54-7.11)		5.29(3.80-7.36)		5.86(4.59-7.48)	
COPD drugs	0.97(0.87-1.07)		1.24(0.81-1.88)		0.93(0.64-1.36)		0.95(0.67-1.36)		0.74(0.58-0.96)	
Place of death										
Hospital death	0.14(0.13-0.16)		0.66(0.43-1.01)		0.44(0.29-0.66)		0.38(0.26-0.55)		0.26(0.19-0.34)	
Home death	4.77(4.29-5.30)		0.73(0.46-1.14)		1.71(1.15-2.54)		2.12(1.47-3.05)		4.36(3.34-5.69)	
Death in nursing home of residence	1.72(1.50-1.96)		3.97(2.17-7.29)		1.81(0.99-3.33)		1.93(1.14-3.26)		1.04(0.70-1.56)	

Abbreviations: PHC: palliative home care; DBD: Days before death; ICU: intensive care unit; ODC: one day care; GP: general practitioner; CPR: cardiopulmonary resuscitation; n.a.: not applicable. n.s.: not significant

PART 2

DEVELOPING AND TESTING A PILOT INTERVENTION

CHAPTER 3

"A palliative end-stage COPD patient does not exist": a qualitative study of barriers to and facilitators for early-integrated palliative home care for end-stage COPD[iv]

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Abstract

The early-integrated palliative home care (PHC) can positively affect people with Chronic Obstructive Pulmonary Disease (COPD). However, PHC as a holistic approach is not well integrated into clinical practice for end-stage COPD. General practitioners (GPs) and community nurses (CNs) are highly involved in primary and home care and could provide valuable perspectives about barriers to and facilitators for early-integrated PHC in end-stage COPD. Three focus groups were organised with GPs (n=28) and four with CNs (n=28), transcribed verbatim and comparatively analysed. Barriers were related to the unpredictability of COPD, a lack of disease insight and resistance towards care of the patient, lack of cooperation and experience with PHC on behalf of the healthcare professionals, lack of education about early-integrated PHC, insufficient continuity of care from hospital to home and lack of communication about PHC between professional caregivers and the person with end-stage COPD. Facilitators were the use of trigger moments for early-integrated PHC, such as after a hospital admission or when the person becomes oxygen-dependent or housebound, positive attitudes towards PHC in informal carers, more focus on early-integrated PHC in professional education, implementing advance care planning in healthcare and PHC systems and enhancing communication about care and PHC. The results provide insights for clinical practice and the development of key components for successful practice in a phase 0-2 Early-integrated PHC for end-stage COPD (EPIC) trial, such as the improvement of the integration of care, encouragement of the disease insight of the person with COPD and the training of PHC nurses in care for end-stage COPD. Funding: IWT/SBO: 140009.

Background

Chronic Obstructive Pulmonary Disease (COPD) is one of the leading causes of death[1], with an illness trajectory characterised by a progressive and inexorable decline interlaced with acute exacerbations[2]. People with end-stage COPD (which we chose to define as 'mostly GOLD stage III or IV[3] and low to very low functioning'), mainly suffer from symptoms such as dyspnea, pain, fatigue, anxiety and low mood. This leads to a poor quality of life in the final stages of the disease[4]. Despite numerous therapies to treat symptoms, end-stage COPD impacts heavily on emotional and social functioning and daily activities[4] and physical and psychosocial symptoms are poorly addressed.[5]

We know from former research that palliative care (PC), if integrated into standard care earlier than the final weeks of life, can offer support for these symptoms which in fact signal PC needs, and may have a positive impact on the person with end-stage COPD[6,7]. The Global Initiative for Chronic Obstructive Lung Disease (*GOLD*) also recommends early-integrated PC as a way to improve symptoms that reflect PC needs (such as dyspnea, anxiety, pain, fatigue), which would potentially be better treated if PC was not introduced only right at the end of life[3].

However, there is no unifying definition or common understanding in literature of what early-integrated PC is. This might be due to the polymorphous nature of integrated care itself[8]. For this study, the meaning of early-integrated PC can be derived from combining the definitions of PC and of integrated health services given by the World Health Organisation (WHO). The WHO definition of PC incorporates: 1) encouraged collaboration between all healthcare professionals (which we define as general practitioners, specialist physicians, nurses, physiotherapists, dentists, pharmacists, midwives, and paramedics) in order to connect their expertise and 2) early assessment of PC by integrating it with disease-based 'curative' therapies[9]. Furthermore, the WHO definition of Integrated Health Services emphasises 'the management and delivery of health services so that patients receive a continuum of preventive and curative services, according to their needs over time and across different levels of the health system.'[10]

People with end-stage COPD often die in intensive care units in hospitals or nursing homes rather than at home[11] whereas they actually prefer home care[12]; the majority of people with all types of disease wish to die at home[13]. If PC is provided at home by a PC nurse or other PC professional, it can also improve quality of life and care[14,15], increase the chances of dying at home[16] and reduce the burden of symptoms without affecting the levels of grief of informal carers[17]. Moreover, early-integrated palliative home care (PHC) can help to avoid hospital admissions and escalation of costs related to the final months of life for people with end-stage diseases.[18] Lastly, a qualitative study has shown that people with end-stage COPD have indicated needs for PHC and fully accept early-integrated PHC.[19]

In practice, however, early-integrated PHC for end-stage COPD is not without its challenges as the unpredictability of the illness trajectory and the chances of survival can complicate its early integration.[6]

In Belgium, COPD accounted for 10.7% of all deaths in 2015, which made it the third most common cause of death[20]. Furthermore, a study in Flanders revealed that of all deaths from end-stage COPD in 2013, only 37.3% were referred to PC, of which 7.2% involved PC at home. For half of the referred patients, time of onset of PC was only six days prior to death[21]. Reasons for not referring were, according to the physicians involved, lack of time, because PC was not meaningful or that PC needs were addressed in standard care[21]. As research on implementing early-integrated PHC for end-stage COPD is thin on the ground, with studies only exploring the patient's acceptance of integrated PHC[19], investigating PC and end-of-life discussions for COPD in general[22] or not specifically focusing on end-stage COPD[16,23], a more detailed examination of the challenges and possibilities of early-integrated PHC for end-stage COPD is needed to gain insight into reasons why it is currently lacking and how to tackle this.

Likewise, little is known about the opinions of the parties involved in the early-integrated PHC for end-stage COPD, with the exception of the patient's perspectives[19] and those of pulmonologists[24]; the views of general practitioners (GPs) and community nurses (CNs) are lacking. These perspectives are crucial in identifying specific reasons why implementing this type of care is difficult in end-stage COPD[25,26] as GPs and CNs in Belgium are active in primary and home care and well informed about PHC services. In order to gain useful data for clinical and policy-related solutions, this study aims to identify (1) barriers and (2) facilitators from the perspective of GPs and CNs for early-integrated PHC in standard care for people with end-stage COPD. This qualitative study is performed as part of a larger study to develop a complex phase 0-2 intervention trial on early integrated PHC for end-stage COPD (EPIC) in Flanders, Belgium.

Methods

Study design

A qualitative approach using focus groups was chosen for its group dynamic features that stimulate interaction between participants and allow the moderator to use more active interview techniques than with face-to-face interviews[45]. This approach was supported by the methodological orientation of grounded theory[45], as we constructed new insights based on data obtained from the focus groups. The research protocol and topic guides were approved by the Ethics Committee of Ghent University Hospital (Reference: 2016/0171).

Study setting

The study was based in workplace settings in urban and semi-urban regions in Flanders, Belgium, in 2016, as it was part of the development of a phase 2 intervention on early-integrated PHC for end-stage COPD in Flanders, Belgium.

Study population and sampling

The study population consisted of GPs and CNs involved in primary and home care settings. In selecting the participants, three criteria were stipulated as a guiding line for recruitment: 1) Dutch speaking; 2) at least five years' experience as a GP or CN; 3) having cared for at least three end-stage COPD patients. We also took into account variation in semi-urban and urban areas. We then used 'convenience sampling'. With this technique, the sample was composed of participants or groups who met the criteria and who were available or signed up first[46]. However, individual recruitment of GPs and CNs for focus group participation was difficult and we had to change strategy. Only one focus group with CNs was composed by gathering independent CNs from the same region. This was done by contacting individual CNs from one urban area by phone through a contact list from the Flemish Professional Association for Independent Nurses which is available online: http://www.verplegingthuis.be/ .

As a solution, we used besides the convenience sampling technique, a purposive sampling technique which allowed the research team to select participants based on the researcher's judgment. We organised focus groups which consisted either of one regionally composed group of GPs or one regionally composed group of CNs. This type of recruitment could offer us a sample of GPs and CNs representing a wide range of experience related to the topic (maximum variation sampling), even if not all participants met the inclusion criteria. For GPs, these were local peer review GP groups (LOK), geographically determined groups of GPs from both individual and group practices. They meet four times a year to share and critically evaluate their medical practice (peer review) and to improve their quality of care. For CNs these were regionally composed groups from the National Association of Catholic Flemish Nurses and Midwifes (NVKVV) who meet monthly to discuss their practice and share work-related experiences[47].

Recruitment strategy

The participants were initially identified by a member of the research team and other key contacts who were either GPs, CNs or policy members of organisations involved in community care. Further recruitment for GPs was undertaken by contacting several people responsible for local peer review (LOK) GP groups in Flanders in person, by phone or e-mail. Further recruitment of CNs was done by contacting the '*Wit-Gele Kruis*', a Flemish organisation for CNs. This organisation was asked to help with the recruitment by forwarding the call for participants to its members. Through this organisation, we contacted those responsible for regionally composed groups of CNs by phone to organise the focus group when that group had a meeting. Potential groups of GPs or CNs were invited to take part in a focus group by e-mails containing information about the study and participation. Suitable dates and venues were arranged with the people in charge of the local peer review GP groups or regionally composed CN group, if all group members agreed to participate in the study.

Data collection

Recruitment and focus group conversations took place between March and September 2016. A semi-structured topic guide (pilot tested), consisting of four main questions and a set of prompts for each question, was developed and reviewed within a multidisciplinary research team of sociologists, a GP, a lung specialist and an oncologist (for content of the topic guide: Box 1). End-stage COPD was described during the focus group as mostly GOLD stage III or IV[3] and low to very low functioning and PHC as the support of the multidisciplinary PHC teams.

Each focus group was moderated by one male senior researcher (sociologist or psychologist) and observed by one female junior researcher (sociologist or psychologist) who made field notes, all experienced in conducting focus groups due to training in former education and conducting qualitative research in previous studies. The focus groups took place in a quiet room, were conducted in Flemish, lasted on average one and a half hours and were audio taped, for which all participants gave informed written consent. All participants filled in a short questionnaire regarding their own demographic characteristics, clinical experience and experience with care and PC or PHC for end-stage COPD. After conducting two focus groups with GPs, the research team slightly adapted the topic list by leaving out the first question on perceived main problems for people with end-stage COPD, as this question did not lead to significant information regarding early-integrated PHC. We continued recruitment and sampling until data saturation was achieved. Saturation was defined as when no new themes on barriers and facilitators occurred during the focus group.

Data analysis

The focus groups were completely transcribed verbatim. Then we used NVivo 9 software to code and analyse the data according to the research questions. Two researchers (CS and KC) first read and coded the data in themes which were derived from the data from four full focus group transcripts and compared similarities and differences in their analyses until a primary coding framework was constructed. Then all seven focus group transcripts were independently read, compared with the primary coding framework by the two researchers and these results were discussed with all members of the research team. Codes were added, modified or merged when necessary. A third and fourth researcher (PP and LD) made final changes to the codes, which were approved by the other two coding researchers. Once coding was finalised, all transcripts and the coding framework were revised and refined, resulting in (sub)categories of barriers and facilitators. Quotations were selected and approved by the research team to illustrate the results. Transcripts were not sent back to participants for correction but respondent validation of the results was undertaken by sending the results of the study by e-mail to all participating GPs and CNs for consent.

Box 1 Topic list based on research questions

Introduction

1. What are the main problems for people with end-stage COPD, physically, psychologically and socially?
    - Which problems of people with end-stage COPD have the biggest impact on their wellbeing and health?
2. How is the current palliative home care for people with end-stage COPD organized?
    - Who is involved in the current care and what are their roles?
    - What is the quality level of communication and information towards people with end-stage COPD?
3. How could the current problems with PHC for people with end-stage COPD be better addressed (through involvement of palliative home care teams)?
    - How could some solutions help improve quality of life for people with end-stage COPD?
    - Which professional caregiver could play a role in the improvement?
4. How could early-integrated palliative home care be implemented in standard care for people with end-stage COPD?

Results

Participant characteristics (Table 1)

Three focus group interviews with GPs and four with CNs were held with a total of 28 GPs (n= 8, n= 10, n= 10) and 28 CNs (n= 4, n= 7, n= 5, n= 12) that attended one of seven focus groups. The majority of participants were between 40 and 60 years old, and 32 were male. Clinical working experience was variable, with the largest groups (each seventeen participants) working for zero to nine years and working for 20 to 29 years; 32 of 56 participants did not introduce PC to an end-stage COPD patient in the previous year.

As we recruited GPs through local peer review groups and CNs through area-specific group meetings for six of the seven focus group conversations, not all participants met the predefined inclusion criteria: 11 of 56 did not have five years or more clinical working experience and 9 participants had not cared for at least three end-stage COPD patients in the last year. We also found out during the focus groups that ten participants were, either currently or in the past, members of a PHC team as a PHC physician or PHC nurse, without our prior knowledge.

Barriers to early-integrated PHC for end-stage COPD (table 2)

1. Disease trajectory of end-stage COPD

Because of the *unpredictable disease trajectory of end-stage COPD (1.a)*, people with end-stage COPD often experience unexpected exacerbations or other infections and a sudden death. This made it difficult to decide when or whether PHC is needed. According to participants in $FG2_{gp}$ and $FG5_{cn}$, it was also unclear when to go from curative care to PHC as the *deteriorating functioning of the patient is often invisible (1.b)* to the professional caregiver as the disease evolves slowly.

> *'I once saw a terminal COPD patient, with heavy exacerbations, as if he was almost gone, but he can now live further and wrestle through all of that again. And I think that maybe that has something to do with it, that we [professional carers] don't quite see it [deterioration] like that, right?' (FG1, GP).*

2. Perceived patient attitudes

A lack of disease insight (2.a) was mentioned, as some people with end-stage COPD did not seem to understand cognitively the severity of end-stage COPD and the possibility of death. This made it difficult for healthcare professionals to start talking about PHC because the person did not grasp the need for it; the healthcare professionals associated this attitude more with those with end-stage COPD than with other diseases such as cancer. Ignorance of the severity of end-stage COPD even when aware of the possible negative consequences was another example of lack of disease insight:

> *'You also have these [end-stage COPD] patients, we see that visually, whose health is declining. Blue lips, blue as... They rarely accept that when you tell them [that they are going to die] - No, no ... I am not going to die. That is the denial, that is that denial' (FG5, CN).*

R*esistance towards care (2.b)* was also mentioned, an attitude which depended on the personal context and personality of the patient concerned. For example, some people did not want further help from professional caregivers because they wanted to be left alone, while others refused it because of the wish to live life the way they wanted, thereby accepting the consequences. One participant described an end-stage COPD patient who continued smoking even when severely ill, stating it was too late for help anyhow. Other patients seemed to wait too long to contact a doctor, which made early-integrated PHC impossible as they died before care could be given.

> *'But, information... there are many who do not want to hear it [information about further care possibilities such as palliative home care], they [the patient] tell us [healthcare professionals] to leave them alone' (FG7, CN)*

Finally, participants mentioned that the attitude towards PHC was one of resistance because of the perceived affiliation with death (2.c), as seen in this quotation:

> *'We [healthcare professionals] try to stimulate that [palliative home care] for our [end-stage COPD] patients, but it is really hard. Palliative care has a bad connotation, you know. When patients hear they are palliative, they believe they are going to die' (FG5, CN).*

3. Professional caregiver practices

Th*e lack of a coherent and proactive care plan* (3.a) in professional practices formed a barrier, firstly because healthcare professionals experienced care coordination problems in the home situation. For example:

> *'On improving care: you have the cleaning help, the family help, the nurses and so on, and they all have something to say about the [end-stage COPD] patient, like maybe you should try this or that sometime, maybe try that again, and then you, the general practitioner, arrives there, and there you are, with your scientific background and all the scientific evidence that you have learned, and all of those suggestions are fired at and you have to say "yeah, but that will not help, and that will not help either, and I sometimes find it difficult, that everyone [healthcare professionals] has their opinion' (FG1, GP).*

Secondly, conflicting therapies between professionals were said to prevent the early-integrated PHC as well:

> *'To me, a good general practitioner is someone who does nothing. He only manages and says "I think you are suffering from that illness, you should go see that specialist physician." I think that is great. Because they cannot know everything, I fully agree. But too often, you see general practitioners who think they have the answer, while they are totally wrong and that gives complications when it comes to patient compliance. Like when you [and end-stage COPD patient] show up with a specialist's advice and your general practitioner says "hmm, you should not do that". Come on, that cannot happen' (FG5, CN).*

Next, insufficient experience with and a negative vision of PHC for end-stage COPD (3.b) was noted during the focus groups as PHC in itself was either not well known or its usefulness for end-stage COPD was not clear to participants due to a lack of experience in PC for this particular patient group. During the focus groups, participants often claimed that 'a palliative end-stage COPD patient does not exist'. Others asked the moderator to explain what PHC could do for people with end-stage COPD:

> *'The reason I would not immediately use PHC is that I need to know what they can offer in that context. So we want them to be able to offer comfort at a critical moment. But what can they do for someone who is suffocating? So then we need to hospitalise them after all' (FG2, GP).*

Related to this, professional caregivers did not clearly see the added value of early-integrated PHC for end-stage COPD as PC is perceived to curtail all curative options. Stopping curative care and starting PHC was said to feel unnatural, especially for GPs, as they want to cure the patient.

4. Education for professional caregivers

Basic and continuing education about PHC and its advantages for end-stage COPD seemed to be lacking, which also influenced the barriers about professional caregiver practices:

> *'I wonder, if we, as general practitioners, would be better educated and could prescribe oxygen, how we could quickly move on to be giving oxygen. I think that would prevent a lot of hospitalisations' (FG3, GP).*

5. Healthcare and PHC system characteristics

Timeslots for consultations with healthcare professionals which are too short (5.a), due to the fact that they are paid per consultation, prevented discussions about early integrated P(H)C as this topic requires a lot of time to explain properly. Furthermore, coordination between hospital and home care (5.b) was inefficient, as shown by a lack of guidance on how to integrate early PHC into the home in order to enable the person to stay at home until death. In addition, a lack of concrete guidance after discharge from hospital to home was mentioned, with the person with end-stage COPD sometimes leaving the hospital without knowing what the next steps of care are:

> *'I [general practitioner] never knew anything [of information given by someone] from the hospital for COPD' (FG2, GP).*
>
> *'Simply said: 'go home and handle it [the situation where the end-stage COPD patient is in] yourself' (FG2, GP).*

The reimbursement system for PHC (5.c) in Flanders is by law restricted to three months, with the possibility of making a second claim[27], which can be interpreted as an existing structural barrier for referral to PHC. To receive this reimbursement, a patient needs to have a legal palliative status, which depends on life expectancy, i.e. between three months and 24 hours before death (this rule was still in place at the time of the focus groups). As the unpredictable disease trajectory makes it hard to predict whether someone is in the final three months of life, this was also seen as a barrier by the participants. Although early-integrated PHC can be provided without this status, and costs related to PHC are reimbursed even if the person is still alive after three months, GPs and CNs saw this restriction as a psychological obstacle to early-integrated PHC:

> *'Three months, right, if you want to request palliative care for three or six months, we do not know whether that will be the case [for an end-stage COPD patient], and that keeps you from proposing this [palliative home care] to the patient, because of that palliative status' (FG3, GP).*

6. Communication

A lack of proper communication between the involved healthcare professionals (6.a) (GP, pulmonologist, CNs and PHC nurses) was observed due to different roles and perspectives on care:

> *'Specialists also speak from an ivory tower. I'm thinking of a woman [with end-stage COPD] now, who is terminal, and sure, she has a lot of pain and she uses tramadol [an opioid]. Step one in the treatment, according to them [pulmonologists], is medication because it suppresses the respiratory system. But, come on. That is easy to say behind your little desk, wearing your suit, is it not?' (FG2, GP)*

There was also confusion about who should take the initiative to integrate early PHC, along with miscommunications in referral letters, cited by this quote:

> *'Referral letters mentioning no possibilities for curative treatment for a cancer patient [from oncologists to general practitioners] often state: "referral to palliative team". But with terminal COPD*
>
> *it [the referral letter from pulmonologists] just says "lung function borders liveability".' (FG2, GP).*

Another barrier was *communication between professional caregivers and the person with end-stage COPD* (6.b), as talking about further care and PHC needs with them during consultations was referred to as being difficult, especially when family members were involved.

> *'If his wife is not at home, then he [end-stage COPD patient] is incredibly chatty and he can pour out his heart: "and I do not want to live anymore and I want to die." And when his wife gets back, the first thing he says: "do not say anything, my wife is here". But come on, we only get to talk to him for fifteen minutes and the rest of the day he is with her. You realise he cannot discuss his illness with her, right? (FG5, CN).*

Lastly, all focus groups mentioned communication problems due to the terminology of PHC, stating that the term has negative connotations for both those with end-stage COPD and healthcare professionals as it implies impending death.

Facilitators for early-integrated PHC for end-stage COPD (table 3)

1. Trigger moments

Participants expressed the need for trigger moments in the course of the disease trajectory of end-stage COPD as a way to facilitate early-integrated PHC. Examples were *after a hospital admission (1.a)* as a moment to start talking about the future or reorganising care, *a couple of exacerbations (1.b), when the patient becomes oxygen-dependent (1.c)* or *housebound due to a loss of functioning (1.d)*. These moments were seen as turning points when the person realises the severity of the disease more clearly:

> *'Someone [end-stage COPD] who goes home after hospital and gets oxygen, that is an important thing to work on as a team [of professionals]. And that [early integrated PHC] is something we [the professionals] could then discuss' (FG2, GP).*
>
> *'For example, I think that starting oxygen at home is quite the occasion [for early-integrated PHC]. After all, it announces a huge phase' (FG2, GP).*

2. Involvement of informal carers

Mainly GPs thought that providing more information about PHC and increasing positive attitudes towards it among informal carers (such as family members, volunteers of PHC teams) could encourage the latter to support the person with early-integrated PHC:

> *'We [general practitioners] are often asked by the family to come and talk without the patient being present. And then we discuss what will happen, what the palliative home care team could do, practical agreements' (FG2, GP).*

3. Education for healthcare professionals

When talking about knowledge and care for end-stage COPD, there was an urgent *need for more information about early integrated PHC for end-stage COPD and its clinical implementation to be given in standard and further education of healthcare professionals*. This could better prepare them for supporting people with end-stage COPD.

4. Healthcare and PHC system characteristics

Advance Care Planning (ACP) as a standard procedure in clinical practice for all end-stage COPD patients could facilitate conversations about the future, further wishes and needs. This could trigger professionals and end-stage patients to think about integrating PHC earlier. ACP is already a practice in nursing homes in Belgium:

> *'Because at that moment [going to a nursing home] there is a very important changeover in the life stage of a person. And because it is actually common to do advance care planning for someone who ends up in a nursing home. That is a procedure' (FG2, GP).*
>
> *'Reply: we should do this for all our chronic ill patients' (FG2, GP).*

5. Communication

Enhancing *communication by professional caregivers with those with end-stage COPD (5.a)* could be a facilitator, by using practical matters such as *'where would you like to die'* as a way to start talking about early-integrated PHC. Another possibility could be giving clear-cut information about end-stage COPD and future chances of survival in order to make the person realise the severity of their disease:

> *'You do not need that [advance directive] if you are already at the point of dying. But for the things that might come. I think about an end-stage COPD patient who always says that "they [healthcare professionals] will never put me on those machines [in the hospital] anyway, right?" [General practitioner says:] "Sure, but then we do really have to put that on paper, right?" And that is where you have a lead [to start talking about early-integrated PHC]. Those practical questions are hints to talk about how far you want to go [in future care]' (FG2, GP).*
>
> *'Patients should be correctly informed about further possibilities, about what medical care can still do for them. And then the conversation should mainly be about what the patient still wants and what he or she still expects and, and good agreements will have to be made about what will and what will no longer happen to the patient. And if hospitalisation is out of the question, how are we [professionals, patient and informal carers] going to organise the care package, and especially, with what objective?' (FG4, GP).*

Furthermore, even if some respondents felt the need to change the term PHC to supportive home care, others stated that focusing on symptom management, comfort and psychosocial support in conversations with end-stage COPD patients could also help the latter to accept the content of P(H)C:

> *'You do not have to use the term palliative if you can say okay, from now on we will give you [end-stage COPD patient] maximum comfort and we will do everything to take care of you as good as possible without calling that directly palliative [care]' (FG2, GP.)*

Finally, improving *communication between healthcare professionals (5.b)* by appointing a care coordinator to facilitate the information flow between hospital and home settings and integrating different healthcare professionals' perspectives could increase early-integrated PHC. If the specialist physician's medical information was combined with information from home and the primary carers this could provide a better view of the personal, medical and social context of the person. A care coordinator could also introduce the advantages of early-integrated PHC to them and their informal carers, as the person with this role would have more time for these conversations than the other healthcare professionals involved would:

> *'Looking at each end-stage COPD patient to see which network can be provided and making connections with specialist's network. "Which nurse, which GP would you [the patient] like?" Then every end-stage COPD patient will have their own network up to informal care' (FG5, CN).*

Tables

Table 1 Characteristics of general practitioners and community nurses (N=56)

	General practitioners			*Community nurses*				*Total*
Characteristics	**FG1 (n= 8)**	**FG2 (n= 10)**	**FG3 (n=10)**	**FG4 (n=4)**	**FG5 (n=7)**	**FG6 (n=5)**	**FG7 (n=12)**	**56**
Sex								
Male	4	4	4	2	3	4	3	**24**
Female	4	6	6	2	4	1	9	**32**
Age								
≤29	1	1			3		2	**7**
30-39	1	2	2		2		2	**9**
40-49	1	4	1	4	1	1	4	**16**
50-59	4	1	1		1	4	4	**15**
60-69	1	2	6					**9**
≥70								
Practice location								
Urban	8		10	4		2		**24**
Semi-urban or rural		10			7	3	12	**32**
Number of end-stage COPD patients cared for in the last year	(1 non response)	(1 non response)						
None			4	1		1	3	**9**
1-9			1	3	1	2	9	**16**
10-19	4	1	1		5	2		**13**
20-29	1	1	4		1			**7**
≥30	2	7						**9**
Number of end-stage COPD patients introduced to palliative care in the last year								
None	5	2	7	1	4	2	11	**32**
1-3	2	8	3	3	2			**18**
4-6					1	3	1	**5**
7-9								
≥9	1							**1**
Active in a palliative home care team								
Yes		4*	3*	2**	1**			**10**
No	8	6	7	2	6	5	12	**46**
Clinical work experience (years)								
0-4	1	2	1		4		3	**11**
5-9	1	1	0		1		3	**6**
10-19	1	2	2	2		1	3	**11**
20-29	3	3	2	2	2	2	3	**17**
≥30	2	2	5			2		**11**

*General practitioners were recruited as members of a LOK group. Without our prior knowledge, we found out they were part of a palliative home care team as palliative care physicians.

**Community nurses were recruited solely because of experience as a community nurse. Without our prior knowledge, some of them had had experience as a palliative home care nurse in the past or as a second job. One participant was recruited in FG4 because another participant cancelled. This participant had been a palliative home care nurse in the past, but is currently a full-time researcher on palliative care.

Table 2 Barriers according to general practitioners (GPs) (FG1$_{gp}$, FG2$_{gp}$, FG3$_{gp}$) and community nurses (CNs) (FG4$_{cn}$, FG5$_{cn}$, FG6$_{cn}$, FG7$_{cn}$) for early-integrated palliative home care in standard care for people with end-stage COPD

1	*Disease trajectory of COPD*	1.a: Unpredictable exacerbations and death (FG1gp, FG2gp, FG3gp, FG5cn, FG7cn) 1.b: Invisible deterioration of functioning (FG2gp, FG5cn)
2	*Perceived patient attitudes*	2.a: Lack of disease insight: 1. Not understanding the severity of the disease or realising the possibility of death (FG1gp, FG2gp, FG3gp, FG5cn, FG7cn) 2. Denial of the severity of the disease (FG2gp, FG5cn) 2.b: Resistance to care 1. The wish to be left on their own (FG2gp, FG5cn, FG6cn, FG7cn) 2. The wish to lead the life as they wished, accepting the consequences (FG1gp, FG3gp, FG5cn, FG7cn) 2.c: Resistance towards palliative (home) care because of the association with death (FG2gp, FG3gp, FG6cn, FG7cn)
3	*Professional caregiver practices*	3.a: Lack of a coherent and proactive care plan 1. No cooperation between professionals involved at home (FG1gp, FG4cn, FG7cn) 2. Conflicting therapy and treatment between professionals (FG3gp, FG5cn) 3.b: Insufficient experience with and negative vision of palliative home care for end-stage COPD 1. No experience in clinical practice with palliative (home) care for COPD (FG1gp, FG2gp, FG3gp, FG5cn, FG7cn) 2. GPs continue to give life-prolonging care as added value of palliative (home) care for people with end-stage COPD is not clear (FG1gp, FG5cn)
4	*Education for professional caregivers*	Not enough focus on knowledge and advantages of palliative (home) care for end-stage COPD in healthcare professionals' basic and continuing education (FG2gp, FG3gp, FG5cn, FG6cn)
5	*Healthcare and palliative home care system characteristics*	5.a: Consultations: not enough time during consultations to start talking about palliative home care and further care (FG4cn) 5.b: Coordination between hospital and home care 1. Lack of guidance on how to integrate palliative home care early to allow the patient to stay and die at home (FG1gp, FG2gp, FG6cn) 2. Discharge from hospital to home situation without concrete guidelines (FG1gp, FG3gp) 5.c: Reimbursement system for palliative home care services 1. Palliative status for palliative home care is based on predictability of death (FG2gp, FG5cn) 2. Palliative reimbursement of palliative home care is restricted to 3 months (FG2gp, FG3gp, FG7cn)
6	*Communication*	6.a: Inter-professional communication 1. Not knowing each other well enough for proper communication (FG2gp, FG3gp, FG5cn, FG6cn) 2. Unclear who takes initiative to introduce palliative home care to the end-stage COPD patient (FG3gp) 3. Not understanding each other's messages (FG2gp) 6.b: Communication between healthcare professional and end-stage COPD patient 1. Not discussing palliative care (needs) in detail during consultations with the end-stage COPD patient (FG2gp) 2. Difficulties of professionals in talking about palliative care needs with their end-stage COPD patients (FG2gp, FG3gp, FG4cn) 3. Patient-family relationship can prevent communication on palliative home care (FG1gp, FG5cn, FG7cn) 4. Professionals fear talking about palliative home care because of the patient's reaction (FG5cn)

Table 3 Facilitators according to general practitioners (GPs) (FG1$_{gp}$, FG2$_{gp}$, FG3$_{gp}$) and community nurses (CNs) (FG4$_{cn}$, FG5$_{cn}$, FG6$_{cn}$, FG7$_{cn}$) for early-integrated palliative home care into standard care for patients with end-stage COPD

1	***Trigger moments***	1.a: Hospital admission 1. After hospital admission, a moment to start talking about the future (FG1gp, FG2gp, FG3gp, FG4cn, FG6cn) 2. After hospital admission, a moment to reorganise care (FG2gp) 1.b: After a couple of exacerbations (FG2gp) 1.c: When an end-stage COPD patient becomes oxygen-dependent (FG2gp, FG3gp) 1.d: When an end-stage COPD patient is confronted with loss of functioning and becomes housebound (FG1 gp, FG2gp, FG5cn)
2	***Involvement of informal cares***	Increase knowledge about advantages of palliative home care for informal carers for patients with end-stage COPD (FG1gp, FG2gp, FG3gp, FG5cn)
3	***Education for healthcare professionals***	More focus on early-integrated palliative home care for end-stage COPD and concrete implementation in clinical practice in education for healthcare professionals (FG5cn)
4	***Healthcare and palliative home care system characteristics***	Start advance care planning as a standard procedure for end-stage COPD patients living at home (FG1gp, FG2gp, FG3gp, FG4cn, FG7cn)
5	***Communication***	5.a: Communication between healthcare professionals and end-stage COPD patients 1. Talking about practical matters can help professionals to start talking about palliative home care (FG2gp, FG3gp) 2. Inform end-stage COPD patients clearly and firmly about their disease and future (FG4cn) 3. Better explanation of the term early-integrated palliative home care can help acceptance by end-stage COPD patients: talk about it as comfort care, psychosocial support (FG2gp) 5.b: Communication between healthcare professionals: appoint a care coordinator who facilitates the care transition to early-integrated palliative home care (FG3gp, FG5cn, FG6cn)

Discussion

Main findings

The results of this study have revealed perceived barriers and facilitators from the perspective of general practitioners (GPs) and community nurses (CNs) to the early-integrated palliative home care (PHC) in standard care for people with end-stage COPD in Flanders, Belgium. The categories of barriers were 1) unpredictable exacerbations and death in COPD and invisible deterioration of functioning; 2) perceived patient attitudes such as a lack of disease insight and resistance towards care; 3) healthcare professional practices with a lack of a coherent and proactive plan, insufficient experience and a negative view of PHC for end-stage COPD; 4) not enough focus on the knowledge and advantages of PHC and palliative care (PC) for end-stage COPD in the basic and continuing education of healthcare professionals; 5) healthcare and PHC system characteristics: consultations which are too short, insufficient coordination between hospital and home care and a reimbursement system for PHC that is based on life expectancy; and 6) communication: a lack of and unclear communication about care possibilities for end-stage COPD between healthcare professionals and a lack of clear information about PHC between them and their patients.

The categories of facilitators were 1) trigger moments to start talking about early-integrated PHC such as after hospitalisation, after a couple of exacerbations, when becoming oxygen-dependent or housebound; 2) involvement of informal carers; 3) information about the advantages of early-integrated PHC for end-stage COPD in the education of healthcare professionals; 4) including advance care planning (ACP) as a part of healthcare and PHC systems and 5) enhancing communication between professionals by installing a care coordinator and enhancing communication between professionals patients by explaining better and giving practical examples of what early integrated PHC could mean for end-stage COPD.

Interpretation of findings in relation to previous research

The following barriers were in line with previous research on communication about PC in general, early-integrated PHC or PC for end-stage COPD: 1.a: unpredictable exacerbations and death[6]; 3.b.2: continuation of life-prolonging care in end-stage COPD[28]; 5.a: lack of time during consultations to start talking about PHC and further care[28]; 5.b: no coordination between hospital and home care[24]; 6.b.1: not discussing PHC and PC and PC needs in detail during consultations[29]; 6.b.4: the professional's fear of talking about PHC because of the patient's reaction[30].

For facilitators, we saw similarities with former studies on trigger moments 1.a: after hospital admission[31], and 1.c: when the person becomes oxygen-dependent[32]; 3) professional education, with the importance of providing more focus on implementation of early-integrated PHC[24,33]; 4: health system and PHC system characteristics with reported advantages of ACP as a way to introduce PHC[24]; 5.a.2: enhancing communication between professionals and people with end-stage COPD by better informing the latter about PHC possibilities[24]; 5.b: improving communication between professionals by appointing a care coordinator[24].

Due to the specific focus on early-integrated PHC for end-stage COPD, this study also identified new insights into barriers due to conflicting therapies and insufficient communication between healthcare professionals and the lack of guidelines after hospital discharge. A common denominator between these might be insufficient or non-existent communication between hospital and home care settings[24]. The healthcare professionals in hospital and those in home care might need to cooperate better and more often. By doing this, care and therapies could be adjusted to better meet the wishes of the person[34], while not forgetting to involve them and their informal carers in discussions about care. One option could be an electronic patient file accessible to the patient, their informal carers and the healthcare professionals in the hospital, the primary and the home care settings[35]. This file could contain a classification system that emphasises their PHC needs and functioning instead of the disease, such as the comprehensive ICF core set for COPD developed by the World Health Organisation[36]. Another possibility could be organising multidisciplinary consultations to take place each time a serious deterioration of functioning occurs, similar to multidisciplinary oncology consultations in Belgium. More research is needed to explore whether these examples could work for early-integrated PHC in end-stage COPD.

Although it is known that PC and PHC increases quality of life for people with end-stage COPD when integrated early[7], the content of PHC needs adaptation if it is integrated before the terminal stage, depending on the disease population and the personal needs of the patient[37]. Research has shown the need for management of troublesome symptoms and short-term PC if integrated early[6]. Managing breathlessness or relieving psychosocial symptoms which are often seen in end-stage COPD despite optimal medical care[5] might require the involvement of other care professionals besides a PHC nurse, such as a physiotherapist, psychologist or social worker. Re-evaluating the content of PHC if given early and integrated for end-stage COPD is therefore necessary in order to be fully effective.

The large volume of results on professional caregiver-patient communication showed there is plenty of room for improvement. Participants claimed that some people with end-stage COPD did not fully understand the disease, sometimes refused care and often interpreted the term PC or PHC as a sign of impending death. However, previous research found that people with end-stage COPD did express the desire to talk about end-of-life care[30] and fully accepted PHC and early-integrated PHC[19]. This could thus mean that participants in our study either misinterpreted their end-stage COPD patient’s wishes and communication preferences about PHC, or that the patient did not clearly share their care needs which would confirm other research finding that patients often do not fully understand the severity of end-stage COPD[38], or did not know what future care they would prefer[22]. In contrast, another study found that patients did convey the need for involvement and education about end-stage COPD and PC, which could improve PC communication[39]. A previous trial tested patient feedback by giving self-reported patient questionnaires on end-of-life preferences for communication, therapy and experiences. These were then given to the involved healthcare professionals which resulted in better patient-professional communication[40]. As neither the literature nor the results of our study provided a clear answer to these communication issues, further testing of communication systems is suggested, while improving undergraduate and postgraduate education for healthcare professionals on bad news delivery, ACP and shared decision-making.

The unpredictable disease trajectory of end-stage COPD was mentioned as a factor impeding timely referral to and conversations about early-integrated PHC, largely confirmed by research stating the need for clear identification criteria for pulmonologists to introduce PC in a timely manner[24]. The trigger points identified in the results of our study could fulfil this purpose, as they signal an increase in PHC needs due to a decline in functioning such as after a hospital admission, a couple of exacerbations, beginning oxygen-dependency or becoming housebound. These trigger moments were not related to life expectancy as the latter was seen as an inappropriate basis for deciding whether early integrated PHC was needed, which is in line with a study proving that criteria to predict survival in end-stage COPD do not work[41]. Moreover, at the time of the focus group conversations, eligibility for PHC in Belgium was dependent on a palliative status based on life expectancy (less than three months before death), which was seen as a psychological barrier to the early-integrated PHC as the unpredictability of COPD prevents professionals from deciding whether an end-stage COPD-patient is likely to survive for three months. Nevertheless, somewhat contrary to our results, a previous qualitative study found that admission for exacerbation was considered too chaotic and not an appropriate occasion to discuss PC, although it could be a milestone leading to PC discussions[31]. Pulmonologists also stated that conversations about treatment preferences should be initiated when the patient is stable again[32]. It is important to mention that the trigger moments in the results of our study could give rise to an opportunity for talking about early-integrated PHC as they could help the person realise the severity of the disease, but initiating the conversations should take place when they are back in a stable context, preferably at home, after the events had occurred. More research is needed to explore the feasibility of addressing PHC needs following the different triggers.

Strengths and limitations

The research team involved in data analysis consisted of people with different backgrounds including psychology, sociology, general practice, primary care, PHC, pulmonology and oncology. This enhanced the interpretation of the data due to the multitude of perspectives. Furthermore, to the extent of our knowledge, this is the first qualitative study reporting GPs' and CNs' insights into barriers to and facilitators for early-integrated PHC for people with end-stage COPD. We engaged a varied sample of GPs and CNs with different backgrounds, care experience and perspectives on PHC. The high number (56) of participants in seven different focus groups also constituted a key strength of this study as it improved transferability of the findings beyond the context of the individual participant's experiences.

However, it is worth noting that due to altering recruitment strategies at the start of the study not all participants reached the inclusion criteria we predefined. Eleven out of 56 had less than five years working experience, and nine of 56 had not had someone with COPD in their practice in the previous year. This could have influenced the results as professionals with less working experience or less experience with COPD might have faced difficulties in answering questions about early-integrated PHC for end-stage COPD, as they would have lacked the clinical experience to which to relate their answers. Nevertheless, we believe that due to the setting of a focus group where there were other participants with much experience, this limitation did not cause substantial problems for the quality of the conversations and the results. During the focus group conversations, the experienced professionals inspired those less experienced to reflect critically on the questions asked by the moderator. The strength of the answers also relied on the vivid discussion between the participants who challenged each other. Therefore, we did not exclude the less experienced participants from the analysis as their participation helped in obtaining the results.

Furthermore, 32 of the 56 participants had not introduced end-stage COPD patients to PC or PHC in the previous year. This might have affected the results due to a lack of experience with PC or PHC for end-stage COPD between the participants. However, this does not mean that they did not know what PC or PHC can do for patients, as they had all had experience with PC, though mainly with people with cancer. Therefore we believe that these participants were able enough to form an opinion on why they never or hardly ever introduced PHC for end-stage COPD compared with cancer and what could be done to alter this.

Another limitation of this study was the lack of insights from other healthcare professionals involved such as pulmonologists and physiotherapists. Neither did we consult people with end-stage COPD or informal carers. However, gaining insight into early-integrated PHC was the primary focus of the study and therefore we interviewed healthcare professionals active in primary and home care. Notwithstanding these limitations, the results could provide valuable information on the development of feasible interventions, practical implementation and policy-related recommendations on early integrated PHC for end-stage COPD.

Implications for policy and practice, and future research

Given the complexity of implementing early-integrated PHC for end-stage COPD, we suggest a multilevel strategy approach in order to successfully change related policy and practice[42]. The micro level could be adapted by increasing the patient's insight into end-stage COPD and early integrated PHC using government-funded campaigns about PC and PHC on national television which could raise awareness of PC and PHC among the general population. Meso level changes could be made by focusing professionals' basic and continuing education more on clinical PHC practice through obligatory internships in PC and PHC settings, enhancing knowledge about end-stage COPD, PC and PHC needs and the advantages of early integrated PHC and focusing on skills in communication and ACP.

Finally, macro changes by adapting the healthcare and PHC system would be needed; these could include disconnecting eligibility for palliative status and reimbursement of PHC-related costs from life expectancy and instead linking it to lower functioning, PC and PHC needs in end-stage COPD[27]. Although the Flemish government has decided to change this system, the law itself has not yet changed. Additionally, incorporating ACP as a standard procedure within early-integrated PHC to facilitate patient-professional caregiver communication and appointing care coordinators as an additional role in existing care could provide continuous support for people with end-stage COPD over different care settings[42]. However, this would require an economic costs and benefits analysis.

As this study was performed to develop the phase 2 EPIC trial, the results suggested using a comprehensive PHC model in the intervention with inclusion criteria representing high PHC needs as a proxy to start early-integrated PHC for end-stage COPD[43]. Based on our results, these inclusion criteria representing high PHC needs could be GOLD III or IV combined with low functioning such as frequent hospitalisations for COPD, exacerbations due to COPD, becoming housebound or oxygen-dependent. Key components could cover several dimensions of appropriate PHC, from improving the disease insight of the person concerned to training the PHC team in knowledge and therapy for end-stage COPD and integrating care by trying to improve cooperation and communication between involved professionals. Previous interventions in early PC and PHC for end-stage COPD mainly focused on one symptom, for example managing breathlessness[44] or provided training about one care aspect such as nutrition[23]. Instead, we suggest using several components to provide a holistic PHC approach, in order to fully tackle the lack of early-integrated PHC for people with end-stage COPD.

Conclusion

Our study uncovered barriers in terms of the disease trajectory, patient attitudes, professional practices, the healthcare and PHC system and communication problems. Facilitators suggested there are possibilities at many levels for the successful implementation of early-integrated PHC in practice or development. This would require a multilevel approach with the involvement of healthcare professionals active in hospital and home settings, while not forgetting to include in the process the people with end-stage COPD themselves and their informal carers.

Data availability

The data that support the findings of this study are available from the corresponding author (CS) upon reasonable request.

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Competing interests

The authors declare no competing interests.

Author contributions

C.S., L.D., K.C., G.J., S.V.B., and P.P were involved in the study conception and design and in obtaining ethical approvals. C.S. and K.C. were involved in the data collection. C.S, K.C. and P.P, experienced qualitative researchers with backgrounds in sociology (C.S. and K.C) and medical, palliative home and primary care (P.P.) analysed the data. Analysis was discussed with all contributing authors. The first and following drafts were written by C.S. All authors commented on the first and following drafts, revised them critically, and agreed with the final version. All authors are accountable for all aspects of the work.

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CHAPTER 4

Development of a complex intervention for early-integrated palliative home care into standard care for end-stage COPD patients: a Phase 0-I study[V]

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Abstract

Background: Research suggests that palliative home care should be integrated early into standard care for people with end-stage COPD. The majority of people also express the wish to be cared for and to die at home. However, a practice model for early-integrated palliative home care (PHC) into standard care for end-stage COPD has not been fully developed.

Aim: To develop an intervention for early-integrated PHC into standard care for end-stage COPD patients.

Methods: We conducted a Phase 0–I study according to the Medical Research Council Framework for the development of complex interventions. Phase 0 aimed to identify the core components and inclusion criteria of the intervention by way of an explorative literature search of interventions, expert consultations and seven focus groups with general practitioners and community nurses on perceived barriers to and facilitators of early-integrated PHC for COPD. In Phase 1, the intervention, the inclusion criteria and components were developed and further refined by an expert panel and two expert opinions.

Results: Phase 0 resulted in identification of inclusion criteria and components of interventions and the barriers to and facilitators of early-integrated PHC for end-stage COPD. Based on these findings, a nurse-led intervention was developed in Phase I consisting of training for PHC nurses in symptom recognition and physical therapy exercises for end-stage COPD, regular visits by PHC nurses to the patient's home, two information leaflets on self-management, a semi-structured protocol and follow-up plan to record the outcomes of the home visits and integration of care by enabling collaboration and communication between home and hospital-based professional caregivers.

Conclusion: This Phase 0-I trial succeeded in developing a complex intervention for early-integrated palliative home care for end-stage COPD. The use of three methods in Phase 0 gave reliable data on which to base the components and the inclusion criteria of the intervention. The preliminary effectiveness, feasibility and acceptability of the intervention will subsequently be tested in a Phase II study. Funding: IWT-SBO.

Background

Chronic Obstructive Pulmonary Disease (COPD) is one of the leading causes of death[1] and was in 2015 responsible for 2.6% of global disability adjusted life years[2]. The disease involves a progressive, inexorable functional decline and acute episodes of exacerbation[3]; end-stage COPD patients display symptoms including dyspnea, fatigue, anxiety and low mood, leading to a reduced quality of life[4]. Even with medical care, these symptoms impact heavily on daily activities and emotional and social functioning[4] while physical and psychosocial needs are inadequately addressed[5].

Integrating palliative care (PC) early into regular care could address these unmet needs and could have a positive impact on end-stage COPD patients[6,7]. Conversations about prognosis should be an integral part of care; strategies for professional caregivers to facilitate such discussions include being aware of the implications of the diagnosis, the need to build a good relationship with the patient and to start the discussion of prognosis early in the disease course[8]. While patients with end-stage COPD often die in intensive care unit settings in hospital rather than at home[9], they actually prefer to be cared for at home[10] and to die at home[11]. Therefore, if PC was provided at home it could improve quality of life[12,13] and increase the chances of dying at home[14].

Moreover, if palliative home care (PHC) was provided early enough it could avoid unnecessary hospital visits and admissions, overly aggressive care and high end-of-life-related medical costs[15]. Patients with end-stage COPD themselves express the need for integrated PHC as an addition to standard care[16]. However, implementing PHC early is not without its challenges because the unpredictability of the illness trajectory and survival time can complicate decisions about when to introduce it[6]. There are other challenges e.g. that some healthcare professionals view PC for end-stage COPD as not valuable or believe that PC needs can be addressed by standard care alone[17].

Furthermore, research on implementing and testing integrated PHC early in clinical practice for end-stage COPD is fairly limited, consisting of a study exploring place of death and costs of medical care for people with COPD receiving PHC[14], a trial on acceptance of home support and integrated care among end-stage COPD patients[16], a trial on the early introduction of specialised PC for COPD[18,19], a PHC trial focusing mainly on managing one symptom i.e. breathlessness[20] and another on the identification of people with end-stage COPD in need of proactive PC[21]. In contrast, interventions in cancer research have tested many models of early and/or integrated PC demonstrating positive effects on quality of life and quality of care[22–26], while it has been shown that end-stage COPD brings similar PC needs and symptom burden, particularly when compared with lung cancer[5]. A practical model to implement early-integrated PHC in standard home care for people with end-stage COPD is lacking; therefore, our study aim was to develop an evidence-based intervention supporting the early-integrated PHC into standard care for people with end-stage COPD.

Methods

Study design

The intervention was developed using the Medical Research Council (MRC) framework for complex intervention design[27]. This framework provides multiple steps (from Phase 0 to Phase IV) for developing and evaluating complex interventions. This study consists of a Phase 0-I trial involving the identification and modelling of the core components and the development of the complex intervention.

The process from development to implementation of a complex intervention may take different forms, with several Phases consisting of key functions and activities (Figure 1). Reporting is not shown as a separate activity, because it is regarded as an important element of each stage in the process[27].

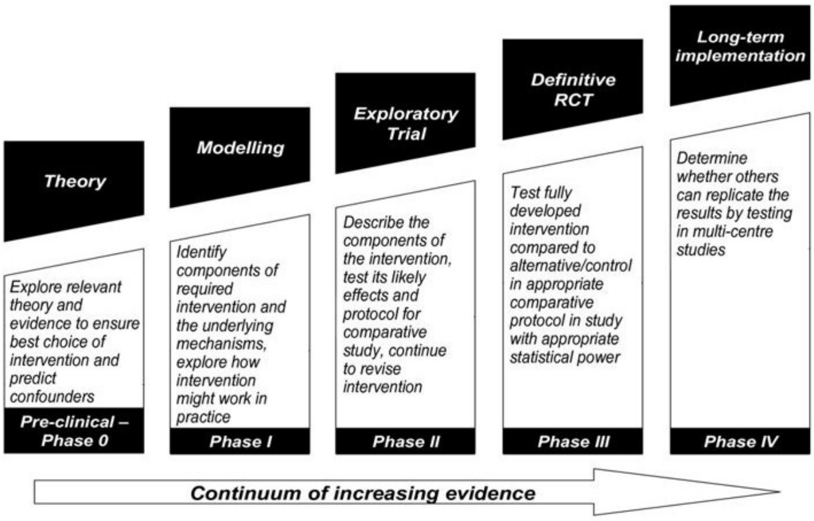

Fig. 1: Medical Research Council framework for development and evaluation of complex interventions

Phase 0 – Identifying the evidence base and developing the theory

We used three methods to obtain data for the development of the key components of the intervention. Key components - the core of the intervention - are intended to be or have been demonstrated through research to be positively associated with the outcomes that address identified needs[28,29]. Next, we also obtained data on possible inclusion criteria for participants.

The first method was an exploration of the relevant literature between April 2015 and November 2016. This search identified published trial results and the protocol papers of uncompleted trials on PC and/or symptom management for COPD. The used methodology was an explorative literature search. A search strategy was developed by CS and KC for PubMed. A combination of controlled vocabulary and free text words was used to search in titles and abstracts: *COPD and intervention in combination with PC, early PC, general practitioners (GPs)* and *symptom management*. The reference list of all identified studies was screened for additional relevant studies. A study was included if it reported: (1) intervention results or an intervention protocol (the most recent results of one trial needed to be included), (2) components related to PC or symptom management for end-stage COPD and (3) clear reference to inclusion criteria of the intervention participants. The eligibility of selected studies was independently assessed by CS and KC and this selection was critically revised by the research team. Appraisal was undertaken by CS and KC by critically reviewing all selected studies. No appraisal tool was used as the design was exploratory and not systematic.

The second method, undertaken between May and September 2016, was to consult experts for their views on possible components and inclusion criteria based on their experiences and ideas about the future of PHC; 27 national and international experts from clinical and/or research settings were selected for their research and/or clinical expertise in PC and/or COPD as a criterion. An extra criterion was stipulated for Belgian experts, i.e. their knowledge of the Flemish healthcare context concerning care for COPD, as this was information we could not gather from the literature search and from international experts. By recruiting both experts in PC and/or in COPD we tried to obtain a sample representing a wide range of experience related to the topic (maximum variation sampling). Other international and national experts in COPD and/or PC were recruited through the professional contacts of experts we interviewed (snowball sampling). We interviewed pulmonary specialists, a physiotherapist, experienced researchers, policymakers, people working in a PHC unit and GPs. A topic guide in English and in Dutch can be seen in Appendix 1.

Thirdly, we conducted focus groups between September 2015 and September 2016 to gain more insight into PHC practices, current standard care, barriers to be overcome and facilitators to promote timely integration of PHC for people with end-stage COPD in Flanders, Belgium. In this way, we tried to complement the results of the literature search and expert consultations with information from the healthcare professionals' context in which the intervention will be implemented. The methods of the focus groups are published elsewhere[30].

Phase I: Modelling the intervention for clinical practice

In Phase I, the intervention was modelled using Phase I from the MRC-framework as a guiding methodology[31]. Outcomes were stipulated to be improvement in quality of life for people with end-stage COPD and improvements in quality of care. The research team developed a first draft of a complex intervention testing early-integrated PHC for end-stage COPD. The draft was based on the results of Phase 0, by selecting the most commonly used and mentioned inclusion criteria and intervention components, while also taking into account the research setting, the Flemish context, possibilities of replicating the intervention and feasibility and acceptability issues. This draft was refined by one expert panel and two individual expert opinions to further select the best courses of action in order to enhance implementation of the intervention in clinical practice. These Flemish experts identified possible implementation barriers which could occur and searched for solutions to adjust the components in order to overcome them.

We deliberately selected the Flemish experts based on their experience with people with end-stage COPD, in clinical practice, in PHC or in social work. The expert panel and inquiry of expert opinions were held in December 2016; the former took one and a half hours, was audiotaped and transcribed verbatim (the panel), while the latter collected, were via e-mail. The expert panel (n=8) consisted of three GPs, a pulmonologist, a pulmonary nurse, a community nurse (CN) and a psychologist working in a PHC team. Some of them had also been consulted during Phase 0 in the expert consultations or the focus groups. The two expert opinions were from a GP and a social worker. The results of the expert panel and opinions were categorised for each component and analysed within the research team to finalise the intervention. We followed the same methods for selecting inclusion criteria, but the final selection of inclusion and exclusion criteria was revised and adapted by a well-experienced pulmonologist on accuracy, feasibility and acceptability in clinical practice. A flow diagram of the methods used from Phase 0 to I is given in Table 1.

Ethical aspects

The research protocol and topic guides for the focus groups were approved by the Ethics Committee of Ghent University Hospital (Reference: 2016/0171). Furthermore, a signed informed consent was obtained from each participant in the focus groups and the expert consultations, panel and opinions. Anonymity was assured by preventing the participants being identified from the transcripts.

Table 1 Use of the theory and modelling Phase from the Medical Research Council framework

Definition	*Steps undertaken*
(1) Phase 0 – theory	
(1.1) Identifying the evidence base by carrying out an explorative literature search	(i) Reviewed existing interventions on palliative care and symptom management for end-stage COPD on their design, components, inclusion criteria, and results on outcomes. (ii) Reviewed existing intervention protocols on palliative care and symptom management for end-stage COPD on their design, components, inclusion criteria, and chosen outcomes.
(1.2) Identifying international and national insights on possible core components and inclusion criteria by carrying out expert consultations	(i) Interviewed 21 experts on their view about successful interventions for early-integrated palliative home care for end-stage COPD, based on the components and inclusion criteria we identified in the explorative literature search, and on other components the experts identified during the consultations.
(1.3) Identifying insights on the Flemish context of early integrated palliative home care for end-stage COPD, which could not be derived from 1.1 and 1.2	(i) Conducted three focus group conversations with general practitioners and four with community nurses on barriers and facilitators for early-integrated palliative home care for end-stage COPD in Flanders.
(2) Phase I – modelling the intervention	
(2.1) Selecting inclusion criteria by using a pragmatic approach based on the critical consideration of the research team, using the results from Phase 0 and taking into account the Flemish clinical practice context, the research setting, feasibility and acceptability issues	(i) Linked all results on inclusion criteria from the different methods in Phase 0 and analysed them. (ii) Selected the most commonly used or positively mentioned inclusion criteria from both literature and expert consultations. (iii) Sorted the inclusion criteria on their relevance to the intervention, taking into account the Flemish clinical practice and palliative home care context by also consulting the obtained results from the focus groups on the facilitator: trigger moments.
(2.2) Selecting intervention components by using a pragmatic approach based on the critical consideration of the research team, using the results from Phase 0 and taking into account the Flemish clinical practice context, the research setting, feasibility and acceptability issues, and possibilities for replicating it. Outcomes of the intervention should be improvement of quality of life for end-stage COPD patients and quality of care.	(i) Linked all results on key components from all methods used in Phase 0 and compared the results. (ii) Identified the most commonly used or positively mentioned components from both literature and expert consultations. (iii) Compared the most commonly used or positively mentioned components from the literature search and the expert consultations and sorted them on their relevance for the intervention. This was done by taking into account their applicability in the Flemish context as we reviewed the identified barriers and facilitators from the focus group study in relation to these components. (iiii) Selected and designed five key components in a first draft of the intervention, using combinations of components from previous interventions, material from previous projects for COPD and newly developed components by the research team members themselves.
(2.3) Identifying implementation issues concerning the chosen inclusion criteria and components specific for the Flemish context	(i) Reviewed the most common inclusion and exclusion criteria identified in Phase 0 by a pulmonologist with long experience in clinical practice for end-stage COPD on implementation issues and feasibility and adapted several criteria for better implementation chances. (ii) Consulted the involved palliative home care team on feasibility and acceptability issues of the selected components. (iii) Consulted an expert panel and two expert opinions on their views, comments and suggestions of the first draft of the intervention, focusing on implementation, feasibility and acceptability issues.
(2.4) Finalising the intervention model	The research team analysed the remarks from the pulmonologist, involved palliative home care team, expert panel and expert opinions and adjusted the intervention components and inclusion criteria in a final draft.

Results

Phase 0 – Identifying the evidence base and developing theory

Key components and inclusion criteria

A. Exploration of relevant literature

From the explorative electronic database search, 68 records were identified. After removal of duplicates and irrelevant reports, the title and abstract of 58 records was screened and 30 full-text articles were retrieved for detailed evaluation. Contact with the first authors and a search in reference lists of included articles yielded eight records. Seventeen articles met all inclusion criteria and were included for data-extraction and quality assessment (Fig. 2). Eleven were intervention studies and six were intervention protocols.

The inclusion criteria used in the intervention and intervention protocol studies are summarised in Table 2. The most commonly used inclusion criteria were hospitalisation for an exacerbation (recently or one or more times in the last year), end-stage dyspnea (according to the Medical Research Council Dyspnea score) and end-stage COPD (mostly GOLD III/IV).

Key subjects of previously successful or partly successful interventions and protocol papers were (1) advance care planning: training general practitioners (GPs)[32] and respiratory nurses[33], or testing whether advance care planning affected the end-stage COPD patient's decision-making about future preferences[34]; (2) respiratory rehabilitation: simple home and intensive hospital-based pulmonary rehabilitation programmes[35], the involvement of respiratory health workers[36] or the integration of respiratory services with standard care therapy[7]; (3) specialised PC: specialised PC added to standard care[19,21]; (4) training professional caregivers: training GPs in early identification of end-stage COPD patients in need of PC and training on communication about preferences and written advance directives[32], or training on inhalation techniques[37]; (5) educating end-stage COPD patients: educating end-stage COPD patients about identification and treatment of exacerbations[38], decision-making in end-of-life care[39] or cognitive restructuring where patients learn to interpret physical and psychological symptoms about anxiety and dyspnea[40], and (6) self-management of end-stage COPD patients: using tele-monitoring for symptom reporting[41], developing a breathlessness service for managing breathlessness[20,42] or using an action plan with a holistic assessment of physical, psychological, social and spiritual/existential needs[43].

A broader overview of the key components derived from the explorative literature search can be seen in Appendix 2: Key components of existing interventions and intervention protocols on PC and symptom management for end-stage COPD patients based on explorative literature search.

A detailed examination of all analysed studies on inclusion criteria and components can be seen in Appendix 3: explorative literature search on interventions and intervention protocols.

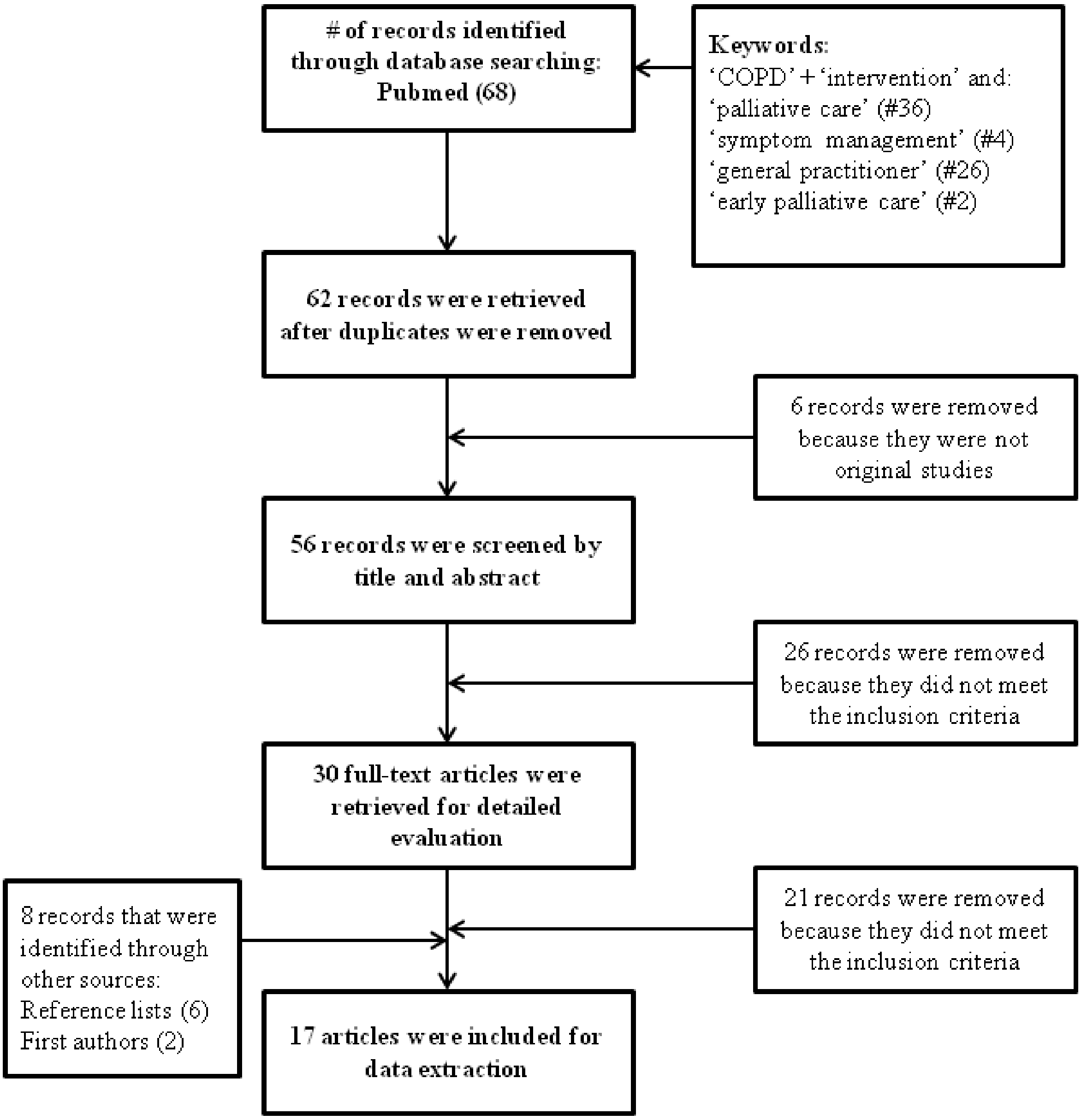

Figure 2 Full electronic search strategy

Table 2 Inclusion criteria of interventions and intervention protocols on palliative care and symptom management for end-stage COPD patients based on explorative literature search

Inclusion criteria	*Used x times in explored studies*
Hospitalisation for an exacerbation (recently OR 1-2 times in last year(s))	10
End-stage dyspnea (Medical Research Council dyspnea Scale score 5)	5
End-stage COPD (mostly GOLD III/IV)	5
FEV1 (airflow limited)	3
Age	3
Smoking habits (ex-smoker or intending to quit/current or former smoker)	3
Hypercapnia/hypoxemia	2
BMI (<21)	2
Free of exacerbation last month	2
Housebound	1
Inhalation therapy	1
Domiciliary oxygen/home ventilation	1
Surprise question (will die within one year or readmission within 8 weeks)	1
Comorbidity	1
Hospital Anxiety and Depression Scale score >=8	1
Visit for pulmonary follow-up	1

B. Expert consultations

Of the 27 experts invited for consultation, 21 accepted the invitation. A list (n=21) of profession(s), country and expertise of each expert can be found in Table 3. Nine were from Belgium, of whom six had expertise in PC and three in COPD. Twelve were from other countries, of whom seven were PC experts, two were experts in COPD, and three were experts in both PC and COPD.

A summary of the main results on possible inclusion criteria and components can be seen in Table 4. The experts considered inclusion and exclusion criteria for the intervention by suggesting which criteria indicated PHC needs and which not. They mentioned positive (facilitators) and negative (barriers) comments for each criterion (Table 4). The most commonly mentioned inclusion criteria were: after admission to hospital for exacerbation (eight experts in favour), depending on lung function test (eight in favour, but also six not), depending on functioning of the patient (four in favour) and being housebound (three in favour).

Possible components of early-integrated PHC for end-stage COPD were discussed: advance care planning, psychosocial support and symptom control were recommended respectively by fourteen, eleven and eleven experts, although advance care planning was also seen as less suitable by nine and the benefits of psychosocial support were questioned by four. Increasing the patient's knowledge and disease insight and providing pulmonary rehabilitation were each recommended by nine experts but barriers were also mentioned by two and four respectively. Eight experts stressed the importance of incorporating self-management into the intervention, while two reported barriers to that. Lastly, six experts saw possibilities for the involvement of relatives in a PHC intervention, and three questioned it.

The in-detail description of the mentioned barriers and facilitators for inclusion criteria and components can be consulted in Appendix 4: Overview of barriers and facilitators on inclusion criteria and components from the expert consultations.

Barriers to and facilitators for early-integrated palliative home care in standard care for COPD

Three focus group interviews with general practitioners (GPs) and four with community nurses (CNs) were held with a total of 28 GPs (n= 8, n= 8, n= 10) and 28 CNs (n= 4, n= 7, n= 5, n= 12) who each attended one of seven focus groups. The categories of barriers related to early-integrated PHC were 1) unpredictable exacerbations and death and invisible deterioration of functioning; 2) perceived patient attitudes such as a lack of disease insight and resistance towards care; 3) professional caregiver practices with a lack of a coherent and proactive plan, insufficient experience and a negative view of PHC for end-stage COPD; 4) lack of focus on knowledge and advantages of PHC and PC for end-stage COPD in a healthcare professional's basic and continuing education; 5) healthcare and PHC system characteristics: consultations that are too short, insufficient coordination between hospital and home care and a reimbursement system for PHC that is based on life expectancy and 6) communication: a lack of and unclear communication about care possibilities for end-stage COPD between healthcare professionals and a lack of clear information about PHC between them and their patients.

The categories of facilitators were 1) trigger moments to start talking about early-integrated PHC such as after hospitalisation, after a couple of exacerbations, when an end-stage COPD patient becomes oxygen-dependent or housebound; 2) involvement of relatives in early-integrated PHC for COPD; 3) information about the advantages of early-integrated PHC for end-stage COPD in healthcare professionals' education; 4) including advance care planning as a part of healthcare and PHC systems and 5) enhancing communication between professionals by installing a care coordinator, and enhancing communication between professionals and patients by explaining better and giving practical examples of what early-integrated PHC could mean for them. The elaborated results on barriers and facilitators for early-integrated PHC are published elsewhere.[30]

Table 3 Characteristics of consulted experts

Expert	*Profession*	*Country*	*Expertise*
1	Palliative home care head nurse Coordinator palliative home care team	Belgium	Palliative care
2	Palliative home care nurse	Belgium	Palliative care
3	General practitioner Palliative home care physician Scientific researcher	Belgium	Palliative care
4	General practitioner Scientific researcher	Belgium	Palliative care
5	General practitioner Scientific researcher	Belgium	COPD
6	General practitioner Scientific researcher	Belgium	Palliative care
7	Pulmonary physician Scientific researcher	Belgium	COPD
8	Pulmonary physiotherapist	Belgium	COPD
9	Respiratory physician Scientific researcher	Switzerland	Palliative care COPD
10	General practitioner Palliative home care physician	Belgium	Palliative care
11	Respiratory physician Scientific researcher	Australia	COPD
12	Respiratory physician	Australia	Palliative care COPD
13	Respiratory physician Scientific researcher	Spain	Palliative care
14	Palliative care physician Scientific researcher	Spain	Palliative care
15	Researcher social sciences	Germany	Palliative care
16	Palliative care physician Researcher medical science	Canada	Palliative care
17	Member of a Scientific Institute Professor in medicine	United Kingdom	Palliative care
18	Member of an expertise centre in Palliative Care Prof. in Pain and Palliative Medicine	Netherlands	Palliative care
19	Scientific researcher	Netherlands	Palliative care
20	Involved in the Breathlessness Intervention service	United Kingdom	Palliative care COPD
21	Respiratory and sleep physician	Australia	COPD

Table 4 Summary of possible inclusion criteria and components for early-integrated palliative home care according to expert consultations

Inclusion criteria	*Facilitators mentioned by experts**						*Barriers mentioned by experts**					
	A	**B**	**C**	**D**	**E**	**Total**	**A**	**B**	**C**	**D**	**E**	**Total**
After admission to hospital for exacerbation			12, 22	14, 16, 17, 19, 20	21	**8**		4	22			**2**
Functioning of the patient			22	14, 16	10	**4**						**0**
Depending on lung function test		4	12, 22	14, 15, 16, 18, 19		**8**	9	4		15, 16, 19, 20		**6**
Depending of social context						**0**				16		**1**
Opinion of caregiver	7					**1**						**0**
Being housebound			12	14, 16		**3**			22			**1**
Oxygen dependency			12, 22			**2**						**0**
Component	*Facilitators mentioned by experts**						*Barriers mentioned by experts**					
	A	**B**	**C**	**D**	**E**	**Total**	**A**	**B**	**C**	**D**	**E**	**Total**
Advance Care Planning	5	1, 2, 3, 4, 11	12, 22	15, 17, 18, 19, 20	13	**14**	5	3, 11	12, 22	15, 20	13, 21	**9**
Involvement of relatives	9		12, 22	15, 16	21	**6**	9		22	16		**3**
Knowledge and disease-insight	9	1, 2, 11	22	15, 17, 18	10	**9**				15	10	**2**
Pulmonary rehabilitation	9	1, 2, 3, 4	22	17, 18	21	**9**	9			17, 18	21	**4**
Psychosocial support	5	1, 2, 6		14, 15, 16, 17, 18	10, 21	**11**		3		14, 15, 16		**4**
Self-management		1, 2	22	15, 17, 18	10, 21	**8**				15, 16		**2**
Symptom control		1, 2, 3, 4, 11	12	15, 17, 18	10, 21	**11**						**0**

*The results are presented in following order: **A**: Belgian experts in COPD; **B**: Belgian experts in palliative care; **C**: foreign experts in COPD; **D**: foreign experts in palliative care; **E**: foreign experts in COPD and palliative care, mentioned with the numbers given to experts in table 3.

Phase I: Modelling process and outcomes

Inclusion criteria

Based on the results in Phase 0, inclusion and exclusion criteria were developed. This was done by evaluating and discussing the most commonly used or mentioned inclusion criteria from the literature and the expert consultations. The research team cross referenced these inclusion criteria to clinical practice for end-stage COPD in Flanders and decided to incorporate lung function tests as a basic criterion in order to identify end-stage COPD, by selecting GOLD III and GOLD IV[44].

Next, as recommendations from GOLD[44] and the results in Phase 0 also stipulated that lowering of functioning and frequent exacerbations are equally important predictors of end-stage COPD, the research team and the pulmonologist who also developed the criteria decided to combine lung function tests with two (in case of GOLD III) or one (in case of GOLD IV) criteria/criterion representing frequent and severe exacerbations (reflected in criterion: three or more hospitalisations for COPD in the past three years) or lowering of functioning (oxygen-dependent, COPD Assessment Test-scale ≥25, Medical Research Council dyspnea-scale of 4, intubation or non-invasive ventilation in the past year, low BMI or heart failure New York Heart Association of 3). By designing the criteria in this way, we tried to incorporate the diverse ways end-stage COPD can occur in people suffering from it. Furthermore, the exclusion criteria were created in order to reflect a person able to participate in the study such as region of residence, mastery of Dutch and cognitive impairment. We also excluded active cancers as patients would otherwise have a higher chance of referral to PHC because of their cancer diagnosis (Table 5: Final selection of inclusion and exclusion criteria).

Table 5 Final selection of inclusion and exclusion criteria

Inclusion criteria:

GOLD III (cf. GOLD 2017[44])and ≥ two OR GOLD IV (cf. GOLD 2017[44]) and ≥ 1 more of the following criteria

- Oxygen-dependent[45]
- Three or more hospitalisations for COPD in the past three years
- COPD Assessment Test -scale ≥25[44]
- Medical Research Council Scale Dyspnea 4
- Intubation in the past year
- Non-invasive ventilation in the past year
- BMI ≤18
- Heart failure NYHA 3

Exclusion criteria:

Patients living outside the region Ghent-Eeklo, Flanders, Belgium (where the intervention will take place)
Patients in the last days of life (bedbound and/or semi-comatose and/or take only fluid and/or no longer able to take oral drugs[19])
Patients with cognitive impairment: Mini Mental status Examination ≤23 at the day of inclusion of patients[46]
Lung cancer diagnosis
Patients with active cancer
Patients who are not living at home any more
Patients with no knowledge of Dutch
Patients with a general practitioner already involved in this study for an intervention/control group patient

Components

The five final components were developed by the research team by combining the results from the literature search, the expert consultations and the focus group study. The intervention needed to focus on predefined outcomes: improving quality of life for end-stage COPD patients and improving quality of care in line with previous literature emphasizing those as the main outcomes of integrated PC[4]. Therefore, we first selected the most commonly used or mentioned components from the literature and experts and prioritised them. This revealed that advance care planning, pulmonary rehabilitation, patient knowledge and disease-insight and symptom control were of utmost importance. Next, there was also evidence for including the involvement of relatives, psychosocial support and self-management as a component. As we wanted to design an intervention with a holistic PHC approach, we decided to incorporate as many relevant components as possible in the design. Furthermore, we looked at the barriers and facilitators related to PHC for end-stage COPD in Flanders from the results of the focus group studies. These revealed that advance care planning, training professionals, increasing knowledge about COPD and PHC for patients and involving relatives were perceived to enhance the early-integrated PHC.

However, the final selection of intervention components was informed by what was considered by the research team as relevant to the Flemish context of PHC, was likely to be feasible for the involved PHC team and research setting, likely to be replicated in other studies and could be implemented as a complex intervention in clinical practice. This made us, for example, exclude pulmonary rehabilitation as a component on its own, as this could not be provided fully by the involved PHC team of the intervention and is not included in care services of PHC in Flanders. It also made us incorporate advance care planning and involving relatives in one component instead of making it two separate components, as PHC teams in Flanders already offer advance care planning to patients and support for relatives as standard PHC.

The chosen content was then modelled and further operationalised into five concrete components using elements from previous studies and projects and from elements developed by the research team itself. Further adjustments were made by the expert panel and the two expert opinions for improving integration and implementation in the Flemish PHC practice. The components are: (1) training of the PHC team in care for people with end-stage COPD, (2) monthly home visits by a PHC nurse, (3) information leaflets, (4) a semi-structured protocol for home visits and (5) integration of care between involved professionals.

Component 1 - Training of the PHC team in care for people with end-stage COPD

Training in knowledge and care for people with COPD will be given to the nurses of the PHC team. The team expressed the need for more information about end-stage COPD as they lack knowledge about it in their current practice. The PHC team will also learn to work with the semi-structured protocol and the information leaflets which are a part of the intervention. The expert panel confirmed the need for training the team and agreed on the topics (see infra) included in the training. One expert advised the inclusion of information about the value of physical activity and dietary advice as many people with end-stage COPD suffer from nutritional deficiencies and low muscle mass. The research team decided to include this recommendation.

The topics of training are:

- providing information on the disease trajectory of COPD and the symptom burden for people with end-stage COPD
- recognising and managing an exacerbation
- providing information about COPD, including the role of exercise, coping with the disease and self-management skills
- learning to work with the semi-structured protocol that will be used during home visits
- learning to work with the information leaflets ‘Breathing and saving energy’ and ‘Preventing and coping with complaints’

Component 2 - Home visits by a PHC nurse

Home visits by a PHC nurse are already part of *care as usual* provided by the PHC team to support the patient, relatives but also the professionals active in home care (e.g. GPs, CNs, physiotherapists) in their care for patients. However, people with end-stage COPD are not receiving PHC systematically in Flanders and when they do it is only in the terminal phase[47]. In Phase 0, it became clear from the literature[48] that end-stage COPD patients need more systematic support for their symptoms and concerns, and not only in the terminal phase. Therefore, home visits were incorporated as a component with a minimum frequency of one per month over a period of six months. This could be increased if more follow-up was needed. This was seen as appropriate by the expert panel.

Component 3 - Information leaflets

In current PHC practice in Flanders, concrete tools for self-management, knowledge and disease insight are insufficiently used, although this could vary among different PHC teams. In contrast, both the literature[20,42] and our expert consultations provided evidence of the benefits of appending self-management tools to PHC for people with end-stage COPD. Therefore, we decided to make information leaflets on self-management of COPD symptoms an intervention component which could be explained by the PHC nurse during home visits. The expert panel recommended that Flemish leaflets should be used to improve comprehensibility for Flemish people, but as there were none in existence at the time we decided to use Dutch-translated leaflets from the ‘Living well with COPD’ Canadian project, which were originally developed in English[49]. These are part of a Canadian learning method for COPD patients and their families and focus on raising awareness and knowledge about COPD and on teaching people possible coping mechanisms, giving information about the disease, breathing exercises, knowledge and use of medication.

The Dutch-translated leaflets were developed for people living in the Netherlands and therefore contain information e.g. brand names of medications only available in the Netherlands which will not be relevant to our intervention in Flanders, Belgium, as advised by the expert panel; we have therefore replaced that information with a list of medication available in Belgium. Some words used in the Dutch-translated leaflets are not commonly used in Flemish, but as we considered the general content very clear for Flemish people, we decided to leave them unchanged. Nevertheless, we will take into account this possible bias when analysing the feasibility and acceptability of this component in the Phase II intervention. The leaflets can be consulted in Appendix 5.

Component 4 – Semi-structured protocol during home visits

Currently, most PHC teams in Flanders do not use a standardised registration document listing all topics of care covered in home visits. PHC nurses also say they have difficulty knowing exactly what the specific needs and symptom burdens are for people with end-stage COPD. As the results of Phase 0 show that holistic PCH requires different types of support for psychosocial, symptomatic and spiritual/existential needs, as well as knowledge of advance care planning and support for those close to the person who is dying, we developed a standardised document containing a semi-structured protocol for further care, support and management of end-stage COPD-specific symptoms. This could enhance the discussion about end-stage COPD symptoms and needs, taking into account all support measures during home visits. The structure of the protocol is inspired by the interventions of Weber et al[18], Buckingham et al[43] and Vanbutsele et al[24] and contains nine focus areas: disease-insight and coping, symptom management (flagged by completing the Dutch translation of the Edmonton Symptom Assessment Scale (ESAS)), care planning, support for relatives, psychosocial support, spiritual support, other non-predefined support e.g. financial, practical and administrative, an action plan and coordination of care. The expert panel had some doubts about using the Dutch-translated ESAS; it recommended changing some words into Flemish in order to improve interpretation and suggested adding 'tightness in the chest' next to 'breathlessness' as the former referred to a different symptom from the latter, which we did. An in-detail overview of the focus areas can be seen in Table 6 and the protocol can be consulted in Appendix 6.

Table 6: focus areas in the semi-structured protocol for the palliative home care nurse

1. Disease insight and coping

- Anamnesis of the disease and the patient
- Listening to the patient's experience of his/her dyspnea
- Information about dyspnea and COPD (through conversation and info-leaflets) and medication (if needed)

2. Symptom management

- Standard care package of the palliative home care team
- Assessment of symptoms (ESAS)

3. Care planning

- Values and wishes of the patient for the future
- Preferences for end-of-life care (for example on hospitalisation)
- Living will/advance directive

4. Support for those close to the person who is dying (if needed)

- Identification of those closest to the person
- Assessment of their needs
- Providing available resources if needed

5. Psychosocial support

- Assessment of needs (psychological, social, financial, administrative, activities of daily living)
- Providing available resources if needed
- If needed, referral to other professional caregivers or social workers if patient agrees

6. Spiritual/existential support

- Assessment of needs (how he/she sees the future, who he/she gets existential/spiritual support from, if there are particular worries)
- Providing available support

7. Other support

- Assessment of other concerns or needs (for example: practical needs related to housing)
- Follow-up of problems if help can be given

8. Coordination of care

- Listing all involved professionals, their function, treatment goals and interventions
- Involving professionals in the follow-up of the patient and their vision of further care
- Communication about coordination of care with the involved general practitioner

9. Agreed actions

- Listing agreed actions the patient can undertake to tackle certain problems, identified in one or more of the other focus areas
- Patient, general practitioner, community nurse, physiotherapist and pulmonologist receive an overview of these actions after each visit

Component 5 - Integration of care between involved professional caregivers

In current PHC in Flanders there is no standard reporting or communication procedure between PHC nurses and other healthcare professionals except for regular updates with the GP, who instigates the PHC. As seen in Phase 0, the focus groups stressed the need for a care coordinator as a proactive care plan is lacking in current practice and conflicting treatment between professionals often happens. Consequently, we incorporated 'integration of care between involved professionals' as a final component in order to systematise the integration of reporting mechanisms and communication between all professionals involved. With the agreement of the patient, the PHC nurse will send the report of each home visit to the GP, CN, physiotherapist and pulmonologist.

The protocol will also contain an action plan (with a summary of actions needed) and will in some cases contain directions to relevant professionals e.g. the physiotherapist in the case of exercise actions. The PHC nurse will directly or via the GP contact them if needed. The GPs will be more highly involved in this model and the PHC nurse will always contact them if further action or care is needed and if important changes in health status occur.

Lastly, a care plan will be included, listing the contact details and speciality of all healthcare professionals so that each one knows who is responsible for what and what care he or she provides. One expert had stressed the importance of identifying and noting down the roles, goals and care interventions of each person involved in the care plan and had asked for a definition of a care intervention as this was not clear. The research team eventually decided not to add these further specifications, but did include an example of a care intervention in the protocol, so the PHC nurse would understand what was needed. Table 7 gives an overview of how the results from Phase 0 related to the selection of the final five components.

Table 7: Describing components of an intervention to integrate palliative home care early in standard care for people with severe COPD

Component 1: Training in care for people with severe COPD for palliative home care team

Explanation of the component	*Barriers and facilitators addressed by the component**
Five nurses of the palliative home care team who will execute the intervention will follow a half-day training course on care for COPD patients. This is to prepare them for the intervention with COPD patients, as the majority of those they currently support are cancer patients. A pulmonologist and a pulmonary physiotherapist/smoking cessation consultant from Ghent University hospital will give this part of the training. Another part will consist of learning to use the intervention tools (information leaflets and semi-structured protocol: see infra under component 3 and component 4) as the palliative home care nurses are not experienced in using them. This will be given by the executive researcher of the study, a sociologist from Ghent University.	➢ No experience in clinical practice with palliative care for COPD (focus group - barrier) ➢ Lack of focus on knowledge and advantages of palliative care for COPD in basic and continuing education (focus group-barrier) ➢ More focus on early-integrated PHC for COPD and concrete implementation in clinical practice in education for professionals (focus group facilitator) ➢ Training professionals in early identification of patients in need of palliative care and structuring advance care planning (literature)

Component 2: monthly home visits by a palliative home care nurse

Explanation of the component	*Barriers and facilitators addressed by the component**
After the general practitioner has been brought into contact with the palliative home care nurse and the patient has been discharged at least two weeks from hospital (if the inclusion happened during hospitalisation), the patient will meet the palliative home care nurse during a first home visit where the nurse will introduce himself/herself and explain what the palliative home care team can do for the patient during the intervention. Following this introductory visit, the palliative home care nurse will plan home visits at least once a month for a period of six months in total, the length of the study. If more adequate follow-up is needed, a higher frequency of visits will be given.	➢ Specialised palliative care consultations integrated with standard care (literature) ➢ Palliative status for palliative home care is based on predictability of death (focus group-barrier) ➢ Palliative reimbursement of palliative home care is restricted to 3 months (focus group-barrier) ➢ Not enough time during consultations to start talking about palliative care and further care (focus group-barrier) ➢ Not discussing palliative care (needs) in detail during consultations with the end-stage COPD patient (focus group-barrier) ➢ Professional caregivers fear talking about palliative home care because of the patient's reaction (focus group-barrier) ➢ Difficulties for professional caregivers to talk about palliative care needs with their end-stage COPD patients (focus group-barrier)

Component 3: Information leaflets

Explanation of the component	*Barriers and facilitators addressed by the component**
A palliative home care nurse will give the patient two information leaflets during one or more of the home visits. The information leaflets have the goal of raising awareness and knowledge about COPD and informing the patient about possible coping mechanisms. These leaflets are Dutch-translated from the originally English leaflets and are part of the Canadian 'Living well with COPD' project, which is a learning method for patients and their families. Titles of the information leaflets are 'Preventing and coping with complaints' and 'Breathing and saving energy'. The palliative home care nurse will explain the information leaflets during visit 1 and visit 2 (and in case of lack of time during visit 3) as well as possible and teach the patient how to use them. It is recommended to start with 'Preventing and coping with complaints' and then 'Breathing and saving energy'.	➢ Educating patients with COPD (literature) ➢ Self-management of patients with COPD (literature) ➢ Not understanding the severity of the disease or realising the possibility of death (focus group-barrier) ➢ Denial of the severity of the disease (focus group-barrier) ➢ Inform patients clearly and firmly about their disease and the future (focus group-facilitator) ➢ Knowledge and disease insight (expert consultations)

Component 4: Semi-structured protocol during home visits

Explanation of the component	*Barriers and facilitators addressed by the components*
During each visit, the palliative home care nurse will use a semi-structured protocol to structure the visit and report it (see table 6). This semi-structured protocol will tackle the following areas: disease-insight and coping, symptom management, care planning, support for relatives, psychosocial support (psychological, financial and administrative), spiritual support, other non-predefined support, an action plan and coordination of care. During every visit, the palliative home care nurse will fill in the semi-structured protocol, which will contain fill-in boxes for the nine focus areas, a box to note down actions and how many minutes of their visit were spent on each area. An action plan and a care plan will be included as well and will be updated during each visit.	➢ Communication between healthcare professional and patient (focus group– barrier) o Not discussing palliative care (needs) in detail during consultations with the patient o Difficulties for professionals in talking about end-of-life preferences and palliative care needs with patients o Patient-relative relationship can prevent communication about palliative care o Professionals fear talking about palliative care because of the patient's reaction ➢ Increase knowledge about advantages of palliative home care for relatives of patients with COPD (focus group- facilitator) ➢ Start advance care planning as a standard procedure for all severe COPD patients living at home (FG - facilitator) ➢ Communication between professional and patient (focus group– facilitator) o Talking about practical matters can help the doctor start talking about palliative care o Better explanation of the term palliative home care can help acceptance by patient ➢ Advance care planning as a part of palliative care (literature) ➢ Self-management of patients with COPD (literature) ➢ Advance care planning as a component of palliative care trials (expert consultations) ➢ Psychosocial support (expert consultations) ➢ Symptom control (expert consultations) ➢ Involvement of those close to the patient (expert consultations)

Component 5: Integration of care between involved professional caregivers

Explanation of the component	*Barriers and facilitators addressed by the component**
The palliative home care team, responsible general practitioner, community nurse, physiotherapist and pulmonologist systematically receive, if the patient agrees, a report of every visit with a summary of the assessments and agreed actions. The palliative home care nurse sends this report directly to them via e-mail or post. The general practitioner (and if needed other relevant professionals such as the community nurses) will be contacted by the palliative home care nurse to develop the care plan for the patient. If needed, any medical interventions by other professionals can be coordinated together with the responsible general practitioner.	➢ Lack of a coherent and proactive care plan (focus group barrier) o No cooperation between professionals involved at home o Conflicting therapy and treatment between professionals ➢ Interprofessional communication (focus group barrier) o Not knowing each other well enough for proper communication o Unclear who takes initiative to introduce PHC to the patient o Not understanding each other's messages ➢ Communication between professionals: appoint a care coordinator who facilitates the care transition to palliative home care (focus group– facilitator)

*An overview of barriers and facilitators for early-integrated PHC can be consulted in a previous paper[50].

Discussion

Summary of the results

In this article, we described the development and modelling of an intervention for the early-integrated palliative home care (PHC) into standard care for people with end-stage Chronic Obstructive Pulmonary Disease (COPD), with the goal of improving their quality of life and quality of care. Phase 0 resulted in the identification of possible inclusion criteria and components and barriers to and facilitators for the integration of PHC early in the care trajectory of end-stage COPD. Based on these findings, in Phase I, a nurse-led intervention was developed consisting of: 1) training on symptom recognition and physical therapy exercises for the PHC team, 2) regular home visits by PHC nurses, 3) two educational booklets on self-management of COPD, 4) a semi-structured protocol to record the outcomes of the home visits and the follow-up plan and 5) integration of care by encouraging collaboration and communication between healthcare professionals in hospital and in home care.

Strengths and weaknesses

We conducted a Phase 0–I study according to the Medical Research Council (MRC)-framework, which is a key strength of this study as it provided a high-quality structured and phased process towards development of complex interventions[29], confirmed by previous intervention studies on end-of-life care and advance care planning[7,28]. To our knowledge this is the first nurse-led intervention exploring the early-integrated PHC into standard care for end-stage COPD patients, using a holistic and comprehensive model, in line with recommendations from Buckingham[43]. Among previous interventions there were studies focusing on holistic palliative care (PC) but these were not sufficiently integrated into standard care[19] or introduced early in the disease trajectory[43]. Other interventions focused mainly on managing breathlessness[20] or did not fully take into account early-integrated care[16]. Instead, we used several components to provide a holistic PHC approach to be given early and integrated with standard care, in order to try to tackle the lack of early-integrated PHC for people with end-stage COPD in current clinical practice.

One limitation of this study is that we did not directly consult people with end-stage COPD and those close to them although the primary focus was in fact to gain insight into care possibilities for the early-integrated PHC. The views of end-stage COPD patients on PHC have been captured in previous research[16], although without taking into account the specific Flemish context. Future research on the perspective of end-stage COPD patients and their relatives in specific regional contexts could explore this further. Furthermore, we will conduct interviews with half of the end-stage COPD patients and their relatives from the intervention group in the Phase II evaluation study, where we will explore their perspectives on the intervention components and on possible improvements for a Phase III intervention trial.

Another limitation is that we have not fully included pulmonary rehabilitation as a component of our intervention despite both literature and expert consultations identifying it as a valuable part of PHC for end-stage COPD, either in the form of physical therapy sessions[35] or for the relief of breathlessness[7]. As pulmonary rehabilitation is formally not included in standard Flemish PHC services, there are no pulmonary physiotherapists in PHC teams in Flanders. As the PHC team involved in our intervention was not experienced in providing pulmonary rehabilitation, we decided not to incorporate this as a main component in the intervention. However, we included rehabilitation techniques and breathing exercises in the component 'training for the PHC team' and if pulmonary rehabilitation is needed the PHC team will refer the patient to a pulmonary physiotherapist. Furthermore, in the Phase II evaluation study, we will evaluate the necessity of incorporating pulmonary rehabilitation as a component in future interventions, by interviewing intervention patients, pulmonologists and general practitioners (GPs).

Comparison with existing literature

One component developed in the intervention, the 'semi-structured protocol', consists of a consolidation of certain elements in the interventions of Vanbutsele et al [24], Weber et al [19] and Buckingham et al [43]. While the two latter interventions did not fully lead to the targeted effects, the components of all three studies seemed stronger and more effective when combined, after we had analysed them in Phase 0. The components of Weber et al[19] were used for shaping the content of the focus areas: symptom control, spiritual/existential, psychosocial and support for relatives, knowledge about the disease and coordination of care. The components of Buckingham's intervention[43] inspired us to add a concrete self-management tool in the form of an action plan. From the intervention of Vanbutsele et al[24] we took the structure of the semi-structured protocol document, with indications of how long (in minutes) a PHC nurse spent discussing one topic in the protocol. This led to a semi-structured protocol that encompasses a complete care support programme.

When comparing the intervention we developed with the results of studies identified in a recent review[6] of PC and management of troublesome symptoms for COPD we saw similarities but also some differences. The review summarised current evidence on how deleterious symptoms and concerns in COPD could be addressed using PC interventions, and deduced potential models for integrative working e.g. symptom-triggered services, short-term integrated PC, advanced COPD clinics and integrated respiratory care services (pulmonary rehabilitation, early supported discharge, hospital at home etc.). The findings also indicated that these models could be triggered by indications for PC such as complex troublesome symptoms, hospitalisation or change in place of residence, acute inpatient care for respiratory failure and the commencement of oxygen therapy. In the meantime, respiratory medicine and primary care can be offered simultaneously to the patient[6].

These suggested models focus mainly on managing specific symptoms such as breathlessness; this differs from the holistic focus of our intervention which aims to encompass spiritual/existential, social and practical support while incorporating a care and action plan, but symptom-specific services as described above could be used for a combination of symptoms and needs together. The studies in the review also support the early-integrated PC with standard respiratory services, in line with our intervention in which we provide possibilities of involving the pulmonologist in helping to decide certain actions the PHC nurse can undertake for the patient, while the latter will also inform the former about the home visits by sending a report of the semi-structured protocol.

Implications for research, education and practice

Future research could explore in detail interventions in PHC for people with COPD. The focus of these studies could be on analysing procedures and difficulties in enrolling and developing interventions. Future Phase II interventions should also report more results on the intervention's feasibility and acceptability of participating end-stage COPD patients, by actively involving the latter in the development and evaluation of interventions. Currently, there is a lack of knowledge about all these aspects. Not only is the number of interventions on PC for end-stage COPD low, especially compared with cancer, but published interventions on PC for COPD do not often report the procedures of the studies, which makes it difficult to repeat them in other contexts. Reviews such as the one from Maddocks et al[6] have proved useful in analysing completed trials and other research on PC for end-stage COPD. More reviews on specific PC services such as PHC and early integrated PC as well as procedures used in implementing interventions could prove to be important in developing future interventions.

Furthermore, our results imply that more knowledge and expertise on care, PC and support for end-stage COPD is needed for PHC nurses but also for other professional caregivers such as GPs and community nurses. We suggest that more emphasis on this topic is provided in basic education with the possibility of learning skills in clinical practice. Further education on PC should also cover more information about disease specific support, for example learning breathing exercises specifically for end-stage COPD, and should not be limited to care for cancer patients. At last, we suggest for clinical practice to re-evaluate the roles of involved healthcare professionals for end-stage COPD, as pulmonary rehabilitation could not be fully incorporated in the service given by PHC nurses. We advise looking at whether this would be a possibility in the future, by training PHC nurses better in this, or that other possibilities should be explored in order for pulmonary rehabilitation to be available at home during the last stage of life, for example by enhancing education about it for physiotherapists. Also, due to the large number of identified components for early-integrated PHC we wonder if early PHC for end-stage COPD does not require the standard involvement of other professionals besides PHC nurses, such as pulmonary physiotherapists and psychologists, as opposed to PHC given in the final stages of life or PHC for cancer. This should be further explored in intervention studies and clinical practice.

Conclusion

This MRC Phase 0-I process succeeded in developing a complex intervention for the early-integrated PHC into standard care for end-stage COPD patients. Using three methods in Phase 0 gave reliable data, with inclusion criteria and components for an intervention focused on holistic PHC. The feasibility, acceptability and preliminary effectiveness of the intervention will subsequently be tested in a Phase II study.

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Conflict of Interest

The authors declare no conflict of interest.

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Appendices

Appendix 1 Topic guide expert consultations in English and in Dutch

Topic guide in English	Topic guide in Dutch
• Introduction and explanation of the goal of the intervention: improving quality of life for people with end-stage COPD by early integration palliative home care • What is your affinity with the study topic and how would you address this in clinical practice? • What is the added value of early integrated palliative care for end-stage COPD? • How can professional caregivers decide when early integrated palliative care should be given for end-stage COPD? For example using trigger moments and inclusion criteria from literature? • How could the current problems with palliative home care for people with end-stage COPD be better addressed (through involvement of palliative home care teams)? • How could some solutions help improve quality of life for people with end-stage COPD? • Which professional caregiver could play a role in the improvement? • Asking their opinion about components used in literature: psychosocial support, symptom management, • How could early-integrated palliative home care be implemented in standard care for people with end-stage COPD using which components in interventions?	• Introductie: Uitleg over mijn onderzoek en waarop we onze interventie zullen toespitsen: nl. het verbeteren van de levenskwaliteit van de patiënt met vergevorderde COPD en het zorgkader voor COPD. Dit door het integreren van vroegtijdige palliatieve zorg in de reguliere thuiszorg • Vragen naar hun affiniteit met het onderwerp en hoe zij dat zouden zien in de praktijk • Vragen over de zin van (vroegtijdige) palliatieve zorg bij COPD-patiënten • Vragen naar welke triggers/inclusiecriteria vanuit de literatuur er bestaan voor de zorgverlener om te bepalen wanneer (vroegtijdige) palliatieve zorg kan ingeschakeld worden bij COPD • Hoe kunnen de huidige problemen voor COPD-patiënten beter geadresseerd worden (door betrekken van palliatieve thuiszorg)? • Welke oplossingen kunnen levenskwaliteit verbeteren? • Welke rol zouden betrokken zorgverleners kunnen spelen in deze verbetering? • Welke interventiecomponenten kunnen gebruikt worden om tijdige integratie van palliatieve thuiszorg te introduceren in standaardzorg voor COPD? • Welke inclusiecriteria kunnen gebruikt worden om tijdige integratie van palliatieve thuiszorg te introduceren

Appendix 2 Key components of existing interventions and intervention protocols on palliative care and symptom management for end-stage COPD patients based on explorative literature search

Key component	*Explanation*
Advance care planning	Incorporating advance care planning was done by training general practitioners in proactive care planning[1] or by testing the effectiveness of written advance directives on decision-making about future preferences, where health caregivers received information about each patient's and surrogate's preferences in the medical record[2]. A study trained respiratory nurses in structured advance care during 2-day sessions, focusing on reflection of patient's goals, values and beliefs, understanding current and future medical situations, possible treatments, outcomes, and communication skills[3].
Pulmonary rehabilitation and respiratory services	Guëll[4] compared home-based and hospital based pulmonary rehabilitation where the patients attended two informative sessions about the disease and four physical therapy sessions. The home-based patients then performed at home low intensity exercises without supervision, while the hospital-based patients carried out a structured exercise programme. Cockcroft[5] evaluated monthly visits to COPD patients by a respiratory nurse, who gave education and support focused on health according to individual needs. They followed a model identifying problems in activities of daily living and setting goals to increase independence in these activities. Higginson tested a breathlessness support service, being a short-term, single point of access service integrating PC, respiratory medicine, physiotherapy, and occupational therapy[6].
Specialised palliative care	The study of Weber[7] integrated early palliative care consultations (one per month for one year by a palliative care professional) into standard care, focusing on symptom management, understanding of illness and coping with the disease, anticipation, relatives support, social support, spiritual support, coordination of the health professionals. The intervention of Duenk[8] let patients meet with a specialised palliative care team (who received special training for palliative care in COPD) within one week after enrolment and at least monthly thereafter in the outpatients setting for at least one year or until death, in the presence of the main informal caregiver.
Trained professional caregivers	Some interventions involved training general practitioners, such as a five hour course on early identification of patients in need of PC and on structuring anticipatory PC planning, an individual coaching session by phone with a physician specialised in PC, and peer group sessions on patient-general practitioner communication regarding the initiation of PC[1]. Another protocol provided training for general practitioners on educating patients to use the right inhalation techniques with their inhalers[9].
Educating COPD patients	In an intervention by Fan et al[10], the patient was given education on COPD over four individual and one group sessions, an action plan for identification and treatment of exacerbations, and scheduled proactive telephone calls for case management[11]. Another trial incorporated the Living Well with COPD Programme and an educational module on end-of-life care and decision-making in an intervention which was delivered in the patient's home over four to eight weeks[12]. Lastly, a study is currently testing the impact of a psycho-educative session (focused on cognitive restructuring) in the patient's home in combination with a telephone booster session where patients learned to interpret and react to physical and psychological symptoms that are related to dyspnea and associated anxiety[13].
Self-management of COPD patients	One trial used tele-monitoring as a way for patients to report their symptoms daily using an electronic diary[14]. Another focused on managing breathlessness by developing a breathlessness intervention service which included among other things a relaxation CD, a hand-held fan and a wellbeing journal for increasing personal wellbeing [15,16], while Buckingham developed a respiratory nurse-led intervention with an action plan on proactive holistic assessment of physical, psychological, social and spiritual needs[17].

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Appendix 3 Explorative literature search on interventions and intervention protocols.

Author, Year, Country, Journal	*Main objectives*	*Design*	*Participants (n)*	*Inclusion criteria*	*Components intervention*	*Primary/secondary outcomes (PO/SO)*
A. Completed trials *(Outcomes marked with *: significant outcomes; marked with #: negative significant outcomes; marked with £: non-significant outcomes but efficient intervention model; marked with &: non-significant outcomes but inefficient intervention model)*						
1. Thoonsen et al *2015* *The Netherlands* *BMC Family Practice*	Training for general practitioners (GPs) in identifying patients in need of palliative care and in structuring anticipatory palliative care planning in order to recognise patients in need of palliative care in a timely way and to structure anticipatory care.	Randomised controlled cluster (RCT)	GPs Intervention: n= 80 Control: n= 79	All GP practices in two regions of the comprehensive cancer centre of the Netherlands were invited by mail to participate. GPs were excluded if they were a consultant in a palliative care team.	The intervention group: GPs were trained in identifying patients in need of palliative care and anticipatory care planning and for each identified patient, they were offered a coaching session with a specialist in palliative care to fine-tune a structured care plan Control group: Usual care	PO: #the number of contacts with the out-of-hours GP cooperative SO: *contacts with their own GP, *place of death and *hospitalisations in the last months of their life
2. Ho et al *2016* *Taiwan* *Scientific reports*	Investigate the effectiveness of telemonitoring in improving COPD patient outcomes.	RCT	COPD patients Intervention: n=53 Control: n=53	COPD patients > 20 years + COPD exacerbation as the main diagnosis, current or former smokers, spirometry-confirmed airflow limitation (FEV1), discharge to home, and accessibility to the internet and phone.	The telemonitoring group: patients had to report their symptoms daily using an electronic diary. Control group: Usual care	PO: #time to first re-admission for COPD exacerbation within six months of discharge. SO: (1)* the time to first emergency room visit for COPD exacerbation, (2)* the number of all-cause hospital re-admissions, and (3)* the number of all-cause emergency room visits.
3. Guëll et al *2015* *Spain* *Archivos de Bronconeumologia*	To compare the effects of a simple home pulmonary rehabilitation program and an intensive hospital-based program in terms of the exercise tolerance and health-related quality of life (HRQOL) of patients with COPD.	Prospective multi center trial	COPD patients Hospital group: n=28 Home group: n= 23	Patients with severe or very severe COPD: age between 50 and 75 years, classification as an ex-smoker or smoker intending to quit, forced expiratory volume in 1 second (FEV1) between 30% and 50% of reference, and stable condition free of exacerbations in the last 4 weeks.	1 group received hospital and 1 group received home pulmonary rehabilitation. Patients in both groups attended 2 informative sessions about the disease and 4 physical therapy sessions. Patients in the hospital group then carried out a structured exercise program while home group	#Respiratory muscle function, arm strength, #leg strength (same results), *Health-related quality of life (only on emotional function higher for hospital group)

					patients performed low intensity exercises at home without supervision.	
4. S. Fan et al *2012* *United States* *Annals of Internal Medicine*	To determine the efficacy of a comprehensive care-management program (CCMP) in reducing the risk for COPD hospitalisation.	RCT	COPD patients: n=426	Patients had been hospitalised for COPD in the 12 months before enrollment. Additional inclusion criteria were a post-bronchodilator ratio of FEV1 to FVC below 0.70 with an FEV1 below 80% predicted, age older than 40 years, current or past history of cigarette smoking (10 packs/years), at least 1 visit in the past year to either a primary care or pulmonary clinic at a medical center, no COPD exacerbation in the past 4 weeks, ability to speak English, and access to a telephone.	Intervention group: COPD education during 4 individual and 1 group session, an action plan for identification and treatment of exacerbations, and scheduled proactive telephone calls for case management, based on the PRECEDE/PROCEED model of health program planning and evaluation. Control group: Guideline based care	PO: #time from randomization to first COPD hospitalisation. SO: *all-cause mortality, number of exacerbations, health-related quality of life, patient satisfaction, COPD-related knowledge, and self-efficacy.
5. Cockcroft et al *1987* *United Kingdom* *British Medical Journal*	To evaluate the role of respiratory health workers.	RCT	COPD patients: n=75	Chronic respiratory disability caused mainly by chronic obstructive airways disease. Admitted to hospital at least twice during the previous three years and new patients who had been seen within the past year.	Intervention group: was visited monthly by a respiratory nurse, who gave education and support, focusing on health rather than on disease, and varying in content according to individual needs. They followed a model identifying problems in activities of daily living and setting goals to increase independence in these activities. Control group: care as usual	PO: *quality of life (by questionnaires). SO: number and duration of admissions to hospital, and *the number of deaths.
6. Higginson et al *2014* *United Kingdom* *The Lancet Respiratory Medicine*	The effectiveness of early palliative care integrated with respiratory services for patients with advanced disease and refractory breathlessness.	Single blind RCT (1:1)	Patients with advanced disease Intervention: n=53 Control: n =52	Refractory breathlessness on exertion or rest (MRC dyspnoea scale score ≥2), despite optimum treatment of the underlying disease, as deemed by the identifying clinician; advanced disease such as cancer, COPD, CHF,	Intervention group: a breathlessness support service: a short-term, single point of access service integrating palliative care, respiratory medicine, physiotherapy, and occupational therapy. Control group: usual care	PO:* patient-reported breathlessness mastery at 6 weeks, a quality of life domain in the Chronic Respiratory Disease Questionnaire. SO: severity of breathlessness on exertion in the previous 24 h,

				ILD and motor neuron disease; willing to engage with short term home physiotherapy and occupational therapy; and able to provide informed consent.		breathlessness, fatigue, and emotional function, quality of life, palliative needs, depression and anxiety and spirometry. *Patient survival rate as a safety secondary endpoint.
7.Buckingham et al *2015* *United Kingdom* *Npj Primary Care Respiratory Medicine*	To identify and address the holistic care needs of people with severe COPD	6 month pilot RCT (ratio 3:1) and interviews	Patients with severe COPD Intervention: n=24 Control: n= 8	People registered with Lothian general practices admitted to Edinburgh Royal Infirmary or St John's Hospital, Livingstone with a primary diagnosis of exacerbation of COPD.	Intervention group: a proactive holistic assessment of physical, psychological, social and spiritual needs delivered by a specialist respiratory nurse shortly after an admission with an exacerbation of COPD (HELP-COPD). Control group: usual care	PO:* Functional assessment SO: *health related quality of life, *physical, *psychosocial, spiritual well-being
9. Teno et al *1997* *United States* *Journal of American Geriatric Society*	To assess the effectiveness of written Advance DirectiveS (ADS) in the care of seriously ill, hospitalised patients. In particular, to conduct an assessment after ADS were promoted by the Patient Self-Determination Act (PSDA) and enhanced by the effort to improve decision-making in the Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments (SUPPORT), focusing upon the impact of ADS on decision-making about resuscitation	Observational cohort study, RCT	Patients with severe illness. Intervention: n= 2652 Control: n= 2152.	Advanced stages of a diseases, such as COPD.	The intervention gave healthcare providers patient-specific prognoses for survival and function, and information about each patient's and surrogate's preferences, including whether the patient had written an advance directive. A nurse clinician specialist placed this information in the medical record or gave it to the attending physician. The nurse also facilitated communication among the patient, the surrogate, and the physician through education and empowering patients and family, arranging meetings, establishing telephone contact, and other techniques to promote decision making that reflected the patients' informed preferences.	*Patients' preferences for pattern of care and for ventilator use; *symptoms; *life sustaining interventions; *and survival prognoses.

10. Farquhar et al 2016 *United Kingdom* *BioMed Central*	A search to establish the effectiveness and cost effectiveness of the Breathlessness Intervention Service (BIS) in advanced non-malignant conditions.	Single-centre phase III fast-track single-blind mixed method RCT	Breathless patients with non-malignant conditions Intervention: n= 44 Control: n= 43 And their carers.	BIS referral criteria (diagnosed appropriately treated cause of breathlessness, were troubled by breathlessness in spite of optimization of underlying illness, and might benefit from a self-management programme)	Intervention group: BIS, multi-disciplinary complex intervention, underpinned by a palliative care approach, utilizing evidence-based non-pharmacological and pharmacological interventions to support patients. Control group: standard care	PO: £0–10 numeric rating scale for patient distress due to breathlessness at four weeks. SO: &Chronic Respiratory Questionnaire, &Hospital Anxiety and Depression Scale, & Client Service Receipt Inventory, &EQ-5D and topic-guided interviews.
11. Horton et al 2013 *Canada* *Journal of Palliative Medicine*	To determine the feasibility of: 1) implementing a customized home-based palliative care service for patients and caregivers living with advanced COPD and 2) measuring outcomes of providing such services.	Single-centre, prospective, cohort observational study	COPD patients: n=33 Caregivers: n=18	Severe COPD: Severe shortness of breath resulting in the patient being too breathless to leave the house; or breathlessness after dressing/undressing (MRC dyspnea score of 5); or the presence of chronic respiratory failure (PaCO2 > 45); or clinical signs of right heart failure OR Moderate COPD: Shortness of breath causing the patient to stop walking after 100 meters or a few minutes on the level (MRC score of 3–4) and at least one the following: BMI < 21; FEV1 < 30% predicted; one or more hospital admissions for acute exacerbation of COPD in the previous year.	Intervention group: COPD self-management educational program based on the Living Well with COPD program plus the eighth educational module on EOL care and decision making delivered in the patient's home over four to eight weeks. Comprehensive palliative care consultation within four weeks of completing educational component. Establish common medical chart in the home to facilitate coordinated care and sharing of information between various caregivers. Ongoing case management.	&Health-related quality of life (HRQoL), &caregiver burden symptom severity, *patient/ caregiver; satisfaction, utilization of acute care services, end-of-life (EOL) outcomes.

Author, Year, Country, Journal,	Main research question	Design	Participants (n)	Inclusion criteria	Components	Primary/secondary Outcomes (PO/SO)
B. Trial protocols						
1. Fernandez et al. 2016 Spain BioMed Central	To evaluate the efficacy of an educational intervention to train GPs in the right inhalation technique for the most commonly used inhalers.	Pragmatic cluster RCT	GPS Intervention: n=10 Control: n=10 COPD patients: n= 267 (10 patients/GP)	GPs: they must be doctors who care for patients included in the COPD PAI, use prescribed inhalation therapy and have consented to participate. Patients: COPD diagnosis, being treated at the primary care centers included in the trial, being prescribed inhalation therapy and consenting to participate in the trial by signing the informed consent form.	The first level is patients with COPD who agree to participate in the trial and receive the educational intervention from their GPs. The second level is GPs who are primary health care professionals and receive the educational intervention. Intervention (for patients & GPs) is one session of the educational intervention with a monitor given to GPs for training in the right inhalation technique. Control group: giving care as usual	PO: correct inhalation technique in patients. SO: functional status (spirometry) and quality of life.
2. Weber et al 2014 Switzerland BMC Palliative Care	To determine the effectiveness of the introduction of specialised palliative care on hospital, intensive care unit and emergency admissions of patients with severe and very severe COPD.	3 year single centre RCT	COPD patients Intervention: n=90 Control: n= 90	Patients with COPD defined according to GOLD criteria with a stage III or IV disease and/or long-term treatment with domiciliary oxygen and/or home mechanical ventilation and/or one or more hospital admissions in the previous year for an acute exacerbation.	Intervention group: early palliative care consultation is added to standard care: 1. symptom management 2. understanding of illness and coping with the disease 3. anticipation 4. relatives support 5. social support 6. spiritual support 7. coordination of the health professionals Control group: standard care only	PO: decrease in intensive care unit and emergency admissions. SO: mood and anxiety of patients, quality of life, use of antibiotics during the last three months, completion of advance directives, documented preferences for resuscitation, or nomination of surrogate decision maker will.
3. Bausewein et al 2012 United Kingdom BMC Pulmonary Medicine	To assess the effect of the Breathlessness Support Service (SSS), a multi- professional and inter- disciplinary outpatient service: on patients' mastery of breathlessness and other breathlessness measures; on	RCT (fast track), face-to-face interviews with patients for outcome measure	Patients (unknown n)	Suffering from breathlessness on exertion or at rest due to advanced disease such as cancer, COPD, CHF, interstitial lung disease, ILD or MND[6].	Intervention group: immediate access to BSS in addition to standard care. Control group: standard best practice and access to BSS after six weeks.	PO: patients' improvement of mastery of breathlessness after six weeks assessed Respiratory Disease Questionnaire (CRQ) SO: breathlessness severity, symptom burden, palliative care needs, service use, and

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[6] Chronic obstructive pulmonary disease (COPD), chronic heart failure (CHF), interstitial lung disease (ILD) or motor neurone disease (MND).

	physiological outcome measures; on caregiver burden; on patients' experiences. To compare NHS resource usage and costs in the two study arms and to explore patients' experiences using the BSS.			Underlying disease should be optimally medically managed. Patients must be able to engage with short term physiotherapy. If patients are suffering from acute exacerbations they are put on a waiting list for two weeks and are then entered into the trial.		respiratory measures (spirometry).
4. Bove et al 2015 Denmark BMJ Open	The efficacy of a minimal home-based psycho-educative intervention versus usual care for patients with COPD.	Single centre RCT	COPD patients (unknown n)	Patients with a confirmed COPD diagnosis, classified as category C or D (GOLD), HADS-A subscale score of ≥8 and were willing to participate and able to provide written consent.	Intervention group: psycho-educative session in the patient's home in combination with a telephone booster session. Patients learn to interpret and react to physical and psychological symptoms that are related to dyspnea and associated anxiety. Control group: usual care.	PO: patient reported anxiety as assessed by the HADS.
5. Duenk et al 2014 The Netherlands BMC Pulmonary Medicine	The primary objective is to assess the effects of proactive palliative care delivered by a specialised palliative care team on the wellbeing of patients with COPD with poor prognosis and their informal caregivers. The secondary objective is to assess survival rate in COPD patients with proactive palliative care integrated with standard care versus standard care only.	Prospective cluster controlled trial (6 hospitals) with pre- and post-test.	COPD patients and main informal caregivers	Inclusion of hospitals: if there is a palliative care team. Inclusion of patients: in hospitalisation for an acute exacerbation and ≥18 years old.	Intervention group: members of the specialised palliative care teams will receive a special training in the provision of proactive palliative care for patients with COPD. Patients in the intervention condition who are assigned for proactive palliative care will meet with a member of the specialised palliative care team within one week after enrollment and at least monthly thereafter in the outpatients setting for at least one year or until death. The main informal caregiver of the patient will be asked to be present at those meetings Control group: standard care for COPD patients given by their treating lung specialists.	PO: change in quality of life (St George Respiratory Questionnaire (SGRQ) of the patient 3 months after inclusion. SO: patient-related a) change in quality of life (SGRQ) of the patient 6, 9 and 12 months after inclusion; b) change in quality of life at the end of life (McGill QOL) 3, 6, 9 and 12 months after inclusion; c) change in psychological wellbeing (HADS) 3, 6, 9 and 12 months after inclusion; d) change in illness understanding 3, 6, 9 and 12 months after inclusion; e) number and length of unexpected hospital admissions; f) number and length of unexpected ICU admissions; g) are the choices of advance care planning documented in the

						medical file? (when yes/when no); h) place of death (ICU/hospital/hospice/nursing home/at home); i) is preferred place of death known? (when yes/when no); j) has this wish come true? (when yes/when no); k) length of survival of COPD patients with proactive palliative care integrated with standard care versus standard care only. SO: informal caregiver-related: a) change in informal caregiver burden (SPPIC) 3, 6, 9 and 12 months after inclusion; b) change in psychological wellbeing (HADS) at 3, 6, 9 and 12 months after inclusion; c) change in illness understanding at 3, 6, 9 and 12 months after inclusion.
6. Houben et al 2014 The Netherlands BMJ Open	To explore whether and to what extent structured advance care planning by a trained nurse, in collaboration with the chest physician, can improve outcomes in Dutch patients with COPD and their family.	A multicentre cluster RCT	Patients with severe to very severe COPD.	1: a diagnosis of severe-to-very severe COPD (GOLD grade III or IV); 2: Discharged after hospital admission for a COPD exacerbation; 3: at least one family member, who will participate in the study.	Intervention group: structured advance care planning: reflection on patient's goals, values and beliefs. Understanding the current and future medical situation, possible treatments and outcomes. Understanding life-sustaining treatments. Determining wishes regarding the current and future care. Encouraging discussions on advance care planning with healthcare providers and loved ones. Appointment of a surrogate decision-maker Control group: standard care	PO: Quality of communication about end-of-life care; (HADS) For patients who died during the study period: quality of end-of-life care and quality of death and dying. SO: concordance between patient's preferences for end of-life care (patient's preferences for CPR and mechanical ventilation; end-of-life preferences interview and received end-of-life care); psychological distress in bereaved family members of deceased patients with COPD; Inventory of Complicated Grief.

Appendix 4 Overview of barriers and facilitators on inclusion criteria and components from the expert consultations

COMPONENTS	*FACILITATORS**	*BARRIERS**
Advance Care Planning	**ACP and palliative care (PC)** ➢ If you meet the criteria for ACP, you meet the criteria for (early) PC too (20, 22) ➢ ACP is the perfect facilitator to start with (early) palliative care, beyond the terminal phase (18) ➢ ACP should be a part of PC and curative care, and can integrate both (4) ➢ You can start ACP independently from PC (13) **Professional caregivers** ➢ Education/training about ACP for professional caregivers can help them start the conversations (3, 4, 12, 15, 19) ➢ Training for professional caregivers in recognizing PC needs is useful for ACP (20) ➢ GPs are well positioned to start ACP and then refer the patient to the PC team (3, 4, 5, 13, 17, 19, 22) ➢ If the professional caregiver is feeling comfortable talking about ACP and PC, the patient is too (17) ➢ Pulmonologists should be involved in ACP conversations too (4, 13) ➢ An ACP-educator (e.g. a nurse) can start ACP conversations with every patient who gets diagnosed with COPD(12) **Content and practical issues related to ACP** ➢ ACP should be an ongoing, gradual process, starting early in the disease trajectory (4, 13, 15, 17) ➢ ACP should be started independently of the disease trajectory, as COPD is unpredictable (4) ➢ It is better to structure ACP and embed it in the current care for better applicability (13, 20) ➢ ACP is only useful when taking into account the specific situation of each patient (4, 15) ➢ ACP is good to start in the non-terminal phase for improved quality of life (1, 2, 3, 12) ➢ After an hospital admission is a good moment to start ACP (3, 17, 19, 22) ➢ Start the conversation with the patient by explaining clearly that this does not mean they will die within a month (19) **Patient** ➢ Especially people with a weaker social context and support benefit from planning ahead (22)	**Professional caregiver** ➢ It is not easy for professional caregivers to do ACP as they lack skills (12, 21) ➢ It is time consuming for professional caregivers (5) ➢ It is not well included in the education programs of medicine in Belgium (3) ➢ It is an optional course for GPs in Belgium, but not obliged (3) ➢ Pulmonologists do not have the communication skills to do ACP (15) ➢ GPs lack communication skills to do ACP (20) **Content and practical issues related to ACP** ➢ Sometimes it is more direct planning instead of advance planning, if the situation requires it (22) ➢ Unclear when to introduce ACP because of the unclear disease trajectory of COPD(3, 13) ➢ When the focus is on documentation instead of the conversation, it becomes problematic (13) ➢ It became a key performance indicator for professional caregivers, so professional caregivers started to do ACP too soon and incautious, scaring patients (21) **Patient** ➢ If a patient is in a stable phase, it is hard to start ACP conversations as they do not want to think/talk about the future at that moment (3, 11) ➢ Family and patient do not understand the risk of dying (12)

	➢ Guidance for patient and professional caregiver about future issues and care needs (4, 11, 15, 19, 22) ➢ It is a good way to provide control for the patient about future situations (15, 17) ➢ It reduces anxiety for the patient (5)	
Involvement of loved ones	**Loved ones in the (PC) care for COPD patients** ➢ Because they are involved in the decision-making processes and will help making better decisions for the patient if they receive the information too (22) ➢ People are more concerned about the impact of decisions on the family, rather than the content of the decision (21, 22) ➢ If loved ones are not convinced about a care option for the patient, they will not allow it (21) ➢ Taking care for a COPD patient can be a burden for loved ones, as they experience e.g. isolation, pressure to look after them 24/7. Better involvement of loved one can help finding relief for those burdens(16) ➢ In between a moderate COPD and a very terminal COPD, early PC could be really helpful for the patients and whole family, as it is a very tough, long period to cope with (16) ➢ PC in the form of involvement of loved ones would make the loved ones realize that COPD is life-threatening, and would thus make the loved ones more supportive towards the patient (12, 9) **Content** ➢ Mapping the family structure and involving the loved ones in order to provide the best PC, adjusted to the specific situation (15) ➢ Loved ones can discuss together with the patient the best care options for both of them (15)	➢ Partners often do not realize the seriousness of the disease and force the patient to do things they are not able to do anymore (9) ➢ Loved ones sometimes continue smoking despite the disease of their partner (9, 22) ➢ The longer the disease takes, the more loved ones stop their involvement eventually (16)
Knowledge and disease-insight of the patient	**Professional caregiver** ➢ A lot depends on the way information is given (22) ➢ GPs should inform the patient before they are introduced to the PC team (1 & 2) **Content and practical issues** ➢ Repeatedly explain what is said over an extended period, so patients remember, realize and understand it (15) ➢ Group meetings with other (severely-ill) COPD patients to talk about their disease and the problems that can arise (15, 22) ➢ Info brochures with information about COPD (10) **Knowledge, disease insight and PC**	**Content and practical issues** ➢ Info-leaflets will not be read by patients as they are not used to it (in Spain) (15) ➢ Knowledge giving is more part of prevention strategy instead as a part of PC (15) **Patient** ➢ Patients often have a low disease insight, which makes it harder to explain their situation (10)

	➢ The content of PC can be explaining the patient that COPD is a terminal illness and which consequences this can have (11, 15, 17) ➢ Explaining that COPD is a chronic, unstable illness, which is the trigger to start talking about the future (15) ➢ Nurses can explain what PC is to the patients, with a focus on giving information (10) **Patients** ➢ Patients need information (18) ➢ Patients want information (15, 22) ➢ If the patient understands its illness, they perform behavior which increases quality of life (f.ex. quit smoking) (9)	
Pulmonary rehabilitation (PR)	**Content** ➢ Replacing old therapies for respiratory therapy in the home care (9) ➢ Less use of cortisone as it is bad for the muscles (3, 9) ➢ Start rehabilitation on the moment of diagnosis (9) ➢ Preventive work (9) ➢ Focus on possible activities of daily living, degree of activity (9, 17, 18) ➢ Focus on muscle strengthening of the legs or other parts of the body which improves metabolism of the oxygen, and makes the patient use oxygen more efficiently (1, 2, 3, 4, 18) ➢ Focus on managing the condition (18) ➢ Focus on body weight. The more weight you carry, the less easy to breathe (18) ➢ Walking aids to improve stability encourages to be active and puts patients in a better position to breathe(18) ➢ Blowing cool air on the face with a hand-held fan, improves the sensation of breathlessness and reduces panic as the nerve system is related to breathing center in the brain (18) ➢ Teach patients breathing exercises, f.ex. to breathe out (3, 18, 21) ➢ Giving very advanced patients little electroshocks to strengthen the legs if they cannot do anything else any more (18) ➢ Relaxation exercises (1, 2) ➢ Patient oriented, focused on the specific situation of each patient (21) ➢ Teach patients to be more active (21) **Pulmonary rehabilitation (PR) and (early) PC** ➢ If you do PR, you should be in a PC program at the same time, as there is clearly something very wrong with the patient (22)	**Content** ➢ Because PR doesn't involve the loved ones, they will ultimately fail as a part of early PC, because you can't ignore the family carers (21) ➢ Sometimes PR is disease focused instead of patient focused, with general directives for all patients with the same disease, which has the risk of not treating the patient according to its own personal situation (21) **Patients** ➢ Patients are used to their own physiotherapist and do not want to change that, even if they give the wrong therapy (9) ➢ Patients are not willing to drive an extra mile for a better home physiotherapist (9) ➢ If patients are too ill, they cannot or do not want to do any exercises or therapy anymore (18 21) ➢ Patients do not understand the word rehabilitation (18) ➢ If the family sees the patient being very breathless because of the exercises, they will stop this therapy for the patient as they do not want to see him/her suffering (21) **Professional Caregivers** ➢ Only some physiotherapists have the knowledge of giving correct PR (9) ➢ There might be insufficient focus on PR in graduate school for physiotherapy (9) **Pulmonary rehabilitation and (early) PC** ➢ It is hard to predict when somebody should start with PR in early PC, because of the unclear disease trajectory (9) ➢ There is insufficient funding to integrate PR in PC (17)

	➢ You can do PR as a part of PC until the patient dies, if you adapt the impact of the therapy. Patients benefit from the smallest improvements in f.ex. breathlessness, level of activity (3, 18) ➢ It would have a big and positive impact on the patient if PR would begin earlier in the PC (3, 9, 21) ➢ PR should be worked out better in the PC home care, f.ex. home visits by physiotherapists and/or occupational therapists, otherwise the patient has to come each time to the hospital where PR is better (3, 18) ➢ PR as a part of PC increases survival, gives a better quality of life, reduces symptoms and is effective as the patient can manage their own deterioration better(17, 18, 21) ➢ PR can stabilize the patient in advance stages instead of further deterioration, which is an improvement (21)	
Psychosocial support	**Professional and informal caregivers** ➢ If volunteers will do the social support, they need some education on COPD and PC in case something would happen during the visits (16) ➢ Volunteers can take over some tasks of the loved ones to continue the social support for the patient while relieving the loved ones from their care tasks (1, 2, 16) ➢ Psychologists as a part of the palliative care team to help the patient with cognitive or behavioral approaches (14, 21) ➢ Social workers as a part of the palliative care team to map the family structures, the main care, needs (14, 15) ➢ Palliative nurses can take up the tasks of psychosocial support (1, 2) ➢ It is better for the patient to stay at home, so the home network should be enlarged, while taking care of the family, assuring the patient they are looked after for (15) **Content** ➢ Through classifications (e.g. ICF) is it possible to map the psychological and social needs of a PC patient (6) ➢ Regular visits until the patients dies by volunteers (16) ➢ Talking about basic topics like 'how they are coping' helps the patient to feel better (16) ➢ Visits to the patient first one time in three months, but later at least every month, maybe every two weeks, depending on the situation of the patient (16) ➢ For an intervention it might be better to have a strict criteria, let's say one visit per month (16)	**Psychosocial support and (early) PC** ➢ Current programs with support included in PC fail to reach the goal of aiding the patient (14) ➢ It is good to start with the support as a part of early PC, but the biggest problem is that you don't know how long the support will take (16) ➢ If you start too early with the support as a part of early PC, it is not good. It is better to start when the patient is really advanced, when they can clearly understand why their functioning is very low (15) ➢ If support would be needed during early PC, it would be because of the personality of the patient (15) ➢ Psychosocial needs are not the big problem for these patients, it is very process-oriented and people seek solutions for it, e.g. not going by bike, but with the car(3)

	➢ A relaxation CD to help the patient become calm (18) ➢ Day programs with a fun and social theme, where the patient can participate in, for half a day or a full day (17) ➢ Reduction of anxiety, as this is the main burden for the patient (5) ➢ Talking/peer sessions for patients who suffer from f. ex oxygen dependency, with the biggest importance of the session is being together (10) **Patients characteristics that indicate support is needed** ➢ One of the most important things for the patient, more than medical care support (14, 16) ➢ Patients are afraid to leave their houses, and thus stay at home, alone (1, 2, 16) ➢ Even during stable periods without exacerbations, they need the support (17) ➢ Patients still lack sufficient psychosocial support , as the broader family do not know how to handle the sick family member (16) ➢ Patients have the feeling their social circle does not understand themselves and they become isolated as a consequence (16) ➢ The longer the diseases take, the less involved the family gets as it takes too long to cope with, while the patient needs them the most at those times (16) ➢ The patient is often feeling lonely when they have no close relatives and just needs company (1, 2, 16, 17) ➢ Advanced COPD patients are often between 50 and 70, most of them still have (many) friends, they just do not see them (16) **Psychosocial support and (early) PC** ➢ Early PC is the perfect timing to start up the support (16) ➢ The support, where caregivers are asking how the mood of the patient is, should be a part of the whole trajectory of the disease, starting from diagnosis, in curative care and continuing during (early) PC (17, 21)	
Self-management of patients	**Content** ➢ Developing tools (e.g. a mantra, online tools) to manage their breathe (18) ➢ Developing an online tool to help patients talk to their family and going through different situations (18) ➢ Learning ways to let the patient cope with their exacerbations, f.ex. self-administration of medicines, relaxation exercises (1 & 2) ➢ Self-management of breathlessness, as being out of breathe is the main reason why people run to the hospital (5, 22)	**Patients** ➢ Low-educated people are not used to the concept of self-control. They do not need self-control in the end stages of their lives/diseases, they just want to be healthy (15) ➢ Contrary, high educated people can have (the feeling of) self-control in every stage of the disease, even if they have severe dyspnea (15) ➢ Self-management is more important in the earlier stages of the disease (15)

	➢ Info brochure for self-administering morphine (10) ➢ Group meetings with other COPD patients to discuss self-help or self-management issues, combined with a fun and social factor (15, 17) ➢ Group activities gives patients a better self-esteem as they feel they could do something fun for themselves (21) ➢ Holistic self-management of the disease (5) **Patients** ➢ If a patient can do more thing on their own, it decreases anxiety (21)	➢ Patients need help with everything, from washing to putting on clothes, to do their hair etc, so they can never reach (full) self-management (16)
Symptom control	**Content** ➢ Small doses of morphine for (subjective sense of) relief in breathlessness (1, 2, 3, 4, 10, 15, 17) ➢ Short periods of medicines seem to work better for the patient than longer periods, as short periods of on-and-off medicines gives them the subjective feeling of control (17) ➢ Control of breathlessness (18, 21) ➢ Rescue teams doing acute symptom control in the home setting can reduce anxiety for the patients (11, 17) ➢ Broad symptom control and full anamnesis focused on the patient itself (10, 18) ➢ You need the same symptom control as used in hospital, but adapted to the home setting, f.ex. a mobile RT-BiPAP (17) ➢ Assessment of emotional aspects of the patient and the family (15) ➢ Using ESAS systematically during the first visit of the PC team (10) **Symptom control and (early) PC** ➢ A patient with bad dyspnea or who cannot sleep at night cannot talk about the future too. So the first step is always symptom control (15, 18, 21) ➢ Starting morphine earlier in the disease trajectory as a part of early PC makes it possible to adjust the doses better, as palliative nurses are more aware of the right amounts (3, 11) ➢ After a rescue team does symptom control and decides whether a patient can stay at home or needs to go to the hospital, the PC team can start doing the further care for the patient (11, 17) ➢ If symptom management happens before PC, there is a more clear view if the patient is in needs for PC or not (15) ➢ Introducing PC is dependent on symptoms, different symptoms ask for different PC (10)	

	➢ Calling the PC teams ‘symptom management experts’ or ‘symptom doctors’ and focusing the care on symptom management helps the patient to accept PC more (10, 12)	
INCLUSION CRITERIA	*FACILITATORS**	*BARRIERS**
After admission in hospital for exacerbation	➢ An admission is a good starting point to ask the patient what they want to do if it happens again as they realize more the seriousness of their situation after this event (14, 20, 21, 22, 17) ➢ After an admission there is quite high mortality in the following 12 months (22) ➢ After second (or more) admission for exacerbation, as they realize more the seriousness of their situation after this (12, 17, 19, 21, 22) ➢ After at least two admissions in the hospital during the last months, for eight months survival(14, 16) ➢ It depends, if you do not want your patient to die during the intervention, you might need to go for inclusion after the first admission (22)	➢ After two or three admissions in the last month, the mortality rate of a patient is around six months (22) ➢ Some patients can only start to talk about PC or further care after the 12th exacerbation, so it depends on the personality of the patient (4)
Functioning of the patient	➢ Declining functionality in the last months (14) ➢ Include the patient, based on its personal level of functioning (16) ➢ If the patient becomes frail (22) ➢ Using the CAT-questionnaire (10) ➢ Using depression scales for inclusion (10) ➢ MMSE score (mini mental state examination) (10)	
Depending on lung function test and prognosis tests	➢ BODE-index 7 for eight months survival(14) ➢ GOLD IV for eight months survival (14) ➢ Results of a full quality of life assessment will indicate whether a patient is eligible for PC or not (16) ➢ Walking speed is a good predictor of illness (18) ➢ The six minute walking test with 30, 60, maybe up to 100 meter in 6 minutes is really slow and shows that the patient is in a bad state (18) ➢ If lung function tests prove the patient is in a severe stage of the disease (22) ➢ Prognosis tests with general criteria, not seen from the individual, as the intervention is limited in time for inclusion of patients (22) ➢ The NNCSI, a care standard developed in the Netherlands which replaces the GOLD criteria (19) ➢ There is nothing good enough, but BODE index can help the caregiver to see if there is something they can do for the patient (15)	➢ Same results on FEV1 have different impacts on patients (9) ➢ Depending on the social context of the patient, there are different implications for the patient (19) ➢ GOLD III or IV indicate a worsening of symptoms and more exacerbations, but that does not mean patients become in need of PC (4) ➢ A patient with GOLD III can be kept alive by PC teams, but not by a pulmonologist (19) ➢ BODE index 5 patients do not have (sufficient) symptoms to start PC (15) ➢ BODE index more than 5 is too late, depending on the patient they can have 6 to 12 months survival (15) ➢ SPICT-tools and surprise questions are not useful as COPD is too unpredictable (16, 20)

	➢ The SPICT or the NECPAL let the caregivers think about if the patient will die within the following year (4) ➢ Combination of GOLD criteria and diffusion test (12)	
Social context		➢ Difficult predictor or PC needs (16)
Opinion of the caregiver	➢ Why the caregiver thinks the patient should not be referred to hospital anymore (7)	
Being housebound	➢ The moment the patient is housebound, they can have their first PC consult, as they are suffering in any case (12, 14, 16)	➢ When housebound, it is too late to start early PC (22)
Oxygen dependency	➢ If a patient becomes oxygen dependent (12, 22)	

*All numbers indicate which expert (who has received a number, see table 1 in manuscript) mentioned this barrier or facilitator.

Appendix 5 Information leaflets from Living Well With COPD


Living well with... COPD

Chronic Obstructive Pulmonary Disease

Een leermethode voor patiënten en hun familie

Voorkomen van en omgaan met uw klachten

- Begrijpen van het zelfreinigende mechanisme van uw longen
- COPD: belangrijkste oorzaken, verschijnselen en klachten
- Vermijden van factoren die uw klachten verergeren
- Medicijnen en inhalatoren

versie 1.3

Dit werkboek is van:


Welkom bij 'Voorkomen van en omgaan met uw klachten' uit de leermethode 'Living Well with COPD'

Het optreden van kortademigheid, hoesten, piepen op de borst en angst zijn vroeg of laat klachten die kunnen optreden bij de ziekte COPD. Door te leren hoe u uw klachten kunt voorkomen en onder controle kunt houden, zult u een beter en actiever leven kunnen leiden.

In deze module zult u leren over:

✓ het zelfreinigende mechanisme van uw longen
✓ de belangrijkste oorzaak van COPD
✓ COPD (chronische bronchitis en longemfyseem) en bijbehorende klachten
✓ omgevingsfactoren die uw klachten kunnen verergeren, hoe u ze kunt vermijden of blootstelling eraan kunt verminderen
✓ medicijnen en hoe belangrijk het is om ze regelmatig te gebruiken zoals is voorgeschreven
✓ het gebruik van inhalatoren en een goede inhalatietechniek

3


Voorkomen van en omgaan met uw klachten

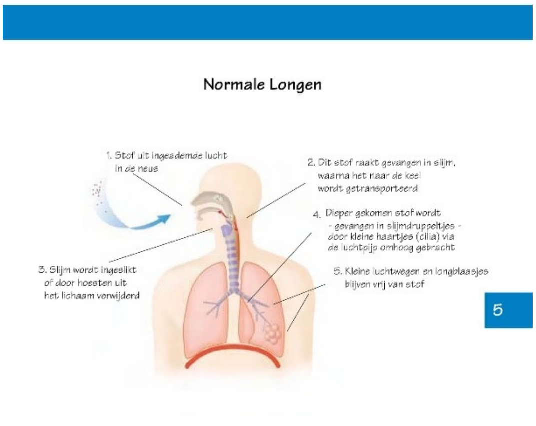
Goed leven met COPD betekent het voorkómen van verslechtering van uw gezondheid, bijvoorbeeld door de klachten van uw COPD te herkennen. Dat betekent dat u blootstelling aan factoren die uw klachten verergeren vermijdt of vermindert, dat u weet hoe uw COPD-medicijnen werken, hoe u ze moet innemen zoals is voorgeschreven en wat de goede inhalatietechniek is.

De lucht die we inademen zit vol met stof en verontreinigingen. Gelukkig heeft moeder natuur ons voorzien van een efficiënt reinigingssysteem voor onze luchtwegen.

Bij iedere ademhaling wordt er lucht in uw longen gezogen met daarin stof en verontreinigingen.

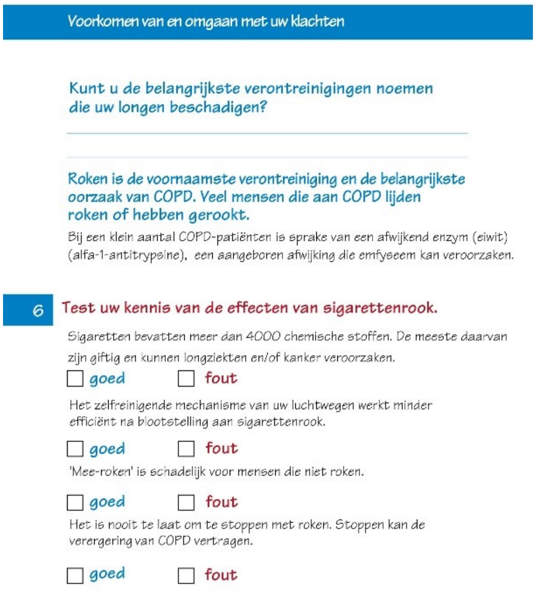
Deze kleine deeltjes worden in uw neus opgevangen. De afscheiding wordt door kleine haartjes, die trilharen (cilia) worden genoemd, omhoog naar uw keel getransporteerd. Als het slijm eenmaal in uw keel is, wordt het doorgeslikt of uit het lichaam verwijderd door hoesten. Dit voorkomt dat deeltjes de onderste luchtwegen bereiken en daar schade aanrichten aan uw kleine luchtwegen (bronchiën) en longblaasjes.

4


Normale Longen

1. Stof uit ingeademde lucht in de neus
2. Dit stof raakt gevangen in slijm, waarna het naar de keel wordt getransporteerd
3. Slijm wordt ingeslikt of door hoesten uit het lichaam verwijderd
4. Dieper gekomen stof wordt - gevangen in slijmdruppeltjes - door kleine haartjes (cilia) via de luchtpijp omhoog gebracht
5. Kleine luchtwegen en longblaasjes blijven vrij van stof

5



Voorkomen van en omgaan met uw klachten

Kunt u de belangrijkste verontreinigingen noemen die uw longen beschadigen?

Roken is de voornaamste verontreiniging en de belangrijkste oorzaak van COPD. Veel mensen die aan COPD lijden roken of hebben gerookt.

Bij een klein aantal COPD-patiënten is sprake van een afwijkend enzym (eiwit) (alfa-1-antitrypsine), een aangeboren afwijking die emfyseem kan veroorzaken.

6 **Test uw kennis van de effecten van sigarettenrook.**

Sigaretten bevatten meer dan 4000 chemische stoffen. De meeste daarvan zijn giftig en kunnen longziekten en/of kanker veroorzaken.

☐ goed ☐ fout

Het zelfreinigende mechanisme van uw luchtwegen werkt minder efficiënt na blootstelling aan sigarettenrook.

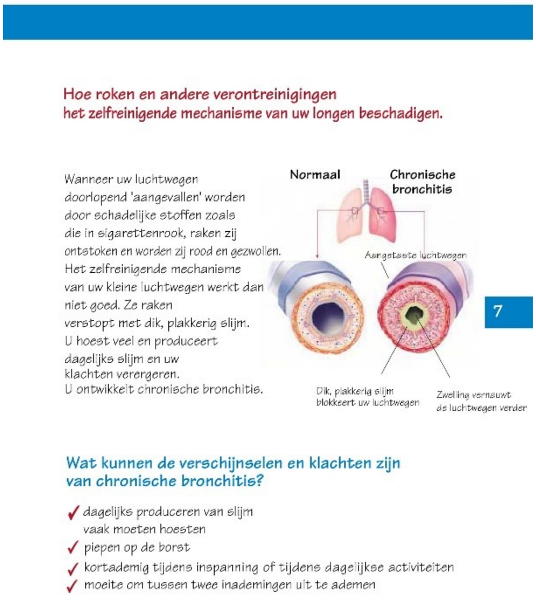
☐ goed ☐ fout

'Mee-roken' is schadelijk voor mensen die niet roken.

☐ goed ☐ fout

Het is nooit te laat om te stoppen met roken. Stoppen kan de verergering van COPD vertragen.

☐ goed ☐ fout



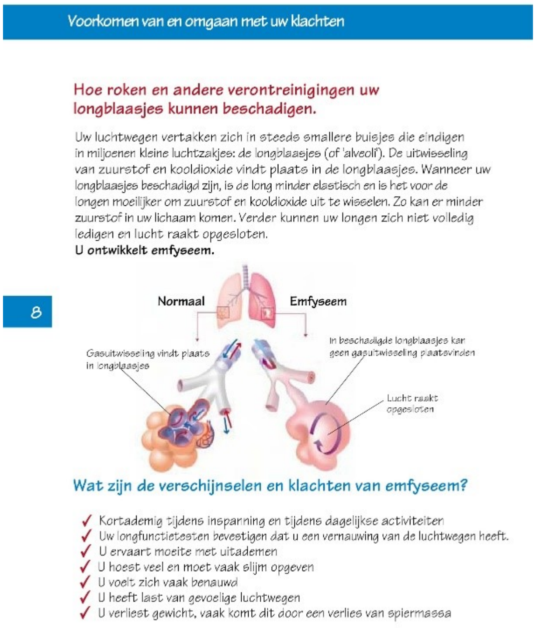
Hoe roken en andere verontreinigingen het zelfreinigende mechanisme van uw longen beschadigen.

Wanneer uw luchtwegen doorlopend 'aangevallen' worden door schadelijke stoffen zoals die in sigarettenrook, raken zij ontstoken en worden zij rood en gezwollen. Het zelfreinigende mechanisme van uw kleine luchtwegen werkt dan niet goed. Ze raken verstopt met dik, plakkerig slijm. U hoest veel en produceert dagelijks slijm en uw klachten verergeren.
U ontwikkelt chronische bronchitis.

7

Wat kunnen de verschijnselen en klachten zijn van chronische bronchitis?

- ✓ dagelijks produceren van slijm
  vaak moeten hoesten
- ✓ piepen op de borst
- ✓ kortademig tijdens inspanning of tijdens dagelijkse activiteiten
- ✓ moeite om tussen twee inademingen uit te ademen



Voorkomen van en omgaan met uw klachten

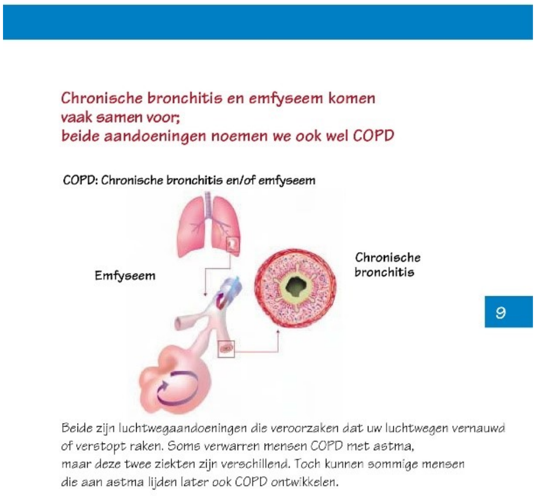
Hoe roken en andere verontreinigingen uw longblaasjes kunnen beschadigen.

Uw luchtwegen vertakken zich in steeds smallere buisjes die eindigen in miljoenen kleine luchtzakjes: de longblaasjes (of 'alveoli'). De uitwisseling van zuurstof en kooldioxide vindt plaats in de longblaasjes. Wanneer uw longblaasjes beschadigd zijn, is de long minder elastisch en is het voor de longen moeilijker om zuurstof en kooldioxide uit te wisselen. Zo kan er minder zuurstof in uw lichaam komen. Verder kunnen uw longen zich niet volledig ledigen en lucht raakt opgesloten.
U ontwikkelt emfyseem.

8

Wat zijn de verschijnselen en klachten van emfyseem?

- ✓ Kortademig tijdens inspanning en tijdens dagelijkse activiteiten
- ✓ Uw longfunctietesten bevestigen dat u een vernauwing van de luchtwegen heeft.
- ✓ U ervaart moeite met uitademen
- ✓ U hoest veel en moet vaak slijm opgeven
- ✓ U voelt zich vaak benauwd
- ✓ U heeft last van gevoelige luchtwegen
- ✓ U verliest gewicht, vaak komt dit door een verlies van spiermassa

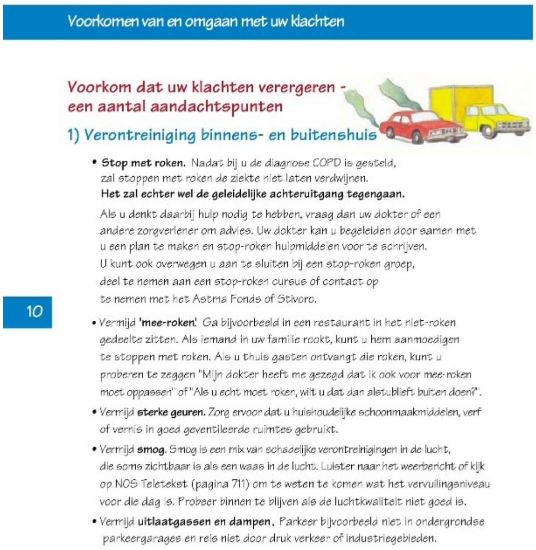


Chronische bronchitis en emfyseem komen vaak samen voor; beide aandoeningen noemen we ook wel COPD

COPD: Chronische bronchitis en/of emfyseem

9

Beide zijn luchtwegaandoeningen die veroorzaken dat uw luchtwegen vernauwd of verstopt raken. Soms verwarren mensen COPD met astma, maar deze twee ziekten zijn verschillend. Toch kunnen sommige mensen die aan astma lijden later ook COPD ontwikkelen.



Voorkom dat uw klachten verergeren - een aantal aandachtspunten

1) Verontreiniging binnens- en buitenshuis

- **Stop met roken.** Nadat bij u de diagnose COPD is gesteld, zal stoppen met roken de ziekte niet laten verdwijnen.
  Het zal echter wel de geleidelijke achteruitgang tegengaan.

  Als u denkt daarbij hulp nodig te hebben, vraag dan uw dokter of een andere zorgverlener om advies. Uw dokter kan u begeleiden door samen met u een plan te maken en stop-roken hulpmiddelen voor te schrijven. U kunt ook overwegen u aan te sluiten bij een stop-roken groep, deel te nemen aan een stop-roken cursus of contact op te nemen met het Astma Fonds of Stivoro.

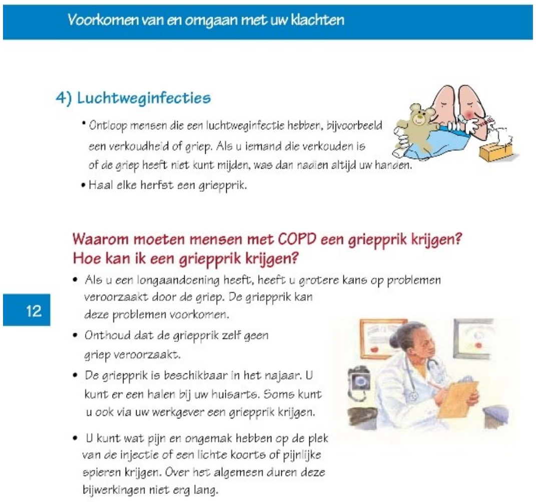
- Vermijd **'mee-roken'.** Ga bijvoorbeeld in een restaurant in het niet-roken gedeelte zitten. Als iemand in uw familie rookt, kunt u hem aanmoedigen te stoppen met roken. Als u thuis gasten ontvangt die roken, kunt u proberen te zeggen "Mijn dokter heeft me gezegd dat ik ook voor mee-roken moet oppassen" of "Als u echt moet roken, wilt u dat dan alstublieft buiten doen?".
- Vermijd **sterke geuren.** Zorg ervoor dat u huishoudelijke schoonmaakmiddelen, verf of vernis in goed geventileerde ruimtes gebruikt.
- Vermijd **smog.** Smog is een mix van schadelijke verontreinigingen in de lucht, die soms zichtbaar is als een waas in de lucht. Luister naar het weerbericht of kijk op NOS Teletekst (pagina 711) om te weten te komen wat het vervuilingsniveau voor die dag is. Probeer binnen te blijven als de luchtkwaliteit niet goed is.
- Vermijd **uitlaatgassen en dampen.** Parkeer bijvoorbeeld niet in ondergrondse parkeergarages en reis niet door druk verkeer of industriegebieden.

2) Emoties

- Moeten omgaan met de veranderingen die COPD in uw leven teweeg brengt, kan stress geven. Als u uw zorgen echter voor u houdt, zult u meer gespannen en angstiger zijn. Als u angstig bent, praat dan met uw vrienden en familieleden over uw gevoelens. Vertel hen de dingen die u dwars zitten en stel manieren voor waarop zij u kunnen helpen.
- Leer uw stressniveau en angstniveau te verminderen door kalm te blijven en uw ademhalings- en ontspanningstechnieken toe te passen.

3) Plotselinge veranderingen in temperatuur

- Vermijd extreme temperaturen. Bedek uw neus met een sjaal als het buiten erg koud of windering is. Probeer bij vochtige omstandigheden in een ruimte met airconditioning te blijven. Airconditioning kan het ademhalen makkelijker maken.

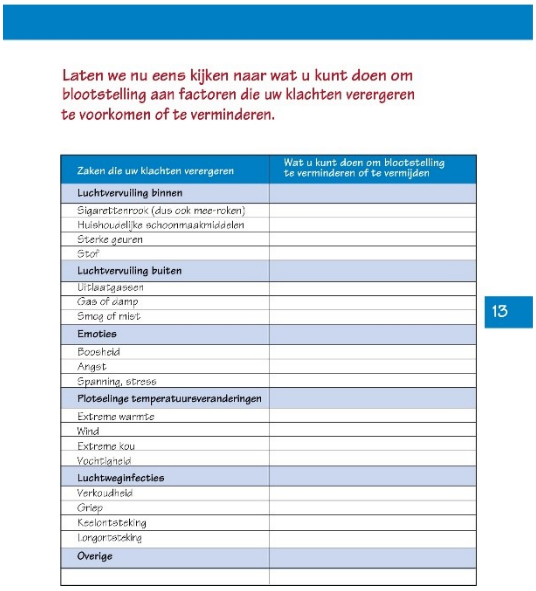


4) Luchtweginfecties

- Ontloop mensen die een luchtweginfectie hebben, bijvoorbeeld een verkoudheid of griep. Als u iemand die verkouden is of de griep heeft niet kunt mijden, was dan nadien altijd uw handen.
- Haal elke herfst een griepprik.

Waarom moeten mensen met COPD een griepprik krijgen? Hoe kan ik een griepprik krijgen?

- Als u een longaandoening heeft, heeft u grotere kans op problemen veroorzaakt door de griep. De griepprik kan deze problemen voorkomen.
- Onthoud dat de griepprik zelf geen griep veroorzaakt.
- De griepprik is beschikbaar in het najaar. U kunt er een halen bij uw huisarts. Soms kunt u ook via uw werkgever een griepprik krijgen.
- U kunt wat pijn en ongemak hebben op de plek van de injectie of een lichte koorts of pijnlijke spieren krijgen. Over het algemeen duren deze bijwerkingen niet erg lang.



Laten we nu eens kijken naar wat u kunt doen om blootstelling aan factoren die uw klachten verergeren te voorkomen of te verminderen.

Zaken die uw klachten verergeren	Wat u kunt doen om blootstelling te verminderen of te vermijden
Luchtvervuiling binnen	
Sigarettenrook (dus ook mee-roken)	
Huishoudelijke schoonmaakmiddelen	
Sterke geuren	
Stof	
Luchtvervuiling buiten	
Uitlaatgassen	
Gas of damp	
Smog of mist	
Emoties	
Boosheid	
Angst	
Spanning, stress	
Plotselinge temperatuursveranderingen	
Extreme warmte	
Wind	
Extreme kou	
Vochtigheid	
Luchtweginfecties	
Verkoudheid	
Griep	
Keelontsteking	
Longontsteking	
Overige	

Voorkomen van en omgaan met uw klachten

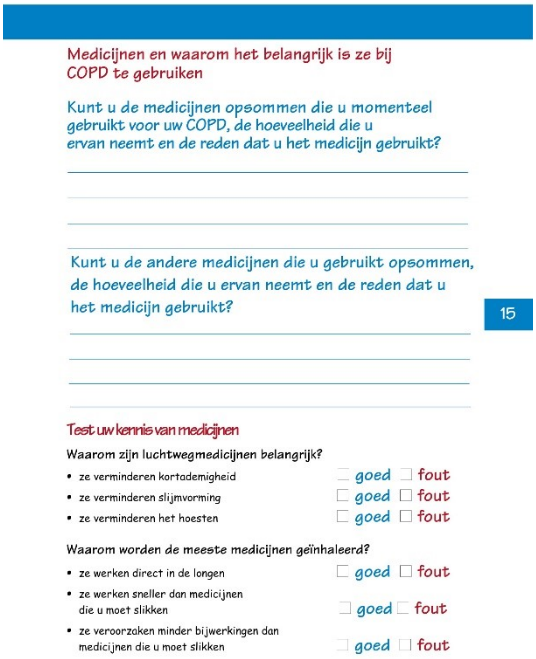
Het vermijden of verminderen van blootstelling aan zaken die uw klachten verergeren is maar een deel van het omgaan met uw COPD. Een ander, heel belangrijk deel, is dat u uw medicijnen regelmatig en met de juiste techniek inneemt als onderdeel van uw dagelijkse routine.

Medicijnen kunnen COPD niet genezen, maar ze kunnen wel helpen om uw klachten te verlichten. Hierdoor zult u zich beter voelen en een betere kwaliteit van leven hebben.

U moet het volgende weten over uw medicijnen:

- de merknaam van elk medicijn dat u gebruikt;
- wat uw medicijnen doen;
- de dosis die u moet nemen;
- wanneer u uw medicijnen moet nemen;
- hoe u uw medicijnen op de goede manier kunt innemen;
- voorzorgsmaatregelen bij medicijngebruik en mogelijke bijwerkingen.

14



Medicijnen en waarom het belangrijk is ze bij COPD te gebruiken

Kunt u de medicijnen opsommen die u momenteel gebruikt voor uw COPD, de hoeveelheid die u ervan neemt en de reden dat u het medicijn gebruikt?

Kunt u de andere medicijnen die u gebruikt opsommen, de hoeveelheid die u ervan neemt en de reden dat u het medicijn gebruikt?

15

Test uw kennis van medicijnen

Waarom zijn luchtwegmedicijnen belangrijk?

- ze verminderen kortademigheid ☐ goed ☐ fout
- ze verminderen slijmvorming ☐ goed ☐ fout
- ze verminderen het hoesten ☐ goed ☐ fout

Waarom worden de meeste medicijnen geïnhaleerd?

- ze werken direct in de longen ☐ goed ☐ fout
- ze werken sneller dan medicijnen die u moet slikken ☐ goed ☐ fout
- ze veroorzaken minder bijwerkingen dan medicijnen die u moet slikken ☐ goed ☐ fout

Voorkomen van en omgaan met uw klachten

Medicijnen zijn er in verschillende categorieën

Meestal is er meer dan één medicijn nodig om uw luchtwegen open te houden. Bij COPD zijn luchtwegverwijders de belangrijkste medicijnen die dagelijks worden gebruikt. Er kunnen echter ook andere soorten medicijnen nodig zijn om andere symptomen te verminderen.

De volgende categorieën medicijnen zullen in de komende pagina's uitvoerig worden beschreven:

A. Luchtwegverwijders – de belangrijkste medicijnen voor de behandeling van COPD, omdat ze helpen om de luchtwegen open te zetten en kortademigheid door inspanning te verminderen.

B. Ontstekingsremmers – ondersteunen de behandeling van de zwelling van de luchtwegen en kunnen opflakkeringen (exacerbaties) helpen voorkomen. Ontstekingsremmers kunnen in combinatie met luchtwegverwijders worden gebruikt.

C. Antibiotica – helpen bij het behandelen van infecties en kunnen nodig zijn tijdens een plotselinge opflakkering of verergering van symptomen, als aanvulling op COPD medicijnen.

16

De belangrijkste medicijnen voor de behandeling van COPD - A) Luchtwegverwijders:

- Ze werken door de luchtwegen open te zetten, waardoor ademhalen gemakkelijker gaat.
- Ze verlichten de kortademighed.
- Omdat ze verschillende werkingsduren hebben, worden ze meestal "kortwerkende" of "langwerkende" luchtwegverwijders genoemd.

Luchtwegverwijders gebruikt u door ze te inhaleren (via de mond). Dit heeft veel voordelen. De medicijnen komen op de juiste plek in de longen terecht en geven zo veel minder bijwerkingen dan bijvoorbeeld tabletten. Ook kunnen ze zo makkelijker worden gecombineerd met andere medicijnen.

- Bepaalde soorten kortwerkende luchtwegverwijders zijn erg belangrijk tijdens een aanval van kortademigheid. Deze middelen worden ook wel "noodmedicijnen" genoemd.

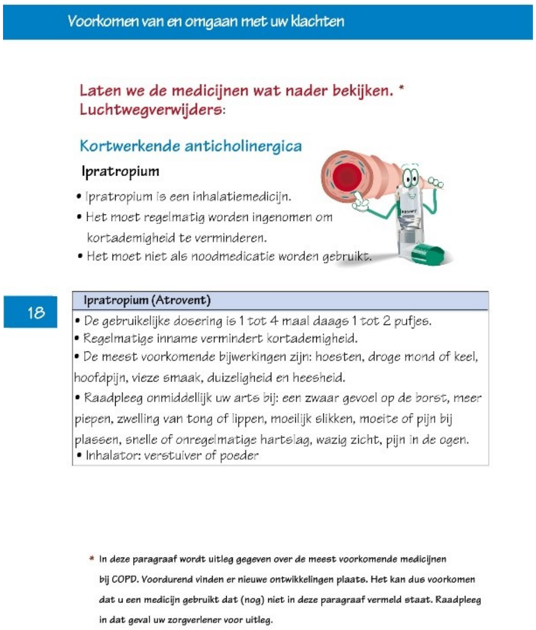
17

Luchtwegverwijders kunnen verder worden onderverdeeld in drie groepen.

Anticholinergica:
- Kortwerkend
- Langwerkend

Beta2-agonisten
- Kortwerkend
- Langwerkend

Combinatie anticholinergicum/beta2-agonist



Laten we de medicijnen wat nader bekijken. *
Luchtwegverwijders:

Kortwerkende anticholinergica

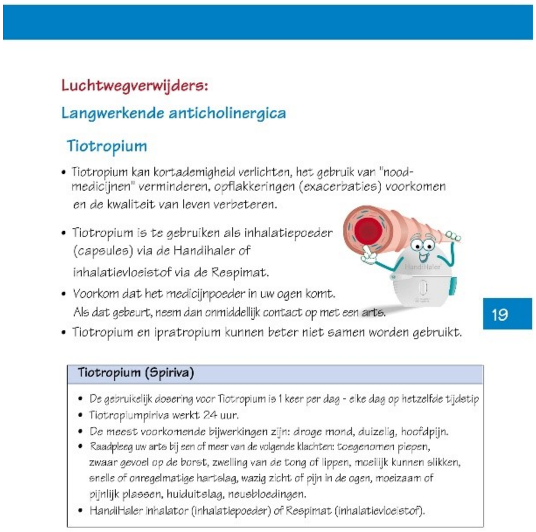
Ipratropium

- Ipratropium is een inhalatiemedicijn.
- Het moet regelmatig worden ingenomen om kortademigheid te verminderen.
- Het moet niet als noodmedicatie worden gebruikt.

Ipratropium (Atrovent)

- De gebruikelijke dosering is 1 tot 4 maal daags 1 tot 2 pufjes.
- Regelmatige inname vermindert kortademigheid.
- De meest voorkomende bijwerkingen zijn: hoesten, droge mond of keel, hoofdpijn, vieze smaak, duizeligheid en heesheid.
- Raadpleeg onmiddellijk uw arts bij: een zwaar gevoel op de borst, meer piepen, zwelling van tong of lippen, moeilijk slikken, moeite of pijn bij plassen, snelle of onregelmatige hartslag, wazig zicht, pijn in de ogen.
- Inhalator: verstuiver of poeder

*** In deze paragraaf wordt uitleg gegeven over de meest voorkomende medicijnen bij COPD. Voordurend vinden er nieuwe ontwikkelingen plaats. Het kan dus voorkomen dat u een medicijn gebruikt dat (nog) niet in deze paragraaf vermeld staat. Raadpleeg in dat geval uw zorgverlener voor uitleg.**



Luchtwegverwijders:

Langwerkende anticholinergica

Tiotropium

- Tiotropium kan kortademigheid verlichten, het gebruik van "nood-medicijnen" verminderen, opflakkeringen (exacerbaties) voorkomen en de kwaliteit van leven verbeteren.
- Tiotropium is te gebruiken als inhalatiepoeder (capsules) via de Handihaler of inhalatievloeistof via de Respimat.
- Voorkom dat het medicijnpoeder in uw ogen komt. Als dat gebeurt, neem dan onmiddellijk contact op met een arts.
- Tiotropium en ipratropium kunnen beter niet samen worden gebruikt.

Tiotropium (Spiriva)

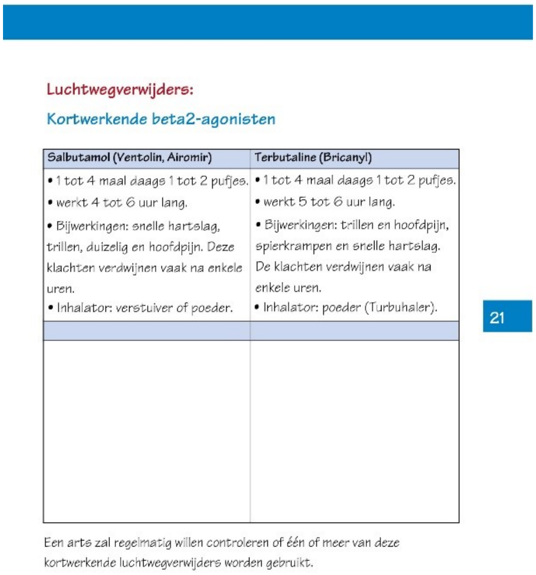
- De gebruikelijk dosering voor Tiotropium is 1 keer per dag - elke dag op hetzelfde tijdstip
- Tiotropiumpiriva werkt 24 uur.
- De meest voorkomende bijwerkingen zijn: droge mond, duizelig, hoofdpijn.
- Raadpleeg uw arts bij een of meer van de volgende klachten: toegenomen piepen, zwaar gevoel op de borst, zwelling van de tong of lippen, moeilijk kunnen slikken, snelle of onregelmatige hartslag, wazig zicht of pijn in de ogen, moeizaam of pijnlijk plassen, huiduitslag, neusbloedingen.
- HandiHaler inhalator (inhalatiepoeder) of Respimat (inhalatievloeistof).

Luchtwegverwijders :

Kortwerkende beta2-agonisten

Salbutamol, Terbutaline

- Deze medicijnen staan bekend als noodmedicijnen, omdat ze snel werken. Zorg dat u ze altijd bij u heeft voor noodgevallen, zoals een aanval van kortademigheid.
- Ze kunnen worden voorgeschreven met ipratropium of tiotropium, omdat ze op verschillende maar elkaar aanvullende manieren werken om uw luchtwegen open te houden.
- Als deze medicijnen vaker worden ingenomen dan het aantal malen dat voor een dag is voorgeschreven, moet u een arts raadplegen. Het kan een teken zijn dat uw COPD niet goed onder controle is.



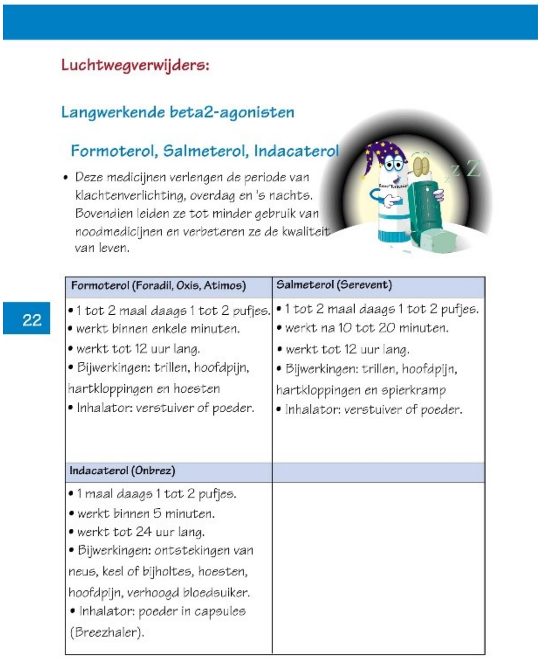
Luchtwegverwijders:

Kortwerkende beta2-agonisten

Salbutamol (Ventolin, Airomir)	Terbutaline (Bricanyl)
• 1 tot 4 maal daags 1 tot 2 pufjes. • werkt 4 tot 6 uur lang. • Bijwerkingen: snelle hartslag, trillen, duizelig en hoofdpijn. Deze klachten verdwijnen vaak na enkele uren. • Inhalator: verstuiver of poeder.	• 1 tot 4 maal daags 1 tot 2 pufjes. • werkt 5 tot 6 uur lang. • Bijwerkingen: trillen en hoofdpijn, spierkrampen en snelle hartslag. De klachten verdwijnen vaak na enkele uren. • Inhalator: poeder (Turbuhaler).

Een arts zal regelmatig willen controleren of één of meer van deze kortwerkende luchtwegverwijders worden gebruikt.

μ



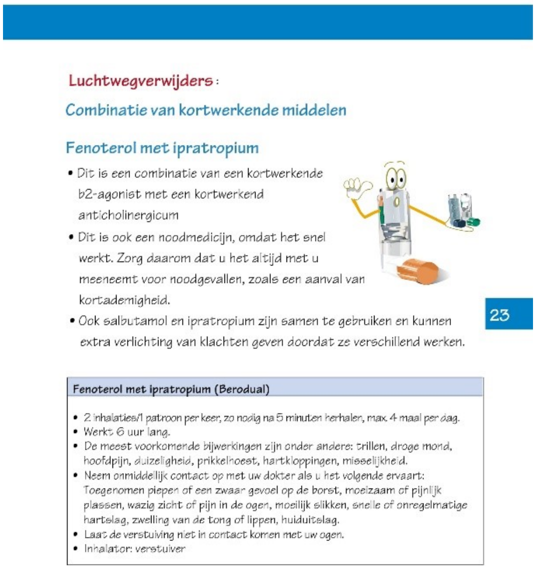
Luchtwegverwijders:

Langwerkende beta2-agonisten

Formoterol, Salmeterol, Indacaterol

- Deze medicijnen verlengen de periode van klachtenverlichting, overdag en 's nachts. Bovendien leiden ze tot minder gebruik van noodmedicijnen en verbeteren ze de kwaliteit van leven.

Formoterol (Foradil, Oxis, Atimos)	**Salmeterol (Serevent)**
• 1 tot 2 maal daags 1 tot 2 pufjes. • werkt binnen enkele minuten. • werkt tot 12 uur lang. • Bijwerkingen: trillen, hoofdpijn, hartkloppingen en hoesten • Inhalator: verstuiver of poeder.	• 1 tot 2 maal daags 1 tot 2 pufjes. • werkt na 10 tot 20 minuten. • werkt tot 12 uur lang. • Bijwerkingen: trillen, hoofdpijn, hartkloppingen en spierkramp • Inhalator: verstuiver of poeder.
Indacaterol (Onbrez)	
• 1 maal daags 1 tot 2 pufjes. • werkt binnen 5 minuten. • werkt tot 24 uur lang. • Bijwerkingen: ontstekingen van neus, keel of bijholtes, hoesten, hoofdpijn, verhoogd bloedsuiker. • Inhalator: poeder in capsules (Breezhaler).	



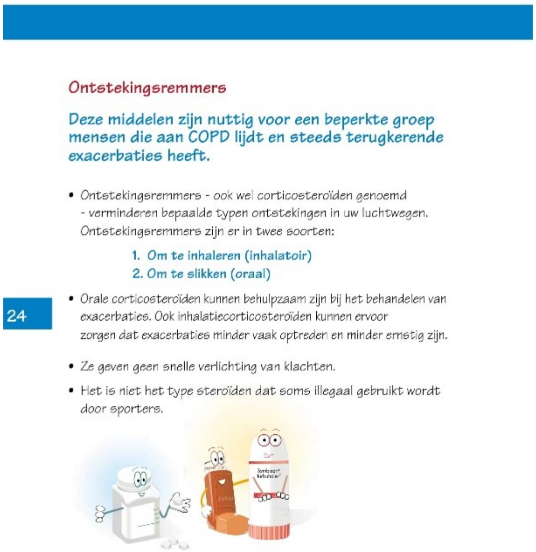
Luchtwegverwijders:

Combinatie van kortwerkende middelen

Fenoterol met ipratropium

- Dit is een combinatie van een kortwerkende b2-agonist met een kortwerkend anticholinergicum
- Dit is ook een noodmedicijn, omdat het snel werkt. Zorg daarom dat u het altijd met u meeneemt voor noodgevallen, zoals een aanval van kortademigheid.
- Ook salbutamol en ipratropium zijn samen te gebruiken en kunnen extra verlichting van klachten geven doordat ze verschillend werken.

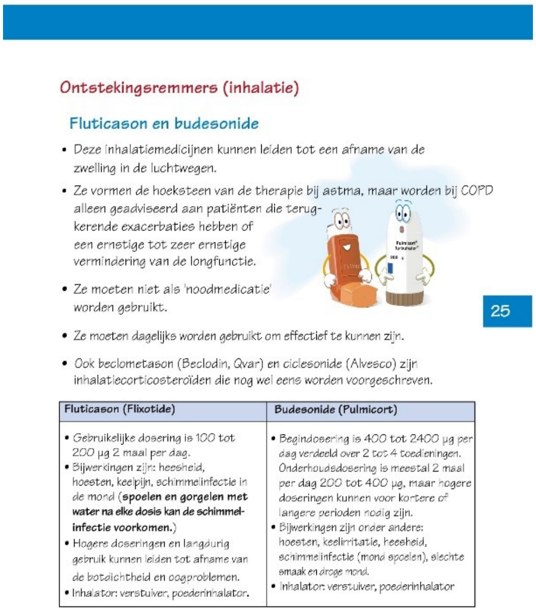
Fenoterol met ipratropium (Berodual)
• 2 inhalaties/1 patroon per keer, zo nodig na 5 minuten herhalen, max. 4 maal per dag. • Werkt 6 uur lang. • De meest voorkomende bijwerkingen zijn onder andere: trillen, droge mond, hoofdpijn, duizeligheid, prikkelhoest, hartkloppingen, misselijkheid. • Neem onmiddellijk contact op met uw dokter als u het volgende ervaart: Toegenomen piepen of een zwaar gevoel op de borst, moeizaam of pijnlijk plassen, wazig zicht of pijn in de ogen, moeilijk slikken, snelle of onregelmatige hartslag, zwelling van de tong of lippen, huiduitslag. • Laat de verstuiving niet in contact komen met uw ogen. • Inhalator: verstuiver



Ontstekingsremmers

Deze middelen zijn nuttig voor een beperkte groep mensen die aan COPD lijdt en steeds terugkerende exacerbaties heeft.

- Ontstekingsremmers - ook wel corticosteroïden genoemd - verminderen bepaalde typen ontstekingen in uw luchtwegen. Ontstekingsremmers zijn er in twee soorten:
  1. Om te inhaleren (inhalatoir)
  2. Om te slikken (oraal)
- Orale corticosteroïden kunnen behulpzaam zijn bij het behandelen van exacerbaties. Ook inhalatiecorticosteroïden kunnen ervoor zorgen dat exacerbaties minder vaak optreden en minder ernstig zijn.
- Ze geven geen snelle verlichting van klachten.
- Het is niet het type steroïden dat soms illegaal gebruikt wordt door sporters.

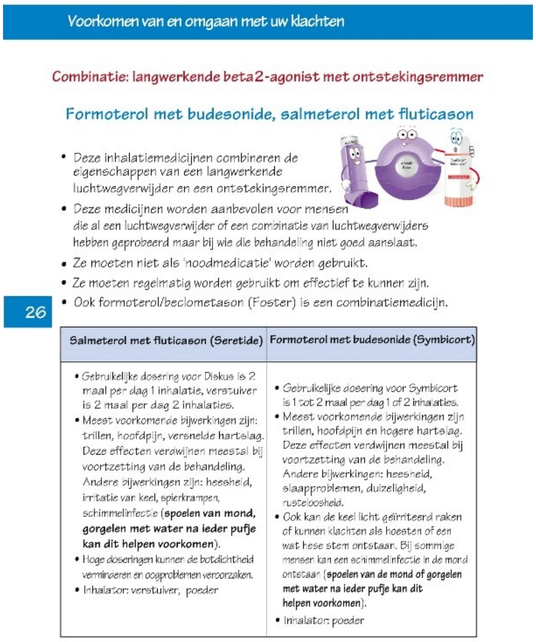


Ontstekingsremmers (inhalatie)

Fluticason en budesonide

- Deze inhalatiemedicijnen kunnen leiden tot een afname van de zwelling in de luchtwegen.
- Ze vormen de hoeksteen van de therapie bij astma, maar worden bij COPD alleen geadviseerd aan patiënten die terugkerende exacerbaties hebben of een ernstige tot zeer ernstige vermindering van de longfunctie.
- Ze moeten niet als 'noodmedicatie' worden gebruikt.
- Ze moeten dagelijks worden gebruikt om effectief te kunnen zijn.
- Ook beclometason (Beclodin, Qvar) en ciclesonide (Alvesco) zijn inhalatiecorticosteroïden die nog wel eens worden voorgeschreven.

Fluticason (Flixotide)	**Budesonide (Pulmicort)**
• Gebruikelijke dosering is 100 tot 200 µg 2 maal per dag. • Bijwerkingen zijn: heesheid, hoesten, keelpijn, schimmelinfectie in de mond (**spoelen en gorgelen met water na elke dosis kan de schimmelinfectie voorkomen.**) • Hogere doseringen en langdurig gebruik kunnen leiden tot afname van de botdichtheid en oogproblemen. • Inhalator: verstuiver, poederinhalator.	• Begindosering is 400 tot 2400 µg per dag verdeeld over 2 tot 4 toedieningen. Onderhoudsdosering is meestal 2 maal per dag 200 tot 400 µg, maar hogere doseringen kunnen voor kortere of langere perioden nodig zijn. • Bijwerkingen zijn onder andere: hoesten, keelirritatie, heesheid, schimmelinfectie (mond spoelen), slechte smaak en droge mond. • Inhalator: verstuiver, poederinhalator

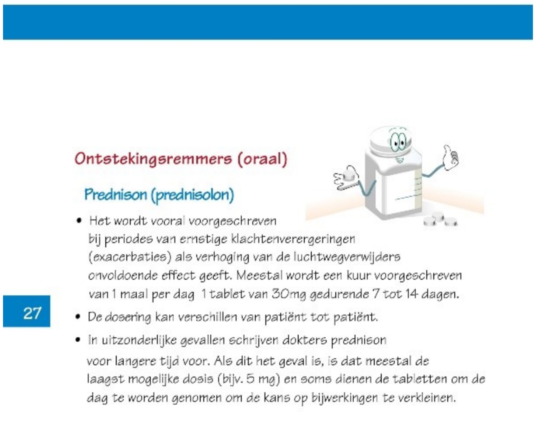


Combinatie: langwerkende beta2-agonist met ontstekingsremmer

Formoterol met budesonide, salmeterol met fluticason

- Deze inhalatiemedicijnen combineren de eigenschappen van een langwerkende luchtwegverwijder en een ontstekingsremmer.
- Deze medicijnen worden aanbevolen voor mensen die al een luchtwegverwijder of een combinatie van luchtwegverwijders hebben geprobeerd maar bij wie die behandeling niet goed aanslaat.
- Ze moeten niet als 'noodmedicatie' worden gebruikt.
- Ze moeten regelmatig worden gebruikt om effectief te kunnen zijn.
- Ook formoterol/beclometason (Foster) is een combinatiemedicijn.

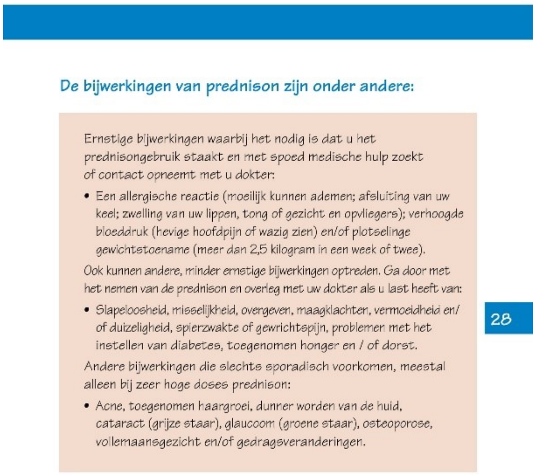
Salmeterol met fluticason (Seretide)	Formoterol met budesonide (Symbicort)
• Gebruikelijke dosering voor Diskus is 2 maal per dag 1 inhalatie, verstuiver is 2 maal per dag 2 inhalaties. • Meest voorkomende bijwerkingen zijn: trillen, hoofdpijn, versnelde hartslag. Deze effecten verdwijnen meestal bij voortzetting van de behandeling. Andere bijwerkingen zijn: heesheid, irritatie van keel, spierkrampen, schimmelinfectie (**spoelen van mond, gorgelen met water na ieder pufje kan dit helpen voorkomen**). • Hoge doseringen kunnen de botdichtheid verminderen en oogproblemen veroorzaken. • Inhalator: verstuiver, poeder	• Gebruikelijke dosering voor Symbicort is 1 tot 2 maal per dag 1 of 2 inhalaties. • Meest voorkomende bijwerkingen zijn trillen, hoofdpijn en hogere hartslag. Deze effecten verdwijnen meestal bij voortzetting van de behandeling. Andere bijwerkingen: heesheid, slaapproblemen, duizeligheid, rusteloosheid. • Ook kan de keel licht geïrriteerd raken of kunnen klachten als hoesten of een wat hese stem ontstaan. Bij sommige mensen kan een schimmelinfectie in de mond ontstaan (**spoelen van de mond of gorgelen met water na ieder pufje kan dit helpen voorkomen**). • Inhalator: poeder



Ontstekingsremmers (oraal)

Prednison (prednisolon)

- Het wordt vooral voorgeschreven bij periodes van ernstige klachtenverergeringen (exacerbaties) als verhoging van de luchtwegverwijders onvoldoende effect geeft. Meestal wordt een kuur voorgeschreven van 1 maal per dag 1 tablet van 30mg gedurende 7 tot 14 dagen.
- De dosering kan verschillen van patiënt tot patiënt.
- In uitzonderlijke gevallen schrijven dokters prednison voor langere tijd voor. Als dit het geval is, is dat meestal de laagst mogelijke dosis (bijv. 5 mg) en soms dienen de tabletten om de dag te worden genomen om de kans op bijwerkingen te verkleinen.



De bijwerkingen van prednison zijn onder andere:

Ernstige bijwerkingen waarbij het nodig is dat u het prednisongebruik staakt en met spoed medische hulp zoekt of contact opneemt met u dokter:

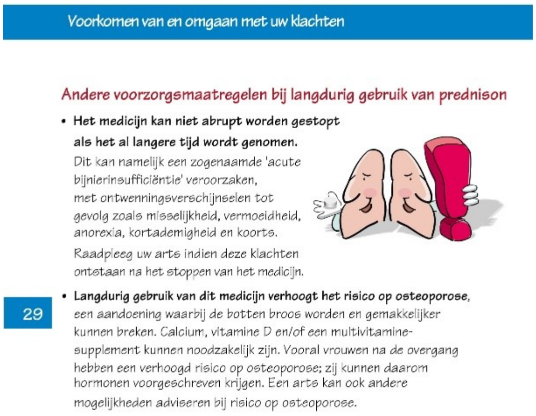
- Een allergische reactie (moeilijk kunnen ademen; afsluiting van uw keel; zwelling van uw lippen, tong of gezicht en opvliegers); verhoogde bloeddruk (hevige hoofdpijn of wazig zien) en/of plotselinge gewichtstoename (meer dan 2,5 kilogram in een week of twee).

Ook kunnen andere, minder ernstige bijwerkingen optreden. Ga door met het nemen van de prednison en overleg met uw dokter als u last heeft van:

- Slapeloosheid, misselijkheid, overgeven, maagklachten, vermoeidheid en/of duizeligheid, spierzwakte of gewrichtspijn, problemen met het instellen van diabetes, toegenomen honger en / of dorst.

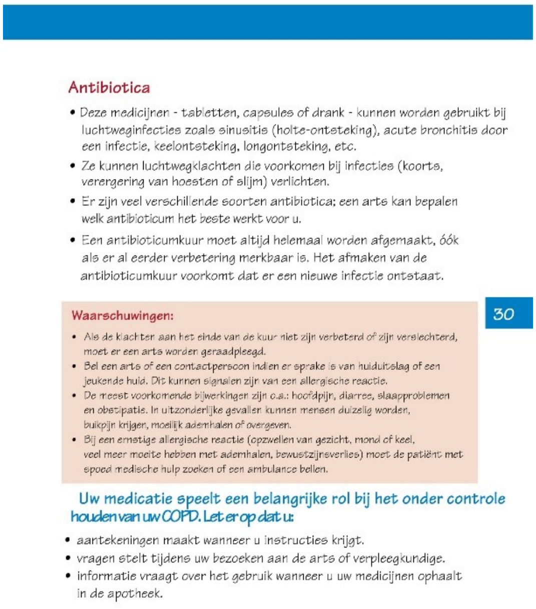
Andere bijwerkingen die slechts sporadisch voorkomen, meestal alleen bij zeer hoge doses prednison:

- Acne, toegenomen haargroei, dunner worden van de huid, cataract (grijze staar), glaucoom (groene staar), osteoporose, vollemaansgezicht en/of gedragsveranderingen.



Andere voorzorgsmaatregelen bij langdurig gebruik van prednison

- **Het medicijn kan niet abrupt worden gestopt als het al langere tijd wordt genomen.** Dit kan namelijk een zogenaamde 'acute bijnierinsufficiëntie' veroorzaken, met ontwenningsverschijnselen tot gevolg zoals misselijkheid, vermoeidheid, anorexia, kortademigheid en koorts. Raadpleeg uw arts indien deze klachten ontstaan na het stoppen van het medicijn.
- **Langdurig gebruik van dit medicijn verhoogt het risico op osteoporose**, een aandoening waarbij de botten broos worden en gemakkelijker kunnen breken. Calcium, vitamine D en/of een multivitamine-supplement kunnen noodzakelijk zijn. Vooral vrouwen na de overgang hebben een verhoogd risico op osteoporose; zij kunnen daarom hormonen voorgeschreven krijgen. Een arts kan ook andere mogelijkheden adviseren bij risico op osteoporose.



Antibiotica

- Deze medicijnen - tabletten, capsules of drank - kunnen worden gebruikt bij luchtweginfecties zoals sinusitis (holte-ontsteking), acute bronchitis door een infectie, keelontsteking, longontsteking, etc.
- Ze kunnen luchtwegklachten die voorkomen bij infecties (koorts, verergering van hoesten of slijm) verlichten.
- Er zijn veel verschillende soorten antibiotica; een arts kan bepalen welk antibioticum het beste werkt voor u.
- Een antibioticumkuur moet altijd helemaal worden afgemaakt, óók als er al eerder verbetering merkbaar is. Het afmaken van de antibioticumkuur voorkomt dat er een nieuwe infectie ontstaat.

30

Waarschuwingen:

- Als de klachten aan het einde van de kuur niet zijn verbeterd of zijn verslechterd, moet er een arts worden geraadpleegd.
- Bel een arts of een contactpersoon indien er sprake is van huiduitslag of een jeukende huid. Dit kunnen signalen zijn van een allergische reactie.
- De meest voorkomende bijwerkingen zijn o.a.: hoofdpijn, diarree, slaapproblemen en obstipatie. In uitzonderlijke gevallen kunnen mensen duizelig worden, buikpijn krijgen, moeilijk ademhalen of overgeven.
- Bij een ernstige allergische reactie (opzwellen van gezicht, mond of keel, veel meer moeite hebben met ademhalen, bewustzijnsverlies) moet de patiënt met spoed medische hulp zoeken of een ambulance bellen.

Uw medicatie speelt een belangrijke rol bij het onder controle houden van uw COPD. Let er op dat u:

- aantekeningen maakt wanneer u instructies krijgt.
- vragen stelt tijdens uw bezoeken aan de arts of verpleegkundige.
- informatie vraagt over het gebruik wanneer u uw medicijnen ophaalt in de apotheek.

Voorkomen van en omgaan met uw klachten

Het is belangrijk om te weten hoe u uw medicijnen op de juiste manier moet gebruiken, omdat inhalatiemedicijnen bedoeld zijn om direct in uw luchtwegen terecht te komen.

Weet u hoe u uw inhalator op de juiste manier moet gebruiken?

Als uw antwoord 'Nee' luidt, bent u zeker niet de enige. Veel mensen met COPD hebben moeite met het gebruik van hun inhalator. Sommige inhalatoren vergen oefening en voldoende oog-hand coördinatie. Inhalatoren hebben bovendien een eigen gebruiksaanwijzing. Dit kan verwarrend zijn.

31

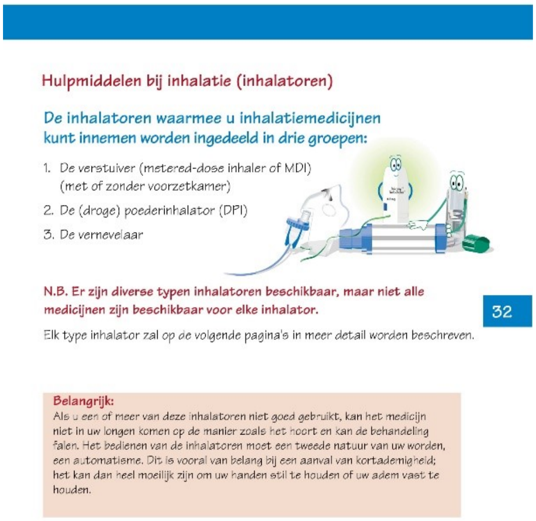
Als uw antwoord 'Ja' luidt, is het tijd om uw kennis door te nemen. Wat uw antwoord ook is, wees voorbereid. U zult gevraagd worden uw inhalatietechniek te laten zien.

Test uw kennis over inhalatoren:

• U moet het medicijn voelen bij het inhaleren om te weten dat het werkt	☐ waar	☐ niet waar
• De Aerochamber is een hulpmiddel dat niet in het openbaar moet worden gebruikt	☐ waar	☐ niet waar
• Een vernevelaar is effectiever dan een poederinhalator	☐ waar	☐ niet waar

Belangrijk:

Een goede inhalatietechniek is een vereiste om de geïnhaleerde medicatie - deeltjes of poeder - in uw luchtwegen te krijgen. Aarzel niet om te vragen uw inhalatietechniek te laten controleren.



Hulpmiddelen bij inhalatie (inhalatoren)

De inhalatoren waarmee u inhalatiemedicijnen kunt innemen worden ingedeeld in drie groepen:

1. De verstuiver (metered-dose inhaler of MDI) (met of zonder voorzetkamer)
2. De (droge) poederinhalator (DPI)
3. De vernevelaar

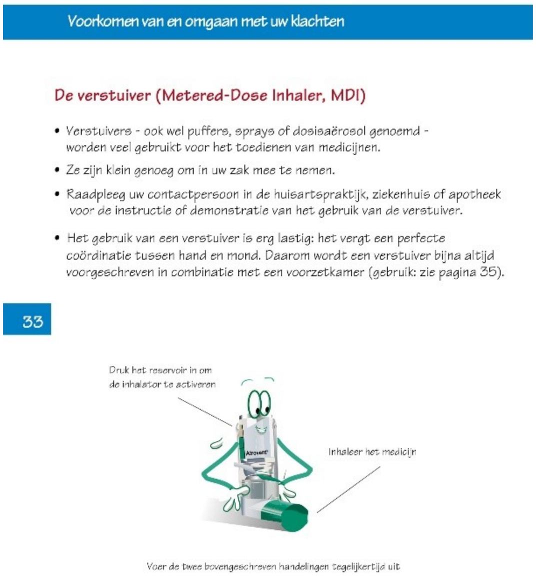
N.B. Er zijn diverse typen inhalatoren beschikbaar, maar niet alle medicijnen zijn beschikbaar voor elke inhalator.

32

Elk type inhalator zal op de volgende pagina's in meer detail worden beschreven.

Belangrijk:

Als u een of meer van deze inhalatoren niet goed gebruikt, kan het medicijn niet in uw longen komen op de manier zoals het hoort en kan de behandeling falen. Het bedienen van de inhalatoren moet een tweede natuur van uw worden, een automatisme. Dit is vooral van belang bij een aanval van kortademigheid; het kan dan heel moeilijk zijn om uw handen stil te houden of uw adem vast te houden.



Voorkomen van en omgaan met uw klachten

De verstuiver (Metered-Dose Inhaler, MDI)

- Verstuivers - ook wel puffers, sprays of dosisaërosol genoemd - worden veel gebruikt voor het toedienen van medicijnen.
- Ze zijn klein genoeg om in uw zak mee te nemen.
- Raadpleeg uw contactpersoon in de huisartspraktijk, ziekenhuis of apotheek voor de instructie of demonstratie van het gebruik van de verstuiver.
- Het gebruik van een verstuiver is erg lastig: het vergt een perfecte coördinatie tussen hand en mond. Daarom wordt een verstuiver bijna altijd voorgeschreven in combinatie met een voorzetkamer (gebruik: zie pagina 35).

33

Druk het reservoir in om de inhalator te activeren

Inhaleer het medicijn

Voer de twee bovengeschreven handelingen tegelijkertijd uit

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Voorzetkamers

Waar denkt u dat een voorzetkamer voor wordt gebruikt?

Juist

In essentie vertragen voorzetkamers de snelheid waarmee het medicijn uw mond binnenkomt. Hierdoor kan het medicijn beter uw onderste luchtwegen bereiken. Er zijn diverse types beschikbaar, die op verschillende manieren werken. Een voorzetkamer moet een eenrichtingsventiel hebben. Zo kan de kamer het pufje uit de verstuiver een aantal seconden vasthouden totdat u klaar bent om te inhaleren. Dit leidt tot minder verlies van medicatie als gevolg van een slechte coördinatie tussen inademen en drukken op de verstuiver.

Voorzetkamers verhogen dus het effect van uw medicatie.

Ook verminderen zij bijwerkingen als een bittere smaak en heesheid.

Onderhoud

Verwijder voor het schoonmaken eerst de verstuiver. Haal vervolgens alle losse delen van de voorzetkamer uit elkaar een maak ze schoon in een lauwwarm sopje. Spoel niet af en laat de voorzetkamer op een schone doek drogen zonder droog te wrijven. Reinig de voorzetkamer wekelijks bij dagelijks gebruiks en vervang hem 1x per jaar door een nieuwe.

Gebruik van verstuiver met voorzetkamer

1. Bij het eerste gebruik, verstuif 2 doses in de lucht. Dan goed schudden.
2. Plaats de verstuiver met de opening naar beneden op de voorzetkamer.
3. Ga rechtop zitten of staan en buig het hoofd licht achterover.
4. Mondstuk van de voorzetkamer tussen de tanden plaatsen en met de lippen omsluiten. Adem goed uit.
5. Druk de verstuiver in, niet meer dan 1 puf in de voorzetkamer afvuren.
6. Vijf keer rustig in- en uitademen.
7. Spoel de mond met water. Spuug het eerste slokje uit.
8. Wanneer de arts meerdere doses tegelijk heeft voorgeschreven, vanaf stap 2 herhalen.
9. Haal na gebruik de inhalator uit de voorzetkamer en plaats het beschermkapje terug.

Vraag uw contactpersoon in de huisartspraktijk, het ziekenhuis of de apotheek om een instructie.

De (droge) poederinhalator (DPI)

De poederinhalatoren geven medicijnen af in poedervorm. Niet alle medicijnen zijn in deze vorm beschikbaar.

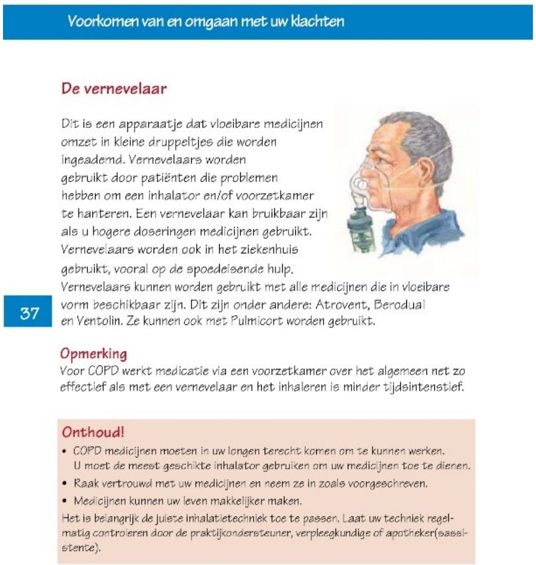
Ze zijn klein genoeg om in uw zak mee te nemen.

In tegenstelling tot de verstuiver, wat een 'druk en adem' inhalator is, worden deze inhalatoren geactiveerd als u inademt. De dosis medicijn die wordt afgegeven, hangt af van de kracht van uw ademhaling. Hoe sneller en dieper u inademt, hoe meer poeder er in uw longen terecht zal komen.

Omdat het poeder erg fijn is, kan het zijn dat u niets voelt bij het inhaleren van het medicijn.

Deze middelen moeten niet gebruikt worden met een voorzetkamer.

Vraag uw contactpersoon om een instructie.



De vernevelaar

Dit is een apparaatje dat vloeibare medicijnen omzet in kleine druppeltjes die worden ingeademd. Vernevelaars worden gebruikt door patiënten die problemen hebben om een inhalator en/of voorzetkamer te hanteren. Een vernevelaar kan bruikbaar zijn als u hogere doseringen medicijnen gebruikt. Vernevelaars worden ook in het ziekenhuis gebruikt, vooral op de spoedeisende hulp. Vernevelaars kunnen worden gebruikt met alle medicijnen die in vloeibare vorm beschikbaar zijn. Dit zijn onder andere: Atrovent, Berodual en Ventolin. Ze kunnen ook met Pulmicort worden gebruikt.

Opmerking

Voor COPD werkt medicatie via een voorzetkamer over het algemeen net zo effectief als met een vernevelaar en het inhaleren is minder tijdsintensief.

Onthoud!

- COPD medicijnen moeten in uw longen terecht komen om te kunnen werken. U moet de meest geschikte inhalator gebruiken om uw medicijnen toe te dienen.
- Raak vertrouwd met uw medicijnen en neem ze in zoals voorgeschreven.
- Medicijnen kunnen uw leven makkelijker maken.

Het is belangrijk de juiste inhalatietechniek toe te passen. Laat uw techniek regelmatig controleren door de praktijkondersteuner, verpleegkundige of apotheker(sassistente).

Laten we nog eens nagaan wat u hebt geleerd.

U heeft geleerd wat COPD is en wat de belangrijkste oorzaak is.

U heeft geleerd dat stoppen met roken belangrijk is om de achteruitgang van COPD af te remmen.

U weet hoe u factoren kunt herkennen die uw klachten verergeren.

U kent het belang van het regelmatig innemen van uw medicijnen met de juiste inhalatietechniek en u weet hoe u de medicijnen moet gebruiken om klachten te verminderen of onder controle te houden.

Neem nu de tijd voor een welverdiende onderbreking.

Leren om te ontspannen is essentieel wanneer u COPD heeft. Ontspanningsoefeningen kunnen medicijnen niet vervangen, maar zij kunnen wel een gevoel van rust en controle creëren en u helpen energie te besparen. Bespreek met uw contactpersoon welke oefeningen u kunt doen om lichaam en geest tot rust te brengen.

Neem, zoals altijd, vooral de tijd om onderdelen waaraan u meer tijd wilt besteden nog eens door te nemen.

38

Voorkomen van en omgaan met uw klachten

Noteer hier uw persoonlijke doelen:

39

Met dank aan

Ecpcfc."Swgdge<
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Appendix 6 Semi-structured care protocol

Protocol for Ghent-Eeklo Palliative Home Care Team

Patient identification

Name of **patient**:__________________________ **Date** of conversation:__ / __ / ____

If present during the conversation, name of **informal caregiver**:____________________

Name of **palliative care nurse**:__________________

Integration with first and second line care

The general practitioner, home nurse, physiotherapist and lung specialist are updated after each visit on the time management form with the proposed care and action plan. The palliative care nurse sends them the report directly after each visit. The patient also receives this report if s/he requests it.

Subject	Summary of conversation	Action taken	X min of conver-sation time spent on this subject
Insight into disease and coping - Patient's experiences with COPD - Info brochure on 'breathing and saving energy' - Info brochure on 'preventing and dealing with your complaints' - Information about medication (in consultation with the GP) For more information about the use of brochures, see annex 1			**…min**
Symptom management Reduction in complaints based on the ESAS - annex 2 If the complaint turns out to be serious (ESAS score ≥4), investigate suitable follow-up or refer to another carer.			**…min**
Care planning E.g. - The patient's values and wishes (what s/he feels is important) - Preferences for EoL care (e.g. concerning admissions to hospital) - Living will			**…min**
Support for loved ones E.g. - Identification of the patient's most important loved one(s) - Assessment of the loved ones' needs - Making the necessary support available to loved ones			**…min**

Psycho-social support …min

E.g.

- Assessment of needs (financial, administrative, activities in daily life)
- Making help/support available
- Organisation by the GP can be referred through to a social worker or psychologist if necessary and the patient agrees.

Spiritual support …min

E.g.

- Assessment of needs
- How do you see the future?
- Who gives you support in existential/spiritual matters?
- Do you have specific concerns?
- Making support available

Other support …min

E.g. Practical help with moving house, requirements (e.g. different mattress etc.)

- Assessment of other issues
- Follow-up of problems if help can be provided

Coordination of care

- Care plan with the carers involved: role, tasks and frequency.
- Plan drawn up in consultation with GP and home nurse

Fill in annex 3, 'care plan'

List action points …min

- Synthesis of action the patient can take to tackle problems

Fill in annex 4, 'action plan'

The information pack the patient receives is in two parts. This is a learning method to teach patients (and their loved ones) to deal with COPD.

Contents

Part 1: Preventing and dealing with your complaints

- Understanding your lungs' self-cleaning mechanism
- COPD: most significant causes, symptoms and complaints
- Avoiding bills that make your illness worse
- Medicines and inhalers, including a list of medicines for COPD

Part 2: Breathing and saving energy

- Physiology of breathing
- Breathing techniques
- Body postures to reduce shortness of breath
- Coughing techniquesUse

The intention is for the palliative care nurse to teach the patient to use these brochures during visit 1 and visit 2 (and possibly also during visit 3 if time is lacking). The nurse does so by going over the contents and showing the patient how the 'learning' system works (i.e. by answering the questions in the brochures etc.). Start with the 'Preventing and dealing with your complaints' pack and then introduce the 'Breathing and saving energy' pack to the patient.

The patient can be given the entire pack straight away, during visit 1. Learning to use the brochures can be included in the action plan (annex 4) as an 'agreed action point', and then the nurse can enquire at subsequent visits whether the patient has used the brochure and filled in the questions in the brochure.

ANNEX 2 - ESAS JOURNAL OF COMPLAINTS[7]

Part A: score on each occasion[8]

0 = best situation imaginable or absence of the complaint/feeling
10 = worst situation imaginable or constant presence of the complaint/feeling

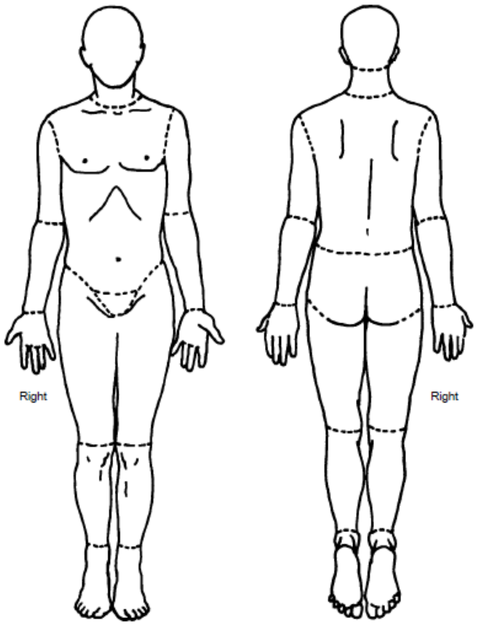
No pain	0	1	2	3	4	5	6	7	8	9	10	Severe pain
I am active	0	1	2	3	4	5	6	7	8	9	10	I am not active
Not nauseous	0	1	2	3	4	5	6	7	8	9	10	Very nauseous
Not miserable	0	1	2	3	4	5	6	7	8	9	10	Very miserable
Not anxious	0	1	2	3	4	5	6	7	8	9	10	Very anxious
Not sleepy	0	1	2	3	4	5	6	7	8	9	10	Very sleepy
Good appetite	0	1	2	3	4	5	6	7	8	9	10	No appetite
I feel well	0	1	2	3	4	5	6	7	8	9	10	I feel ill
Chest is not tight	0	1	2	3	4	5	6	7	8	9	10	Very tight chest
Sleeping well	0	1	2	3	4	5	6	7	8	9	10	Sleeping badly
Not tired	0	1	2	3	4	5	6	7	8	9	10	Very tired
No shortness of breath	0	1	2	3	4	5	6	7	8	9	10	Very short of breath
…………	0	1	2	3	4	5	6	7	8	9	10	…………

Filled in by (tick box)

- ○ Patient
- ○ Palliative care nurse
- ○ Assistant carer
- ○ Loved one

If a given symptom is experienced as severe (≥4 on the scale), the team looks into the extent to which they can deal with it themselves. If they cannot and the patient agrees: referral to GP to schedule an appointment, after which the patient can be put in touch with another specialist if necessary. If the GP agrees, this referral can also be done directly through the palliative care nurse.

Part B: indicate on these pictures where you experience complaints.



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[7] Source: De Graeff A, Hesselmann GM, Krol RJA, Kuyper MB, verhagen EH, Volbaard EJ. Palliatieve zorg. Richtlijnen voor de praktijk. VIKC, Utrecht, 2006

[8] NB Symptoms relevant to the patient can be added to the journal of complaints. The empty boxes can be used for this. ‘Breathlessness’ has already been added for the purposes of this protocol.

Guidelines for using the journal of complaints[9]

Aims

- Gain more insight into the nature and intensity of the complaints experienced by the patient
- Actively involve the patient in mapping the trajectory of his/her complaints
- Pay structural attention to the complaints
- Encourage communication between the patient and carers about the complaints experienced
- Give insight into the relationship between different complaints in the patient's physical, psychological, emotional, psychological/cognitive/social and spiritual experience
- Evaluate the effectiveness of the action taken

Method

- The patient indicates the extent to which s/he experiences the complaint as a 'burden' with a number (0-10).
- Depending on the existing complaints, items can be added such as coughing, phlegm, difficulty concentrating, dependency, immobility and vomiting.
- If the patient would prefer only to score a few complaints, the journal can be adapted. Likewise with the complaint 'pain', for example, the journal can be adapted if the intention is to gain insight into the pain score in various parts of the body.

Instructions

- The complaints are to be given a score once a month, preferably at the same time of day. The symptom is assessed over the past weeks. The patient should preferably indicate the scores him/herself (by circling the correct number) in part A, possibly with the help of the family and/or nurse.
- In part B the patient indicates where s/he experiences complaints, possibly with the help of family and/or the nurse, if filling in part A is difficult.

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[9] http://www.oncoline.nl/richtlijn/bijlage.php?bijlage_id=15

ANNEX 3 - CARE PLAN

This is a summary of the care plan, for_____________, created on __ / __ / ____ in the presence of __________________ (carer).

Both the patient and the other carers receive a summary of this care plan, on paper, digitally or by phone.

Name of carer involved	Role (e.g. physiotherapist)	Contact number	E-mail address	Tasks (e.g. respiratory therapy)	Frequency of visits (e.g. 1x/week)

ANNEX 4 – ACTION PLAN

This is a summary of the agreed actions, for _____________, created on __ / __ / ____ in the presence of __________________ (carer).

The intention is to summarise the action points in the time management form on page 2 and 3 in this plan. For example, several action points can be merged into a single action point, or several action points can be followed up by one person (e.g. the GP). During the next visit, the carer will tick off the boxes for the action points that have been completed in the past month. Any remaining action points are included in the 'action plan' created for the following visit. Both the patient and the other carers receive a summary of this care plan, on paper, digitally or verbally on the telephone.

Action points agreed with the patient and any carers involved (e.g. Read the info brochure 'Preventing complaints')	Who is responsible for this? (e.g. The patient him/herself	Tick off when completed

CHAPTER 5

Early-integrated specialised Palliative home care for end-stage COPD (EPIC-study): A Phase II pilot RCT testing feasibility, acceptability and effectiveness[x]

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[x] Submitted

Abstract

Background: While early-integrated palliative home care (PHC) is believed to be beneficial for COPD patients, trials testing this hypothesis are scarce.
Aim: To test feasibility, acceptability and preliminary effectiveness of early-integrated PHC for end-stage COPD.
Method: Testing early-integrated PHC given by specialised PHC nurses for end-stage COPD during a six-month pilot RCT with five components: (1) pre-inclusion training on COPD support for PHC nurses; (2) monthly PHC visits; (3) information leaflets on coping mechanisms; (4) a protocol on symptom management, support, a care and action plan; (5) integration of PHC and usual care through reporting and communication mechanisms. Patient-reported outcomes were assessed six-weekly. Participants and involved healthcare professionals were interviewed
Results: Of 70 eligible patients, 39 (56%) participated (20:19 intervention-control); 25/39 (64%) completed the trial. A patient received on average 3.4 PHC visits, mainly for disease insight, symptom management and care planning. Nurses distributed all reports but hardly had contact with health professionals except general practitioners (GPs); 8/10 interviewed patients referred to the psychosocial support, breathing exercises and care decisions as helpful. Some GPs criticised PHC being given too early, but pulmonologists and PHC nurses did not. Effectiveness analysis showed between baseline and week 24 fewer hospitalisations in the control group (p=0.03) and a trend of higher perceived quality of care in the intervention group (p=0.06). Other outcomes did not differ between groups for all timing points. A clinically relevant difference was observed at week 24 for health-related quality of life in favour of the control group.
Conclusion: Our intervention on early-integrated PHC for end-stage COPD is feasible and accepted but our pilot trial did not yield the anticipated preliminary effectiveness. Before moving to a Phase III-trial, the intervention should be improved, e.g. by enhanced coordination of care, more GP involvement, more intensive training for PHC nurses in COPD support and revision of the trial design, e.g. of targeted outcomes in line with individual patient goals and care preferences.

Background

Chronic Obstructive Pulmonary disease (COPD) is one of the leading causes of death[1]. Dyspnea, pain, fatigue, anxiety and low mood[2] are a burden for end-stage COPD patients[3]. Next to conventional therapies[2], palliative (PC) can offer support too[3]. The WHO advocates integration of PC earlier in the disease trajectory[4]. They and other research reason that this person-centered approach positively affects health-related quality of life (HRQOL), symptoms[5] and perceived quality of care[5]. Several respiratory societies[67] recommend this for COPD.

Physician-led[8] or nurse-led[9,10] trials show that early specialised hospital PC increases HRQOL in cancer. In one, PC nurses were shortly trained for early symptom assessment and PC was integrated in the care network[9]. A PC trial meta-analysis[11] showing HRQOL improvements for cancer and heart failure urged the need to also test PC models in COPD. Only two trials in COPD[12,13] testing an integrated PC and respiratory care service for refractory breathlessness, improved breathing mastery and survival. The PROLONG-study[14] testing proactive hospital PC did increase advance care planning but not HRQOL.

Furthermore, patients prefer to be cared for and to die at home[15], implying that PC should happen ideally at home. Specialised early palliative home care (PHC) might enhance the chance of home death[16,17] and may avoid hospitalisations[18]. However, PHC use is still low[3] and late[19] in Belgium and other countries. Health professionals lack insight into its benefits for COPD[19] due to insufficient knowledge, fear of talking about PHC with patients who may have less disease insight[20] and the unpredictable illness trajectory[21].

Implementing early-integrated PHC for COPD is thus a challenge. Firstly, effective PC models are still under debate[21] and interventions testing it are scarce[15,22]. Secondly, it has proved only effective for inhalation techniques and self-management until now[15] whereas a PHC feasibility[23] and a pilot[24] trial did not affect HRQOL, symptom burden, anxiety or mood. Thirdly, integrated PHC requires complex reporting, communication and collaboration mechanisms[21]. This is difficult within a centralised hospital[14] let alone in the decentralised home care setting. Last, PHC trials[25] use a great variety of PHC components, primary outcomes, and quality of reporting is moderate. This impedes generalisation, whereas this is needed for practice[25].

Here, pilot trial results of an early-integrated PHC intervention in end-stage COPD are given, addressing abovementioned issues[21]. Developed using the MRC Framework (results presented elswhere[2627,28]), we tested systematic home visits by PHC nurses given earlier in the COPD trajectory. As PHC nurses in Belgium are most experienced in terminal cancer support, a training on COPD-support and a care protocol addressing COPD-symptoms was included, and information and coping leaflets for COPD patients. Integration entailed systematic PHC reporting mechanisms and encouraging PHC nurses to proactively discuss care with GPs.

The aim is to report feasibility, acceptability and preliminary effectiveness results. We hypothesised differences in HRQOL, perceived quality of care and other patient-reported outcomes in favour of the intervention group.

Methods

Study design

This Phase II pilot study[29] was a six-month non-blinded RCT with five recruiting hospitals in the Ghent-Eeklo region of Flanders, Belgium. We aimed at 40 or more recruited patients in line with previous Phase II trials[30]. Research ethics committee approval (number: EC/2017/0212) from Ghent University Hospital (lead centre) and local research committees were granted. There were two amendments (following further approval) to reach the inclusion target: (1) a fifth recruiting hospital after eight months of recruiting and (2) a recruitment period extension of two months. We used a mixed methods approach and pilot trial CONSORT guidelines for reporting[31]

Setting and participants

Pulmonologists from the departments of Respiratory Medicine of five participating hospitals recruited the patients. In Belgium, PHC services are regionally organised and provided by a multidisciplinary team (PHC nurses, PHC physician and psychologist). General practitioners (GPs) apply for a palliative status for the patients in order to be able to refer them to PHC (Appendix 1). In our intervention, PHC nurses of 'the network Ghent-Eeklo' provided PHC. Participants were end-stage COPD patients. Inclusion criteria represented low to very low functioning (Box 1).

Box 1 Inclusion and exclusion criteria of participating patients

Inclusion criteria:
GOLD III (cf. GOLD[6]) and ≥ 2 or GOLD IV (cf. GOLD[6]) and ≥ 1 of the following criteria:
Oxygen-dependent[32]
≥ 3 hospitalisations for COPD in the past three years
COPD Assessment Test-scale ≥25[33]
Medical Research Council Scale Dyspnea 4
Intubation in the past year
Non-invasive ventilation in the past year
BMI ≤18
New York Heart Association Functional Classification (NYHA) 3
Exclusion criteria:
Patients living outside the region Ghent-Eeklo, Flanders, Belgium
Patients in the last days of life (bedbound and/or semi-comatose and/or taking only fluid and/or no longer able to take oral drugs[22])
Patients with cognitive impairment: Mini Mental Status Examination ≤23 on the day of inclusion of patients[34]
Lung cancer diagnosis
Patients with active cancer
Patients who are no longer living at home
Patients with no knowledge of Dutch
Patients with a GP already involved in this study for an intervention/control group patient

Randomised controlled design

Consenting patients were randomised (1:1) in either early-integrated PHC or usual care. We used the permuted block method (block size of 4), stratified according to recruiting hospital. A statistician created computer-generated sequences using the PLAN procedure in SAS. Only the research assistant obtained the allocation sequence, patient study numbers and the corresponding allocation from the statistician for enrolment. Blinding was not possible and the exploratory nature of the trial did not require adequate powering.

The intervention patients received systematic early-integrated PHC (Box 2 and previous publication[28]) alongside care as usual. The control group received care as usual, which could include PHC if requested. This PHC did not include the systematic follow-up with the care protocol and the leaflets. After the intervention, control patients could receive PHC if they preferred(Table 1).

Box 2 Intervention components of the palliative care improvement programme

(1) A training session for the palliative home care team (PHC)

Before the start of the patient inclusions, a half-day training was organised for the PHC team.

The first part was given by a pulmonologist and a physiotherapist specialised in respiratory rehabilitation to inform the PHC team on care, symptom relief and support for end-stage COPD.

The second part, given by the researcher (CS), taught the PHC team to work with the information leaflets (component 3) and the care protocol (component 4).

(2) Systematic home visits by a PHC nurse

At least once a month (more often if needed), a PHC nurse visited the patients and informal carers in their homes for a total of six months.

(3) Information leaflets on self-management

During home visits, PHC nurses gave the patients two information leaflets for self-management improvement derived from *the Canadian Living Well with COPD project*[35] (Dutch version available).

They included information on the disease and its causes, on use of medication, breathing exercises, panic distress .

(4) The care protocol

PHC nurses used a written care protocol during home visits based on a combination of components of previous interventions[9,22,30].

Several areas of care assessment were included: disease-insight and coping, symptom management (flagged by completing an Edmonton Symptom Assessment Scale [ESAS] and a visual representation of the human body to indicate symptom burden), care planning, support for informal carers, psychosocial support, existential/spiritual support, other non-predefined support e.g. financial, practical and administrative.

A care plan containing an overview of all involved healthcare professionals.

An action plan tailored to the needs of the patient: PHC nurses defined actions during each visit for the next month, e.g. practising breathing exercises. They noted down the type of action and the relevant healthcare professional. At the next visit the nurse checked whether actions had been completed.

A summary of the focus areas discussed, agreed actions and the time spent on discussing it during the home visit could be reported in the protocol.

(5) Integration of PHC into standard care

Using systematic communication and reporting mechanisms between PHC nurses and other involved healthcare professionals.

The completed protocol was sent to the pulmonologist, GP and if necessary other healthcare professionals after each visit.

If the ESAS reported a symptom burden higher than 4 out of 10, PHC nurses were encouraged to seek help from other professionals for symptom management.

Finally, during every home visit the PHC nurse decided with the patient if any other actions were needed and, if necessary, assigned these to other healthcare professionals, with the patient’s consent.

Patient-reported outcomes

We assessed following outcomes:

1. *HRQOL*, measured with the Dutch 36 item Short Form Health Survey (SF-36 SF) version 2, validated for COPD[36,37], with a physical and mental composite score (score-ranging: 0-100 [maximum HRQOL])
2. *Anxiety and mood,* measured with the Hospital Anxiety and Depression Scale (HADS)[38,39], with anxiety and depression subscale (validated for small COPD population[40,41]) symptoms (score-range: 0-21 [maximum distress])
3. *COPD-related symptom burden* measured with the COPD Assessment Test (CAT) (score-range: 0-40 [maximum symptom burden])
4. *The amount of exacerbations, primary care interventions, hospitalisations and living will decisions,* measured with patient-reported health records
5. *Perceived quality of care,* measured with the Dutch Patient Assessment of Chronic Illness Care (PACIC), validated for COPD[42], (score-range 0-5 [maximum quality of care]).
6. *Place of death* (hospital, home, nursing home) as reported by the involved healthcare professionals.

Quantitative data collection

Screened and eligible patients were registered with reasons for (in)eligibility and participation. Data was six-weekly collected using questionnaires at the patient's home in the presence of the research assistant at week 0, 6, 12, 18 and 24, which could have differed (with a range of seven days) from each target week (Table 1). Outcome 5 was only measured at baseline and week 24. The research assistant contacted all GPs for accuracy of patient-reported health records (outcome 4). PHC reports were analysed for time spent on different care and support areas, and integration of care elements.

Statistical analysis

We analysed all data collected from April 2017 until September 2018. SPSS software (version 25) did the descriptive analysis of the trial and intervention component data. For the intervention effects, we applied three-level generalised linear mixed models (measurements – patients – hospitals) using the lme4-package in R[43]. First, a model including the main effect of time and group and their interaction effect was fitted. Second, we did variable adjustment between intervention and control group at baseline and between completers and non-completers (i.e. drop-outs, deaths,..). Since the results and conclusions stayed the same, we presented the unadjusted models.

For outcomes 1-3, we included all five measurement periods and fitted a three-level general linear model. This was similar for outcome 5 using only baseline and the fifth measurement. For exacerbations and primary care interventions, we calculated a sum score over all available measurements and a three-level Poisson model with offset adjusting for the number of available measurements. We used three-level logistic regression models (with cloglog link function) to examine the intervention effects on the dichotomous outcome hospitalisations. The intervention effects on living will were examined among participants who had not signed one at baseline. We used a two-level logistic regression model (with cloglog link function) with offset to estimate the effect of the intervention on having signed a living will at the last available measurement period. To facilitate interpretation, estimated marginal means and confidence intervals were calculated using the emmeans-function[44]. Statistical significance was determined at alpha= 0.05 and for trends at alpha=0.10.

Qualitative data collection

Post-intervention interviews assessed experiences with patients of the intervention group (and when preferred, with their informal carers) who had had minimum three PHC visits. Maximum variation sampling, taking into account sex, age, recruiting hospital and enrolment date variations, was assured. We interviewed the GPs and pulmonologists about recruitment, inclusion and the integration component. A focus group with PHC nurses checked overall intervention experiences; all interviewees were asked for improvement suggestions.

Data were collected between December 2017 and September 2018. Patients were interviewed at home or in the hospital. GPs, pulmonologists and PHC nurses were interviewed at their workplace and completed a demographic and clinical questionnaire. The executive researcher (CS, sociologist) conducted the Dutch interviews, which lasted 20-90 minutes. Participants consented for audiotaping the interviews. Topic guides (see Appendix 2) were developed by the research team.

Qualitative data analysis

Two experienced researchers (CS & PP) in qualitative research coded and analysed the fully-transcribed interviews, using NVivo9 software. The entire research team identified, analysed, revised and refined themes and subthemes.

Operationalisation

We operationalised the concepts of acceptability, feasibility and effectiveness as follows:

Feasibility was assured for:

- *Recruitment*: when at least 50% of eligible patients agreed to participate and 40 were included, in line with trials on integrated PC for COPD[12,30]
- *Trial procedures*: at least 70% compliance (patients who completed all five assessments, excluding those who were too ill or died), in line with PC trials for cancer[14] and COPD[12];
- *Intervention:* Component 1: if the entire PHC team followed and used the training; Component 2: if the patients received monthly visits (depending on

their possibilities, e.g. whether they were hospitalised or not); Component 3: if the leaflets were provided and explained to all patients; Component 4: if most aspects of the protocol were used during all visits; Component 5: if all reports were distributed and communication/collaboration with at least one other health professional for each patient was established.
- *Recruitment, trial procedures and intervention:* if at least half of interviewees thought the procedures or components were executable.

Acceptability

- *Recruitment, trial procedures and intervention:* if at least half of the interviewees approved the application of the procedures or intervention.

Preliminary effectiveness

A primary outcome measure was not defined nor did we focus on one measurement point. We examined thus the overall interaction time*group (including all available time points) for differences in favour of the intervention group. Results were considered statistically significant when $p < 0.05$. Being a pilot study, we also interpreted p-values < 0.10 and considered these as trend towards significance. We assessed the clinical relevance of non-significant findings. The results will aid in choosing a primary outcome measure and preferred measurement point for a Phase III trial.

Table 1 Procedures

Training PHC team		PLs, pulmonary physiotherapist and researcher: organised a half day training for the PHC team about information and care for end-stage COPD patients and working with the intervention tools	
Screening and recruitment		PLs of the Department of Respiratory Medicine of five recruiting hospitals[¥]: - screened patient files of all eligible patients using inclusion and exclusion criteria - introduced the study to eligible patients during hospitalisation or ambulatory consultation, using a small guidebook developed by the research team - asked the patient's permission to be contacted by the research assistant for more information	
Information and written informed consent		The research assistant: - provided further information about the study to the patient and if necessary to the informal carers - provided information and explanation of their role within the study to the responsible GP - obtained obligatory written informed consent from the patient and responsible GP - included the patient in the study	
Week	**0**	During a home visit, (or at the hospital if the patient was hospitalised) the research assistant asked: - baseline measurement assessed by the patient (1st assessment)[£] - demographic characteristics assessed by the patient and the informal carer - estimation of the patient's functional status assessed by the patient and informal carer The research assistant sent by post to the responsible GP: - a clinical questionnaire (year of diagnosis with COPD, stage of COPD, comorbidities) and an estimation of the patient's functioning[£]	
		Randomisation	
		Intervention group: early-integrated palliative home care	**Control group: usual care**
Week	1	- responsible GP requested palliative status for reimbursement of related costs (not obligatory, for explanation, see box 1) - telephone call between PHCN and GP for care agreements concerning the patient	- no palliative status was requested - no telephone call needed between involved health professionals
Week	2	1st PHC visit [*][#] and usual care	Usual care
Week	6	2nd PHC visit[*][#] and usual care	Usual care
		2nd assessment[&]	2nd assessment[&]
Week	10	3th PHC[*] and usual care	Usual care
Week	12	3th assessment[&]	3th assessment[&]
Week	14	4th PHC[*] and usual care	Usual care
Week	18	5th PHC[*] and usual care	Usual care
		4th assessment[&]	4th assessment[&]
Week	22	6th PHC[*] and usual care	Usual care
Week	24	5th assessment[&]	5th assessment[&]
		End of intervention	
Week	25[¶]	Depending on the patient's wishes, support by the PHC team can be continued	Depending on the patient's wishes, support by the PHC team is possible

Abbreviations: PHC: palliative home care; PHCN: palliative home care nurse; GP(s): general practitioner(s); PL(s): pulmonologist(s)

[¥] Start of recruitment period: 2 recruiting hospitals, after 1 month of recruiting: 4 hospitals, after 6 months recruiting: 5 hospitals

[£] Patient baseline measurement happened directly after informed consent (when recruited via consultation), or after two weeks of hospitalisation (when recruited during hospitalisation)

[*] Using the care protocol of which copies were send (with patient's consent) to the involved general practitioner, pulmonologist, community nurse and other involved health professionals;

[#] Using the information leaflets;

[&] Completed by the patient together with the research assistant at the patient's home

[¶] In this week or later

Results

Recruitment and trial processes

Population description and feasibility

See Figure 1 for the CONSORT diagram. From 15 April 2017 until 31 March 2018, we screened 117 patients for their eligibility during consultation or hospitalisation; 47 were ineligible, mainly due to the early stage (GOLD I or II) of COPD (n=27) and 20 due to exclusion criteria, mainly residence outside the intervention region. The study was then proposed to the 70 of 117 screened patients (59.8%) who were eligible, of whom 39 (55.7%) agreed to participate. Not participating was mainly because of a lack of interest. Allocation ratio was 20:19 intervention versus control group. Sixteen were unable or declined to complete all five questionnaires of whom six dropped out. Compliance for questionnaires completed at home with the research assistant was 29 (82.9%) of 35 questionnaires at week 6, 31 (91.2%) of 34 at week 12, 28 (87.5%) of 34 at week 18 and 25 (89.2%) of 28 at week 24. Total compliance was 33/39 (84.0%), 14.0% higher than the 70.0% target. Of the 39 patients, six (15.4%) died during the six-month intervention and nine (23.1%) within twelve months of inclusion. The demographics (Table 2) show differences in higher education (30.0% intervention versus 5.3% control) and being fully disabled (5.0 versus 21.0). Baseline results show worse HRQOL, anxiety, mood, COPD-symptom burden and hospitalisations for the control group (Table 4). For qualitative feasibility results, see Appendix 3.

Acceptability (Appendix 3: qualitative results)

Intervention

Feasibility

Quantitative (Figure 2 and Appendix 4) and qualitative data (Table 3) show the *feasibility results. Component 1*: Before inclusion, all involved PHC nurses followed the COPD-care training. This was feasible, but too short and what was learnt was initially difficult to implement; *Component 2*: of all 20 intervention patients, 18 (90%) received a first PHC visit. PHC nurses brought them 67 PHC visits (mean visits per patient: 3.4) and four for one control patient. Post-trial, PHC nurses did 14 visits (the fifth or sixth) for six patients (Figure 2.A). PHC nurses said systematically giving PHC visits was possible but monthly visits not needed for stable patients; *Component 3:* Leaflet one was provided during visit 1 and leaflet two during visit 2 for all intervention patients (Figure 2.C) for disease insight and breathing capacity but were often not actively used by patients. PHC nurses were initially insecure to teach the content during visits. *Component 4:* a PHC visit took on average 84.8 minutes mostly on symptom management (mean: 21.0 min) (Figure 2.C). The ESAS-scale was completed in 97.5% of all visits, the ESAS-figure in 40.7%; the care plan in 54.3%. On average, 2.1 actions were defined per visit and 0.6 completed. Informal caregivers attend 55.6% of visits

(Appendix 4). The protocol structured the PHC visits in a logical way and facilitated conversation about psychosocial symptoms. It was sometimes a burden to complete and the action and care plan was often not used. *Component 5:* PHC nurses contacted GPs 41 times (median per patient: 1 (range: 1-2)) and community nurses 35 times (median per patient: 0 (range: 0-1)). Physiotherapist referral happened for four patients and social worker referral for three. Reports of all visits were distributed (Figure 2.B, but the reports were often left unread due to time constraints and technical issues (importing the report automatically in the patient file was not possible). Some GPs did not receive all reports. One pulmonologist said it facilitated PHC conversations. Communication and collaboration between PHC nurses, GPs, community nurses and pulmonologists did not increase, except with physiotherapists for breathing and muscle strength. Telephone or face-to-face contact for care alignment did not occur between care settings. PHC nurses could not reach pulmonologists, while the latter did not need extra communication.

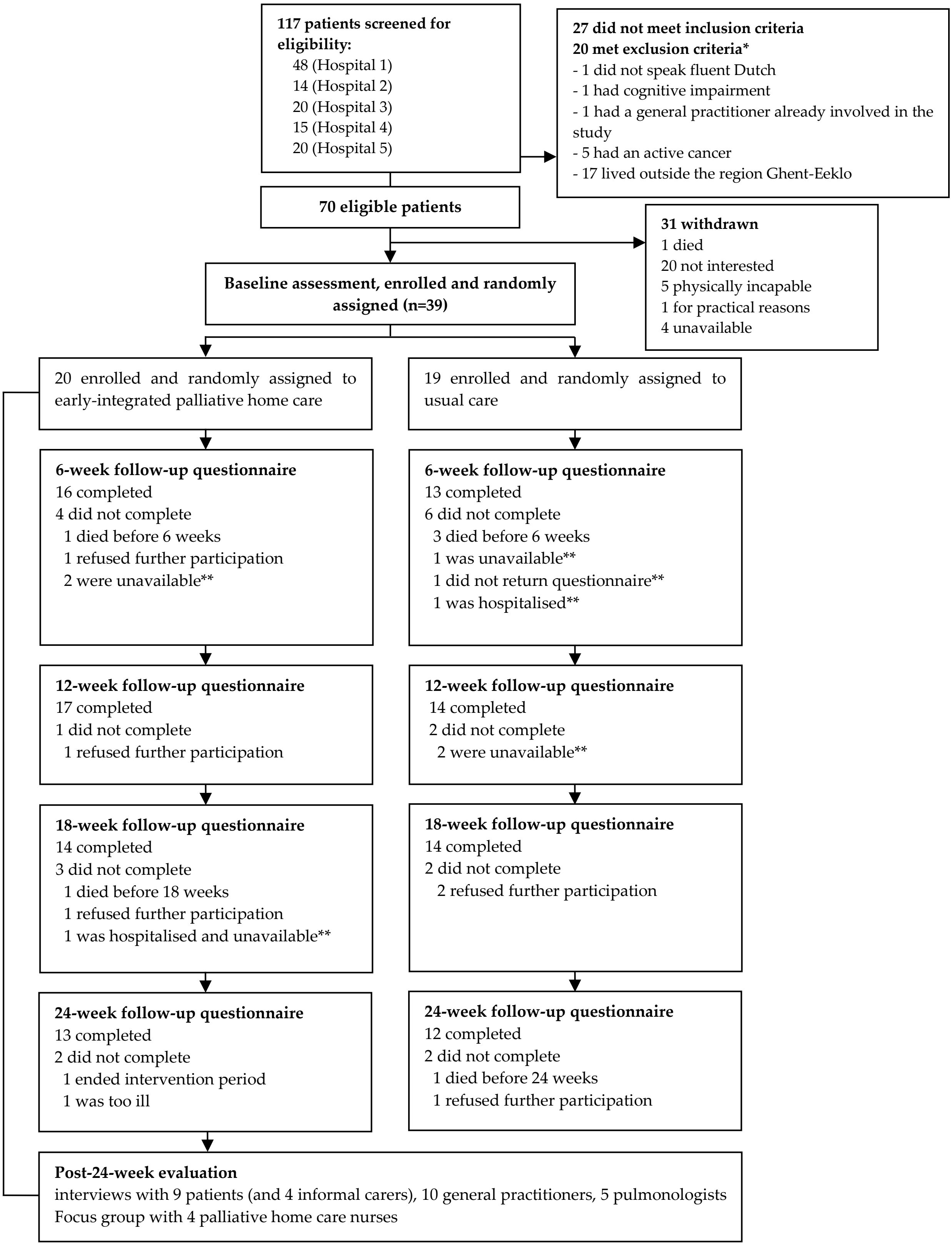
Acceptability (Table 3)

Qualitative results showed that for *Component 1*: PHC nurses indicated a strong need to follow more training, which they thought very useful; *Component 2*: the systematic approach of monthly PHC visits assured follow-up. The majority of patients (and, if interviewed, the informal carers), pulmonologists and PHC nurses agreed with the PHC timing, although the latter said referral was too late for some. Some GPs said it was too early or worried if patients need systematic PHC. Patients appreciated the breathing exercises, care planning and practical help. Some GPs said that psychologist's support is more beneficial in this stage; *Component 3*: PHC nurses and patients said it aided for breathing capacity. Better informed patients did not see added values; *Component 4*: PHC nurses said that while it was a useful tool for structuring visits it was not always needed, especially the action plan. The care plan provided a useful care overview during visit 1. The ESAS-scale aided conversation or confronted patients about symptoms such as anxiety. Patients said the protocol resembled questionnaires; *Component 5:* PHC nurses, pulmonologists and the majority of GPs valued the sent reports for being updated. One GP did not see its relevance and one pulmonologist was not glad to read afterwards that a wheelchair was ordered (since this was bad for muscle strength). Another appreciated the PHC nurse's initiative to organise a meeting; one pulmonologist and some GPs did not need collaboration.

Preliminary effectiveness

Table 4 shows the mixed-model analysis and the estimated means. An overall interaction effect (F) was presented, except for perceived quality of care and health-records for which an interaction effect (b) between baseline and week 24 was done. Missing values were low and most (24/36) for PACIC-items (Appendix 5). Place of death was descriptively analysed. Between week 0 and 24, hospitalisation significantly differed (b= 1.85, SE= 0.83, p= 0.03) in favour of the control group who were less hospitalised (for univariate details see Table 5). A trend towards a significant interaction effect was observed for perceived quality of care (b= 0.65, SE=0.34, p=0.06). It significantly improved in the intervention (b= 0.56, SE= 0.23, p= 0.02), while it stabilised in the control group (b= -0.10, SE= 0.25, p= 0.70). HRQOL (physical and mental), anxiety, mood, COPD-symptom burden, exacerbations and primary care interventions remained unchanged. Every six weeks, 3.5% (95% CI= 0.5-22.5) control patients signed a living will and 11.9% (95% CI= 5.1-26.5) intervention patients (non-significant); 2/20 (10.0%) intervention and 4/19 (21.1%) control patients died at the hospital. Six weeks post-intervention, 2 intervention patients died at home (for reasons: Appendix 6). While the interaction effects were non-significant, HRQOL increased until week 12 for both groups. At week 24, clinically relevant differences for physical (F= 0.89, p= 0.47) and mental (F= 1.13, p= 0.35) HRQOL were observed compared with baseline. Physical HRQOL increased 1.1 points in the control and decreased 2.9 points in the intervention group. Mental HRQOL increased 3.0 points in the control and decreased 1.6 points in the intervention group. Descriptive 24-week results show a lower mean for hospitalised versus non-hospitalised intervention patients for physical (16.3 versus 27.6) and mental (30.1 versus 40.1) HRQOL (Table 4). Both groups also showed clinically relevant mild (7-10) anxiety and depression levels on all timing points (non-significant). Sensitivity analysis, controlling for education and functional status, gave similar results, as did a complete case analysis (not in Table). Appendix 7 shows the used questionnaires.

Figure 1 Recruitment and trial follow-up



*Some patients met more than one exclusion criteria

**Were unavailable to complete the questionnaire at that moment. They did not drop out of the study.

Table 2 Demographic characteristics and baseline assessment

	Early-integrated palliative home care (n=20)	*Usual care (n=19)*
Median age (min-max)	67.5(50-83)	67.0(48-83)
Mean age (years (s.d.))	67.5(8.4)	67.4(7.9)
Sex, n(%)		
Female	9(45.0)	8(42.1)
Male	11(55.0)	11(57.9)
Education, n(%)		
Lower secondary, primary education or less	9(45.0)	14(73.7)
Higher secondary education	5(25.0)	4(21.1)
Higher education	6(30.0)	1(5.3)
Informal carer, n(%)		
No informal carer	1(5.0)	1(5.3)
Partner	13(75)	14(73.7)
Offspring (daughter/son)	3(15.0)	2(10.5)
Sibling (sister/brother)	1(5.0)	0(0.0)
Parents	1 (5.0)	1(5.3)
Other	1 (5.0)	1(5.3)
Living situation, n(%)		
Alone	7(35.0)	5(26.3)
With partner, children or other family	13(65.0)	14(73.7)
Functional status according to patient, n(%)		
Limited for heavy physical activities	8(40.0)	3(15.8)
Ambulant but capable of taking care of oneself	4(20.0)	6(31.6)
Partly capable of taking care of oneself	7(35.0)	6(31.6)
Fully disabled	1(5.0)	4(21.0)
Years diagnosed with COPD (mean (s.d.)	11.4(9.4)	8.1(4.9)
Years diagnosed with COPD (median (min-max)	11.0(1-41)	8.0(2-17)
Co-morbid conditions reported (mean (s.d.)	2.2(1.8)	2.1(1.4)
GOLD stage, n(%)		
GOLD III	2(10.0)	3 (15.8)
GOLD IV	18 (90.0)	16 (84.2)

% are column percentages. Data are mean (s.d.) or n(%). Abbreviations: s.d, standard deviation;

Table 3 Feasibility, acceptability and suggestions for improvement of the intervention from the evaluation interviews with patients (n=9), general practitioners (n=10), pulmonologists (n=5) and palliative home care nurses (n=4)*

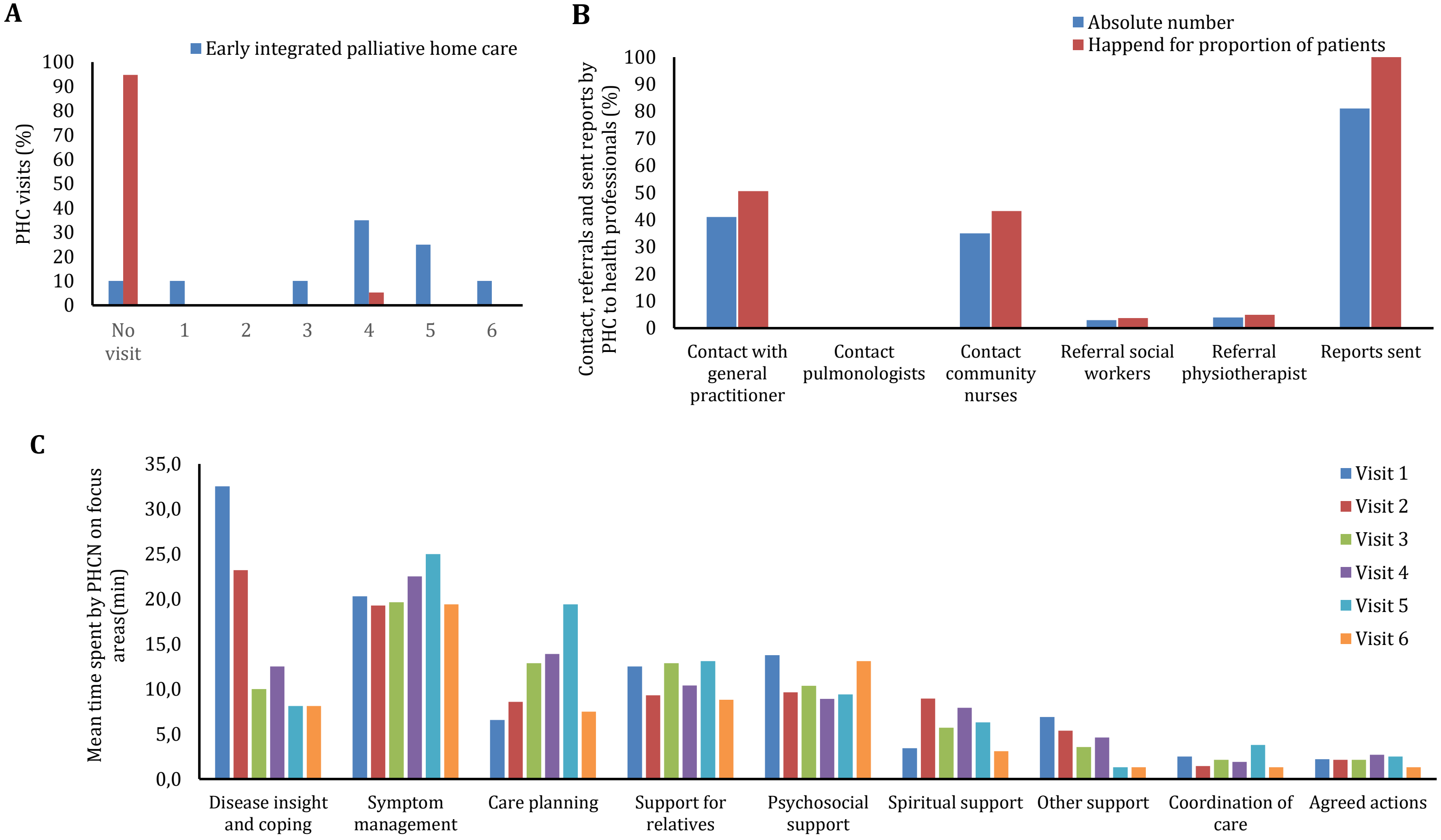
Item		*Feasible*	*Acceptable*	*Suggestions for improvement according to interviewed participants*
Intervention				
1	**Training for the palliative home care nurses (component 1)**	A half day’s training was feasible to attend (4PHCS) Remarks: It was difficult to demonstrate the exercises learned in the training to the P (3 PHCNs) The training was too short to fully learn the exercises (1PHCN)	The content of the training was relevant and needed (4PHCNs) Focus on physical symptom support was good (2PHCNs) Overlap with physiotherapists’ roles: It seemed like taking over physiotherapists’ tasks (1PHCN) It was useful to signal the need for breathing exercises and for referral to the physiotherapist (2PHCNs).	Feedback or multiple training opportunities to better incorporate the training and to practise the breathing exercises (3PHCNs) More explanation on medication use and brand names (1PHCNs) More collaboration with physiotherapists to help with breathing exercises (1PHCN)
2	**Systematic palliative home care visits (component 2)**	In general, home visits were feasible for GPs, Ps, and PHCNs, because they were: Useful for the Ps (3GPs) Easier to talk about care planning, as PHCs have longer time slots during a consultation (1GP) Easier than expected (1P) As expected (1P) Easy to talk about anything, emotions and feelings (4Ps) Possible to receive more explanation of the disease (1P+IC) Easy to arrange a consultation with PHCNs (2Ps) Practical to have a PHCN visit at home, because of reduced mobility (1P) Feasible to do monthly visits, depending on the patient’s will (3PHCNs) Logical to follow the predefined flow of the visits, where the leaflets were given in visit 1 and 2, and care planning in the following visits (2PHCNs) One remark: if Ps were stable, visits 5 and 6 were a bit unnecessary (2 PHCNs)	Positive comments, as the visits: Supported disease insight, care planning and symptom management (mental and physical) (9GPs) Were the right number (1GP) Were helpful for talking about problems (7Ps +3IC) Were helpful for accepting the situation (1P) Were helpful for providing disease information (1P+IC) Were more than care planning (1P) Concerns were mentioned, as the visits were: A bit forced when given early (2GPs) Not needed for Ps in the final phase of life (1GP) Too obligatory due to the systematic aspect (1GP) Not beneficial for disease insight (1GP) Too connected with the negative connotation of PHC (2GP) Discomforting for Ps (1GP, 1 PHCN) Not in line with therapy advice of the PL on maintaining physical activity (1PL) Associated with death (1P+IC) Not different from consultations with GPs or PLs (1P)	Exclude systematic visits, and provide one only when necessary (3GPs) Start visits in the terminal phase (1GP)
3	**Information leaflets (component 3)**	3 Ps (of whom 2 frequently) used them for breathing exercises, 1 read the COPD-related information, and 1 gave it to the physiotherapist. 1 did not receive leaflets. 1 PHCN said it needed some practice to use the leaflets	5 Ps thought they were helpful for breathing exercises, and all PHCNs said they were very useful for supporting the patient’s daily activities	Nothing mentioned
4	**Care protocol in general (component 4)**	It aided with living will decisions, not-COPD related problems, informal carer’s support (each mentioned by one P+IC), practical support (3 Ps). It had a logical structure (1PHCN), it was always completed after the visit (3PHCNs).	Ps were accepting of assessing symptoms in the protocol, 1 felt more relaxed after talking about living will.	Better to show the answers from previous visits (1P) Ask more about the P’s needs (1P+IC)

		Remarks: Living will, informal carer's support, breathing exercises, practical support, were not discussed (each item by 1P + IC) The division between reporting and identifying actions per focus area was confusing (3PHCNs) Completing the protocol on a tablet was not feasible, as this meant double reporting (3PHCNs)		Merge the division between reporting and identifying needs per focus area into one block (1PHCN) Include context, medical and care history (2PHCNs) Switch to a digital protocol (1PHCN)
5	**ESAS-scale and figure (component 4)**	Completing the ESAS-scale was feasible (6 Ps and 3 PHCNs), it was used for indicating pain, and the items visualised symptom burden well (1PHCN). Remarks: Difficult to remember answers from previous visits (1P and 1 PHCN) A pity that a report of the scale results was not provided (2Ps) The scale response was sometimes not in line with what the Ps explained during the conversation (2PHCNs) P resistance to accept referral to other health professionals when high ESAS-score was signalled (2PHCNs) The inverse scoring of the ESAS-scale was confusing (2PHCNs) The items 'shortness of breath' and 'tightness in the chest' were interrelated (2PHCNs) Scores on some items depended on the P's physical effort (different score when Ps were active or not) (1PHCN)	Acceptable: The ESAS-figure was helpful to assess symptoms (1P+IC) The ESAS-scale facilitated conversations about anxiety and low mood (4 PHCNs) Remarks: It was sometimes confronting for the patient to realise the severity of the situation (1PHCN) Completing the ESAS-scale is useful but not really needed in practice (2 PHCNs)	Nothing mentioned
6	**Care plan (component 4)**	Healthcare professionals were noted in the care plan at first visit (2 PHCNs) It was difficult to map PLs when there is no responsible PL (1 PHCN)	Transparency of involved healthcare professionals (3PHCNs) Facilitation of inter-professional contact (1PHCN)	Nothing mentioned
7	**Action plan (component 4)**	Listed relevant actions with follow-up checks (3 PHCNs) Used previous action plan to complete next action plans (2 PHCNs) Listed GP consultations (1PHCN) and practical issues (1 PHCN) Remarks: The example of an action in the protocol was not clear (1PHCN) Confusion about the definition of an action (1PHCN) If the action plan of the previous visit was not used during the next visit, the action plan was not feasible (1PHCN) Identifying actions is laborious (1PHCN)	The feedback principle, where you look back to actions from previous visits, is crucial to use of the action plan (1PHCN) Doubts whether an action plan is useful in practice as it is difficult to identify concrete actions (1PHCN)	Incorporate the previous actions from other visits into one action plan to improve overview (1PHCN) A general report instead of an action plan would be more practical (1PHCN)
8	**Integration between and contact with health professionals and patients (component 5)**	1 face-to-face meeting organised by the PHCN with GP, PHCN, community nurse at the P's home (1GP). Talking about PHC: 6 GPs had contact with PHCNs by e-mail or phone, 2 with PLs, 1 with a community nurse and 4 with Ps. 1 was aware the physiotherapist had been consulted via the PHCN 2 Ps talked with their GP 3 PHCNs called the GP when problems occurred 1 PHCN called the GP for medical information as the ESAS-scale was >4	More support due to increased contact was positive(1GP) Knowing who the PHCN was facilitated a meeting (1GP) The PHCN organising a meeting was desirable (1GP) Contacting and integrating a physiotherapist in the support for the patients is useful in practice (1PHCN) Concerns: More contact besides reports is not necessary (1PL) It is difficult for a GP to talk about PHC with patients as the patient wants positive news from a GP (1GP)	Contact with PHCNs only via e-mail; via telephone is disturbing (1GP) More collaboration between informal and professional care providers is needed to align therapy and care trajectories (1GP) Increase contact between the palliative support team and the PHCNs (1PL) A combination of PHC and home visits by the physiotherapist with care adjusted to

		1 PHCN contacted the physiotherapist on breathing exercises PC communication with community nurses went well (2PHCNs) Referral to other health professionals: 3 Ps had a physiotherapist via the PHCN (3Ps) Contacted palliative support team for hospitalised Ps (1PHCN) Remarks: 4 GPs and 4 PHCNs did not have contact with a PL and vice versa 2 GPs and 3PLS did not have contact with PHCNs The lack of organisation between primary and secondary care hindered integration of care (1PL) Talking about PHC was too time-consuming for specialists (1P) Communication between healthcare professionals was already good (1P) There was no increased contact compared with care as usual (1PHCN) Contact was mainly to report, not to discuss care (1PHCN) Hospitals did not contact PHCN when P was hospitalised (2 PHCNs)	Integration of care is more necessary for primary caregivers (1PL)	the needs and possibilities of the patient (1PHCN)
9	Sending a report (component 5)	Feasible aspects: Sending the report after each visit to GP, PL, community nurse (4PHCNs) Received the report (5GPs, 5 PLs) Content of the report was good (1GP, 2PL) The report was not too long to read (2PLs) Practical that living will decisions were included in the report (1GP) Receiving a report via e-mail is the right medium (2GPs, 2PLs) Remarks Read the report quickly due to a lack of time (6GPs and 3PLs) The report was too long to read (3GPs) Postponed reading the report and therefore forgot it (1GP) Unclear if report was received (4GPs) Reading written and scanned text in an unfamiliar style was not practical (2GPs) Only received one of the five reports (1GP) Receiving a report via e-mail is not practical (2GPs) If not uploaded to the patient file, it is unpractical (2GPs, 1PL) One P expressed distrust about sending the report (1PHCN)	The report contained useful updates on the P's situation (9GPs, 5PLs) It is in the P's interest that all healthcare professionals receive a report (1GP) Receiving a report via e-mail did not interrupt daily activities (3GPs) Knowing the content of the report eased conversations about PHC with the P (1PL) It was good that the GP and PL received an update via the report (2Ps) Receiving a report was not desirable as the information is not relevant (1GP) It was useful to know from the patient that the living will discussions had been initiated via the PHCNs (1GP) Reading afterwards that a wheelchair was ordered by the PHCN was not desirable as this does not improve muscle strength (1PL)	Provide possibility of uploading the report directly to the patient's file (4GPs) Send a summary of the report in concrete action points instead of the entire report (2GPs, 1PL) Send the report via mail instead of via e-mail (1GP) Explain to the Ps during the introduction of the study clearly that information will be shared between health professionals (2PHCNs)

*The results present an overview of all comments from the interviews, mentioning which and how many participants said it. This gives an indication of the importance of the comment. Not every participant expressed an opinion on all topics. Abbreviations: PHC: palliative home care; PHCN: palliative home care nurse; GP(s): general practitioner(s); PL(s): pulmonologist(s); P(s): patient(s). IC: Informal caregiver.

Figure 2 Number and type of palliative home care visits, and integration of care



Except for Figure A, data are based on 81 visits, of which 8 visits (2 for visit 5 and 6 for visit 6) happened outside the intervention period for 6 intervention patients.

(A) Data are proportions of patients based on the total number of intervention and control patients (analysed separately) between baseline and 24 weeks;

(B) Data are proportions of contact, referral and sent reports based on the total number of PHC visits during baseline and 24 weeks for the intervention group.

(C): Data represent the average time (in minutes) spent on the different topics per PHC visit between baseline and 24 weeks. Abbreviations: PHC (palliative home care)

Table 4 Multivariate and univariate results of preliminary effectiveness for baseline, week 6, 12, 18 and 24

Outcome measures	Baseline		Follow-up (week 6)		Follow-up (week 12)		Follow-up (week 18)		Follow-up (week 24)		Interaction effects			
	Control (n=19)	Intervention (n=20)	Control (n=16)	Intervention (n=13)	Control (n=17)	Intervention (n=14)	Control (n=14)	Intervention (n=14)	Control (n=13)	Intervention (n=12)				
Health-related quality of life, anxiety, mood and COPD-related symptom burden scores (mean(95%))											**Overall time*group**		**week24* group**	
											F	**p**	**b(SE)**	**p**
SF-36’physical*£	21.8 (18.4-25.2)	26.5 (23.1-29.8)	24.3 (20.4-28.1)	28.7 (25.2-32.3)	23.4 (19.6-27.2)	28.3 (24.8-31.8)	23.7 (20.0-27.5)	27.1 (23.4-30.8)	22.9 (19.0-26.8)	23.6 (19.8-27.3)	0.89	0.47	-4.00 (2.50)	0.12
SF-36’mental*	34.4 (29.3-39.6)	37.2 (32.0-42.3)	38.1 (32.5-43.8)	38.2 (32.8-43.6)	36.4 (30.9-42.0)	40.7 (35.3-46.0)	38.4 (32.8-43.9)	38.4 (32.9-43.9)	37.4 (31.7-43.2)	35.6 (30.0-41.1)	1.13	0.35	-4.59 (3.23)	0.16
HADS’anxiety*	8.3 (5.3-11.4)	8.5 (5.4-11.6)	7.4 (4.3-10.5)	8.6 (5.5-11.7)	7.1 (4.0-10.2)	7.2 (4.1-10.3)	6.7 (3.6-9.8)	6.7 (3.6-9.8)	6.9 (3.8-10.1)	7.7 (4.6-10.8)	0.46	0.76	0.61 (1.08)	0.57
HADS’depression*	10.2 (8.1-12.3)	7.9 (5.8-10.0)	9.6 (7.2-11.9)	7.9 (5.7-10.1)	8.9 (6.6-11.2)	6.9 (4.8-9.1)	9.5 (7.2-11.8)	8.8 (6.5-11.1)	9.8 (7.4-12.1)	8.1 (5.8-10.4)	0.45	0.64	0.61 (1.30)	0.64
COPD-CAT*	22.4 (17.6-27.2)	20.2 (15.4-25.0)	24.3 (19.4-29.3)	20.4 (15.5-25.3)	22.2 (17.2-27.1)	19.4 (14.5-24.3)	22.2 (17.2-27.1)	19.4 (14.5-24.4)	21.4 (16.3-26.4)	18.8 (13.8-23.7)	0.20	0.94	-0.40 (2.17)	0.86
Number of exacerbations and primary care interventions (mean(95%)), was hospitalised (probability of patients), living will (% patients per six weeks which had a living will decision), and quality of care scores (mean(95%))														
# exacerbations (count)$	0.4 (0.2-1.1)	0.4 (0.2-1.0)	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	0.2 (0.1-0.7)	0.2 (0.1-0.4)	n.a.	n.a.	-0.49 (0.53)	0.35
#primary care (count)$	0.6 (0.3-1.2)	1.0 (0.5-1.7)	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	0.4 (0.2-0.8)	0.7 (0.4-1.3)	n.a.	n.a.	0.08 (0.40)	0.85
Was hospitalized (dichotomous)$	0.6 (0.4-0.8)	0.3 (0.1-0.6)	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	0.13 (0.04-0.25)	0.23 (0.12-0.44)	n.a.	n.a.	1.85 (0.83)	0.03
Living will (dichotomous)$,£	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	3.5 (0.5-22.5)	11.9 (5.1-26.5)	n.a.	n.a.	1.27 (1.10)	0.25
PACIC_quality of careµ	2.6 (2.0-3.2)	2.5 (1.8-3.2)	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	2.4 (1.7-3.0)	2.9 (2.3-3.6)	n.a.	n.a.	0.65 (0.34)	0.06
Place of death (% of patients, univariate analysis)														
Home death	n.a.	n.a.	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	n.a.	n.a.	n.a.	n.a.
Hospital death	n.a.	n.a.	15.8	5.0	0.0	0.0	0.0	5.0	5.2	0.0	n.a.	n.a.	n.a.	n.a.

Abbreviations: Mean: predicted mean; CI: confidence interval; F: overall interaction effect (not interpretable); b: multilevel linear regression coefficient; SE: standard error; p: p-value; SF-36: Short-form 36; COPD-CAT: COPD assessment Test; HADS: Hospital Anxiety and Depression Scale; PACIC: Patient Assessment of Chronic Illness Care; n.a.: not-applicable.

B’s for count variables are on the log-scale; B’s for dichotomous variables are on the cloglog-scale;

*Were measured at baseline, 6, 12, 18 and 24 weeks.

$Were measured at baseline, 6, 12, 18 and 24 weeks, but the results in this table for 24 weeks represent a mean number or probability measured over all measurement moments, controlled for number of measurements each case had.

£The intervention effect on living will was only examined among participants who did not yet have one at baseline. The estimated probabilities indicate a higher probability of living will at the last measurement among intervention patients.

µWas measured at baseline and 24 weeks.

Interpretation of scales and measures: SF-36 physical and mental: (score-ranging: 0-100 [maximum health-related quality of life]; COPD-CAT: (score-range: 0-40 [maximum symptom burden]); HADS anxiety and Depression: (score-range: 0-21 [maximum distress]); PACIC: (score-range 0-5 [maximum perceived quality of care]).

Table 5 Univariate, in-detail results of hospitalisations

Measurement	*Group*	*n*	*#Hospitalisations*				*Detailed information*			*Reasons*			
			1	*2*	*3*	*Total*	*#unplanned*	*days (mean, s.d.)*	*#ER or IC*	*AECOPD & COPD*	*Pneumonia*	*Coma*	*Other*
Baseline	Control	19	8	2	1	11	11	22(17,7)	5	10			1
	Intervention	20	7			7	7	17(13.5)	1	7			
6 weeks	Control	16	1			1	1	7(n.a.)			1		
	Intervention	13	2			2	2	9(5.0)				1	1
12 weeks	Control	17	4			4	4	10(9.3)	2	3			1
	Intervention	14	4			4	4	5(2.9)	1	2	1		1
18 weeks	Control	14	2			2	1	4(n.a.)		1	1		
	Intervention	14	1			1	1	9(n.a.)	1	1			
24 weeks	Control	13	0			0							
	Intervention	12	4			4	4	35(23.4)	3	3		1	

ER: Emergency room admission, IC: intensive care, AECOPD & COPD: acute exacerbation for COPD & COPD-related causes such as breathlesness; s.d.: standard deviation

Discussion

Main findings

In this pilot study, the recruitment and trial processes met the *feasibility* targets and were generally *approved*. On *feasibility and acceptability of the components,* targets were met for the information leaflets and the care protocol, and to a lesser extent for the monthly palliative home care (PHC) visits: mean number was 3.5 and some did not agree about the systematic approach. The training was executable and welcomed but too short, difficult to implement and did not fully prepare for COPD support in this disease stage. Systematic reporting was positively evaluated but did not lead to increased proactive communication or collaboration between PHC nurses and others involved, except with physiotherapists. *Preliminary effectiveness analysis* between baseline and week 24 showed fewer hospitalisations in the control (p=0.03) and a trend of higher perceived quality of care in the intervention group (p=0.06). Other outcomes did not differ. Hospital death occurred for 21.1% control and 10.0% died intervention patients; two of the latter died at home six weeks post-trial. At week 24, a clinical different health-related quality of life (HRQOL) was in favour of the control group.

Strengths and limitations

To our knowledge, this is the first pilot randomised study on early-integrated PHC for end-stage COPD in Belgium. The MRC-framework enabled theoretical evidence and in-depth research. This led to well-executed components and trial procedures and contributed to the need for PHC development and effectiveness reporting[25]. Combining quantitative and qualitative methods captured patient, informal carers and health professional perspectives, often under-represented in interventions[25]. Limitations were 1) a possible crossover effect; staff members were not masked to patient allocation. The pulmonologists may have implemented insights gained from the intervention into the control group. Moreover, because the assessor was not masked, biased outcome reporting was plausible; 2) possibility of selection bias; patients were informed about the PHC approach, so it is likely that those more open to PHC participated; and 3) a complex intervention; knowing which component affected which outcomes and how components were interdependent was impossible.

Interpretation of the results and implications for a Phase III trial

In relation to inclusion criteria, hospitalisations and oxygen-dependency were identified by recruiting pulmonologists as good signifiers of low functional status, similar to those used by the PROLONG-study[45] and GOLD[6], resulting in inclusion of patients ranging from moderate to very low functioning. As only 25.1% died within one year, the criteria captured a cohort relatively early in the disease trajectory and not limited to the end of life, less than the 55% in one PHC trial[23] and more than the 16% in another[24], both using similar criteria.

The use of the term palliative care (PC) during recruitment did not scare patients if well-explained, as in the PC cancer trial of Constantini et al[46] which found no reluctance towards early PC if its purpose was well described. In our trial, PHC visits actually left patients positively surprised about early-integrated PHC. As predicted[20], some older GPs feared the negative connotation of PHC and doubted the usefulness of early PHC for COPD. GP involvement from trial set-up onwards is needed[27]. The slow rate of recruitment through pulmonologists was because this was done in the summer when they saw fewer people for check-ups or via hospitalisations because fewer exacerbations happen. Also many of the patients they saw lived outside our recruiting area, so recruiting via GPs, whom patients consult more often, may be better.

Most intervention components were considered useful and welcome, although the training and care integration lacked implementation strength according to PHC nurses. The two-hour training for COPD support was helpful for early PHC provision[9,14] but was too short for direct implementation in practice. In contrast, the PROLONG-study[14] provided two training sessions (duration unknown), one for training and one for feedback, to increase confidence and skills. However, the ability of a PHC nurse to support someone with complex COPD-symptoms[21] in an early phase[3] may be overestimated; pain and dyspnea remain high until death[47] and require pharmacological treatment and specific breathing and muscle exercises[48]. The HADS also indicated mild anxiety and depression (clinical cut-off point>7)[41].

In relation to the integration component, sending reports to GPs and pulmonologists was feasible and welcomed but this [49] did not provide the structural opportunities for communication and coordination between PHC nurses and others involved that is needed to ensure integration[49]. Time constraints, technological issues and GPs' lack of interest in collaboration were mentioned. Hospital-home care interaction is also demanding[24,27] due to geographical distance[50], lack of a common documentation system[51], unequal power distribution[50] and different care approaches[27]. In contrast, in-hospital integrated PC and pulmonary services seem to encounter fewer obstacles than PHC models[12,13]. We did not assign a fixed care coordinator (an important facilitator of integrated care[27,52]) although PHC nurses were implicitly assumed to fulfil this role (e.g. contacting GPs if ESAS-scale >4). Only one nurse organised multidisciplinary meetings. Deciding who should be coordinating depends on patient preferences or region-specific care dynamics[52]. In Belgium however, PHC nurses operate on the second line[53] which may impede coordination. Primary caregivers such as GPs or community nurses visit patients more and oversee the care network better[54], making them better placed for coordination tasks. Finally, the wheelchair 'conflict' mentioned in the results reflected a lack of proactive therapy alignment and confusion about patient needs. A goal-orientated approach in multidisciplinary meetings and shared electronic health records[55] may better align care with patient needs[55].

At week 24 the trial showed a preliminary negative effect of the intervention, namely fewer hospitalisations (p=0.03) and a clinically relevant but non-significant difference in HRQOL in the control group, itself an unsurprising link, as hospitalisation for exacerbation impacts negatively and independently on HRQOL (in the SF-36)[56]. Between week 18 and week 24, four intervention and no control patients were hospitalised. There are other possible explanations for why the intervention group did not have fewer hospitalisations.

Firstly, the intervention might not have addressed end-stage COPD needs adequately[57]. Belgian PHC nurses are more experienced in terminal cancer care and less in early PC. They felt ill-prepared to support COPD needs, despite the short training. Compared with cancer, prognosis in COPD is unpredictable and deterioration is slower[58]. Cancer patients may rely more on comfort treatment when other therapies are exhausted[14,27] while people with COPD need conventional care (even until death) for dyspnea and pain[47]. COPD phenotypes also impact on different symptoms which makes appropriate care quite complex[24]. Although a holistic PHC approach to prioritise comfort seems most fitting, this was not successful in this and other PHC trials[23,24]. In contrast, other tested interventions like breathlessness-targeting PC[12,59] and anxiety-targeting trials[60] decreased symptom burden using a symptom-tailored intervention. Comparative effectiveness trials in end-stage COPD are possibly more appropriate.

Secondly, at week 24, three intervention patients had life-threatening exacerbations and one entered a coma, all difficult to resolve at home[24,61] and requiring intensive treatment[61]. Patients rely on the emergency room during episodes of escalating symptoms or decreased capacity to cope[23], confirming our findings (Table 5). Furthermore, informal carers are often physically and emotionally exhausted from years of COPD-support[62] making staying at home impossible or undesirable[63]. Of the patients interviewed, many had severely ill or immobile partners who were hospitalised themselves during the intervention.

A positive result was a trend towards a perceived improvement in quality of care (goal-setting, follow-up, problem-solving and care delivery) in the intervention group (p=0.06) and more living will decisions (not significant). PHC nurses are experts in this area and patients appreciated their listening to problems and concerns about future care. PHC may be more effective in COPD[57] for this than for other things; certain GPs and pulmonologists addressed these issues during consultations after receiving a report. One study[65] found that PC for treatment decisions and advance care planning increases quality of end-of-life care, whereas focusing on coping increases HRQOL, as seen in cancer trials[8,10,65,66].

Research, policy and practice implications

Implementation challenges and unexpected effects of this pilot trial provide important lessons for the future. To fulfil its potential, some aspects need adjustment: better training for PHC nurses in COPD support, GP involvement during set-up, recruitment and for generalist PHC, structurally integrated coordination and communication mechanisms (shared health records, ad hoc multidisciplinary deliberation at home/hospital when a deterioration needs changes in care, proactive care alignment) might all be worthwhile. Retailoring the intervention towards targeting needs/symptoms by also involving GPs (for medical care and generalist PHC), psychologists (for anxiety) and physiotherapists (for breathing and muscle exercises) should likewise be explored.[21]

The outcomes were not as expected although patients showed appreciation for help with breathing, listening to problems and discussing future care preferences. Evaluation of this model based on a limited number of test cases with feedback from all involved and in-trial adjustments may be more worthwhile in a pilot phase[67]. On outcomes, qualitative methods may be more appropriate to assess subtleties[23] and context-dependent data and to capture complex COPD situations. Assessing overall PHC experiences, care needed and care preferences (through which appropriate care is decided) are alternative options to the outcome measures used[25,55,68].

Conclusion

The tested early integration of PHC intervention for end-stage COPD is feasible and accepted by patients and their informal carers, PHC nurses, GPs and pulmonologists, but our pilot trial did not yield the anticipated preliminary effectiveness results. Before moving to a Phase III-trial, the intervention should be re-examined and improved, e.g. by enhanced coordination of care, more GP involvement, more intensive training for PHC nurses in COPD support and revision of the design of the trial, e.g. targeted outcomes and evaluation methods.

Competing Interests

The authors declare that they have no competing interests.

Authors' contributions

C.S., L.D., K.C., G.J., S.V.B., K.E. and P.P. were involved in the study conception and design and in obtaining ethical approvals. C.S. (sociologist) and K.E. (psychologist) were involved in the quantitative and qualitative data collection. J.V. (statistician), C.S., K.C. & G.V. were involved in the quantitative data analyses. C.S. and P.P., experienced qualitative researchers with backgrounds in sociology (C.S.) and medical, palliative home and primary care (P.P.) analysed the qualitative data. Analysis was discussed with all contributing authors. The first and following drafts were written by C.S. All authors commented on the first and following drafts, revised them critically, and agreed with the final version. All authors are accountable for all aspects of the work.

Additional material

The protocol of the pilot trial can be accessed through charlotte.scheerens@ugent.be

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Appendices

Appendix 1: Palliative home care in Belgium

Organisation

Belgium has region-bound palliative home care (PHC), which is a separate secondary care service provided by a multidisciplinary team consisting of a PHC physician, PHC nurses and a psychologist. In total, 27 networks (of which 15 in Flanders) are operating in Belgium. PHC is requested by the patient's general practitioner (GP), depending on individual context, this is mostly in consultation with the patient, informal carers, involved community nurses, palliative care nurses in the hospital, or specialists. The main focus of PHC teams are their home visits by the PHC nurses to support the patient and informal carers for psychological, social, physical and spiritual needs (holistic approach). PHC nurses also collaborate with the involved GP if necessary. The PHC physician and the PHC psychologist are involved in weekly meetings and in psychological support for patients and informal carers. Although variation exists, most PHC team do not use standardised documents or scales to assess the symptoms and needs of the patients. Rather, they report in a general electronic patient file, which is not systematically shared with other health professionals. Contact with the latter is mainly by telephone.

Palliative status

Before referring patients to PHC, the responsible GP can request an optional 'palliative status', which is a form for PHC eligibility providing reimbursement of costs related to the palliative phase. The reimbursement system for PHC in Flanders is by law restricted to patients with three months life expectancy, with the possibility of making a second claim[70]. This has recently been altered to six months, although the law remained unchanged up until now. If a palliative status is not requested, PHC can still be provided.

Appendix 2 Topic guides qualitative interviews

For all interviews

Introduction: Short introduction, purpose of the interview

Experiences with the intervention on

Intervention components (visits, integration)
Moment in the disease trajectory to start with the intervention

Suggestions for improvement

Other moment in disease trajectory?
Rol general practitioner or other health professionals?
Communication with health professionals?
Care from the palliative home care team?
Home visits, information leaflets,..?

For patients' (and informal carers) interviews

Experiences with the intervention on

Recruitment
Introduction of the study
Assessments
Home visits, protocol, information leaflets,..?

General practitioners' interviews

Experiences with the intervention on

Inclusion criteria
Recruitment
Collaboration with palliative home care nurses
Collaboration with pulmonologists
Role of the general practitioner in the study

Pulmonologist's interviews

Experiences with the intervention on

Inclusion criteria
Recruitment
Introduction of the study
Collaboration with palliative home care nurses
Collaboration with general practitioners
Role of the pulmonologist in the study

Palliative home care nurses' focus group conversations

Experiences with the intervention on

Inclusion criteria
Recruitment
Collaboration with other health professionals
Protocol
Training
Role of the palliative home care nurse in the study

Appendix 3: Feasibility, acceptability and suggestions for improvement of the trial processes from the evaluation interviews with patients (n=9), general practitioners (n=10), pulmonologists (n=5), palliative home care nurses (n=4)*

Item		*Feasible*	*Acceptable in its current form*	*Suggestions for improvement*
Trial processes				
1	Inclusion criteria	2 GPs said the criteria enabled timely access to PHCN, 2 said the opposite. All PLs agreed the criteria were usable, with especially oxygen dependency (1PL) and hospitalisations (1PL) reflecting a high need for PHC. A wide variability of functioning between eligible Ps was seen (1PL) Difficulties leading to exclusions were: '3 or more hospitalisations in the last 3 years, especially in combination with GOLD III (1PL) Living outside the region of residence (1PL) The CAT-scale being too strict (1 PL) The combination of GOLD and other criteria (1PL)	All GPs said the criteria were more or less acceptable, given the Ps' high needs for support. All PLs accepted the criteria, Concerns were that the criteria: Contradicted with the 3 month life expectancy eligibility criterion for a palliative refund (5GPS) (for more explanation of the refund see box 2) Did not yet reflect a palliative phase (4GPS) On excluding cured lung cancer diagnosis was too strict (1PL) Did not include lung emphysemia Ps (1PL) included Ps who were too ill, as some died before ending the intervention (3 palliative home care nurses) (PHCNs) Inhibit inclusion as the word palliative care (1GP) and the palliative phase (1GP) is difficult for Ps in this phase of the disease to accept. Did not reflect own vision of palliative care for these Ps (2GPs)	GPs suggested to Change the criteria to predictability of 3 months (1GP) Change the criteria for Ps who realise the possibility of a terminal phase (1GP) Rename the word palliative care as it is more supportive care in the intervention (1GP) Take into account being bedbound as a criterion I Take into account the eligibility criterion of a palliative refund (1GP) Acknowledge budgetary boundaries hindering early-integrated PHC (2GPs)
2	Recruitment procedure	On the study introduction: 6 Ps received information via the PL, 2 via the research assistant, 1 could not remember, 1 did not receive an introduction. On receiving notification the P was included: 2 GPs knew it via the PL, 1 via the P, 1 could not remember, 1 GP and 1 PL did not receive it. Feasible aspects: The ability to think about recruiting regularly (2PLs) Having team meetings to discuss recruitment (2PLs) The practical recruitment leaflets with inclusion criteria provided by the research team (1PL) The combination of introducing the study via the PL and further explanation to the P from the research assistant (1PL) The use of newsletters via e-mail to remind PLs of recruiting (1PL)	Recruitment via the pulmonologists was acceptable for 5 GPs and all PLS. Some views on recruitment: A long introduction of PHC is unnecessary (1PL) A GP is not well-experienced with long function test (2PLs) or lacks the time (1PL) to recruit Ps A PL is well-placed to do the recruitment due to experience with PHC for lung cancer (1PL)	Recruitment via the PL but in collaboration with other health professionals such as: GPs (2GPs and 2PLs) Community nurses (2GPs) Palliative support team in the hospital (2PLs) A pulmonary nurse (1PL) Start recruitment in winter during the influenza epidemic, as this increases hospitalisations and consultations in the hospital (3PLs)

		Remarks: Lack of time, lack of courage, inability to think about recruiting (3PLs) Using the word PHC in the study's introduction, which was sometimes replaced by 'extra support' (2PL) The short recruitment period (1PL) Involving other team members in recruiting (1PL) Team meetings to discuss recruitment, due to time constraints (1PL Recruiting eligible ambulant Ps from other departments (1PL) Ps recruited in summer were less ill than in winter (3PHCNs)		Send information on recruitment to all team members and not only to the responsible pulmonologist (1PL) Check the oxygen dependency list (1PL) Recruit via the PL and the GP (2PL) Necessary to explain PHC more in detail to the Ps (1PL)
3	Participation agreement	2 Ps participated without particular reason, 3 to help the researchers and the specialists, and 1 because of several reanimations in the past. Ps participated mainly for the palliative refund (1GP)	Nothing mentioned	Nothing mentioned
4	Assessment procedures	1 Ps said it did not take as long as expected, 1 said it was as expected, and 1 could not remember any details.	2 Ps found the replication of questions every 6 weeks a bit annoying, while 1 said it was perfect. Other Ps did not express a particular opinion.	Nothing mentioned
5	Assessment content	Feasible aspects: Questions were similar to those of the PHCNs (2Ps) and easy to answer (2Ps) Not feasible aspects: difficult to remember answers of the previous six weeks (3Ps), answers depended on context factors not related to COPD (1P), and confronting to express emotions (1P).	3 Ps were acceptable towards the content of the questions. Concerns on the questions were: too difficult to answer (1P), not for COPD (1 P), too repetitive in one assessment, f.ex. those on emotional wellbeing (1P)	Ask general questions without multiple answer categories to capture more context information (1P) Include financial situational questions (1P)

**The results present an overview of all comments given in the interviews, mentioning which and how many participants said it. This gives an indication of the importance of the comment. Not every participant expressed an opinion on all topics.*

Abbreviations: PHC: palliative home care; PHCN: palliative home care nurse; GP(s): general practitioner(s); PL(s): pulmonologist(s); P(s): patient(s)

Appendix 4: Results from the care protocol

	Visit 1	*Visit 2*	*Visit 3*	*Visit 4*	*Visit 5**	*Visit 6***
Received a PHC visit/ intervention group, n	18/20	16/20	16/20	14/20	8/20	8/20
Minutes spent on focus areas during visit						
Total duration visit, mean min. (s.d.)	100.6(22.1)	87.9(23.1)	85.4(43.6)	84.6(35.8)	92.5(40.9)	63.8(16.4)
Disease insight & coping, mean min. (s.d.)	32.5(10.2)	23.2(10.1)	10.8(9.1)	12.5(11.2)	8.1(15.6)	8.1(10.7)
Symptom management, mean min. (s.d.)	20.3(8.8)	19.3(7.8)	21.2(7.1)	22.5(8.3)	25.0(7.1)	19.4(6.8)
Care planning, mean min. (s.d.)	6.6(7.5)	8.6(9.5)	13.8(11.9)	13.9(11.5)	19.4(10.8)	7.5(11.3)
Support informal carers, mean min. (s.d.)	12.5(7.3)	9.3(5.5)	13.8(8.5)	10.4(11.2)	13.1(8.8)	8.8(8.8)
Psychosocial support, mean min. (s.d.)	13.8(7.9)	9.6(7.2)	11.2(7.9)	8.9(10)	9.4(5.0)	13.1(11.3)
Spiritual support, mean min. (s.d.)	3.4(5.4)	8.9(16.9)	6.2(11.2)	7.9(13.7)	6.3(6.9)	3.1(5.9)
Practical support, mean min. (s.d.)	6.9(7)	5.4(5.7)	3.8(6.8)	4.6(8.8)	1.3(3.5)	1.3(3.5)
Coordination of care plan, mean min. (s.d.)	2.5(4.1)	1.4(3.1)	2.3(6)	1.9(3.8)	3.8(5.2)	1.3(3.5)
Action plan, mean min. (s.d.)	2.2(4.1)	2.1(3.8)	2.3(4.8)	2.7(4.8)	2.5(4.6)	1.3(3.5)
# Missings time indication	*2*	*2*	*3*	*4*	*1*	*0*
Other aspects of the care protocol						
ESAS scale completed, n(%)	18(100.0)	16(100.0)	15(93.8)	13(92.9)	9(100.0)	8(100.0)
Visual figure from ESAS completed, n(%)	8(44.4)	9(56.3)	6(37.5)	5(35.7)	2(22.2)	2(25.0)
Care plan completed, n(%)	17(94.4)	9(56.3)	8(50.0)	5(35.7)	2(22.2)	1(12.5)
Actions defined, mean amount (s.d.)	2.3(1)	2.9(1.6)	2.9(1.6)	1.5(1.5)	1.0(1.7)	0.8(1.5)
Actions completed, mean amount (s.d.)	0.7(1.3)	0.6(1.2)	0.8(1.3)	0.4(1.1)	0.9(1.8)	0.8(1.5)
Informal carers present during visit, n(%)	11(61.1)	8(50.0)	9(56.3)	7(50.0)	4(44.4)	3(37.5)

Abbreviations: PHC: palliative home care; S.D.: standard deviation; ESAS: Edmonton Symptom Scale Assessment

*Of which two visits happened after the intervention period

**of which six visits happened after the intervention period

Appendix 5: Missing data analysis of outcome measurement

	Total n items/questions Within assessment	*N patients (%) who completed the assessments*	*Total n missing items of completed assessments*	*Total and % missing items in completed assessments*
Baseline		39/39(100.0)		
SF-36	36		0	0/1404(0.0)
COPD assessment Test	8		2	2/312(0.0)
HADS	14		0	0/546(0.0)
PACIC	20		24	24/780(3.1)
Total	78		26	26/3042(0.9)
Week 6		**29/39(74.4)**		
SF-36	36		2	2/1044(0.2)
COPD assessment Test	8		0	0/232(0.0)
HADS	14		0	0/406(0.0)
Total	58		2	2/1682(0.1)
Week 12		**31/39(79.5)**		
SF-36	36		1	1/1116(0.1)
COPD assessment Test	8		0	0/248(0.0)
HADS	14		0	0/434(0.0)
Total	58		1	1/1768(0.1)
Week 18		**28/39(71.8)**		
SF-36	36		1	1/1008(0.1)
COPD assessment Test	8		0	0/224(0.0)
HADS	20		0	0/392(0.0)
Total	64		1	1/1792(0.1)
Week 24		**25/39(64.1)**		
SF-36	36		1	1/864(0.1)
COPD assessment Test	8		0	0/200(0.0)
HADS	14		0	0/350(0.0)
PACIC	20		0	0/500(0.0)
Total	78		1	1/1950(0.1)

Appendix 6: Numbers, reason and place of death reported at 6, 12, 18, 24, and 30 (post-intervention) weeks

Group	*Timing*	*N(%)**	*Reason*	*Place of death*
Early integrated palliative home care	Before 6 weeks	1(5.0)	Pneumonia and sceptical shock	Hospital(I.C.U.)
	Before 18 weeks	1(5.0)	Pneumonia and influenza	Hospital
	Total	2(10.0)	/	/
	Before 30 weeks$	2(10.0)	Sedation after multiple exacerbations Heart failure	At home At home
Usual care	Before 6 weeks	3(15.8)	Respiratory insufficiency due to terminal COPD	Hospital
	/		COPD exacerbation and pulmonary embolism	Hospital
	/		Respiratory insufficiency due to terminal COPD	Hospital
	Before 24 weeks	1(5.2)	Sedation	Hospital
	Total	4(21.0)	/	/

*N represents amount of patients who died and % the proportion who died based on the total amount of intervention or control patients

$Post-intervention deaths

Appendix 7 questionnaires

Patiëntnr: __________________ **Datum:** / /
Volgnr:_______________

De tijdige integratie van palliatieve thuiszorg in de standaardzorg voor personen met ernstige COPD: een gerandomiseerd gecontroleerd onderzoek.

Zes wekelijkse vragenlijst voor de patiënt en zorgverlener

Waar gaan de vragen over? Deze vragenlijst geeft zicht op uw kwaliteit van leven, COPD gerelateerde symptoomlast, gemoedstoestand, visie op uw ziekte en de zorg voor COPD. Wij waarderen het dan ook zeer als u bereid bent om deze vragenlijst in te vullen.

Hoeveel tijd kost het invullen en wanneer gebeurt dit? Het invullen van de vragenlijst zal ongeveer **20 minuten** duren.

Wanneer vul ik de vragenlijst in? Om de zes weken, nadat ik de vragenlijst per post heb toegestuurd gekregen. ,

Hoe vul ik de vragenlijst in? Deze vragenlijst wordt door uzelf ingevuld:

- In het geval u een antwoord moet **aankruisen** kruist u de antwoordmogelijkheid aan die op u (het meest) van toepassing is.
- In het geval u een cijfer moet aanduiden, omcirkelt u het cijfer die op u (het meest) van toepassing is.
- Bij de open vragen zal u worden gevraagd informatie neer te **schrijven**.

Goede of foute antwoorden zijn er niet. Eerlijke antwoorden zijn het meest zinvol. Als u een vraag helemaal niet kan beantwoorden: vink dan aan 'ik weet het niet'.

Wie krijgt mijn antwoorden? De informatie die u geeft zal strikt vertrouwelijk worden behandeld. Alle gegevens worden volledig anoniem verwerkt en komen enkel in handen van de onderzoekers die gebonden zijn aan beroepsgeheim.

Wat doe ik met mijn ingevulde vragenlijst? De vragenlijst mag u (in een gesloten enveloppe) afgeven aan de onderzoeker. Indien u dit formulier krijgt toegestuurd mag u het ons met de voorgefrankeerde enveloppe terug bezorgen.

Bij wie kan ik terecht met vragen? Bij de betrokken onderzoeker aan de VUB-UGent onderzoeksgroep: Charlotte Scheerens; tel.: 09/332 07 93; e-mail: charlotte.scheerens@ugent.be

Vragen voor de patiënt

Gelieve de onderstaande vragen in te vullen. Tenzij anders vermeld, is er slechts één antwoord mogelijk per vraag.

A. KWALITEIT VAN LEVEN

In deze vragenlijst wordt naar uw gezondheid gevraagd. Wilt u elke vraag beantwoorden door het juiste hokje aan te kruisen. Wanneer u twijfelt over het antwoord op een vraag, probeer dan het antwoord te geven dat het meest van toepassing is.

1 Wat vindt u, over het algemeen genomen, van uw gezondheid?

☐ Uitstekend
☐ zeer goed
☐ goed
☐ matig
☐ slecht

2 In vergelijking met een jaar geleden, hoe zou u nu uw gezondheid in het algemeen beoordelen?

☐ veel beter dan een jaar geleden
☐ iets beter dan een jaar geleden
☐ ongeveer hetzelfde als een jaar geleden
☐ iets slechter dan een jaar geleden
☐ veel slechter dan een jaar geleden

3 De volgende vragen gaan over dagelijkse bezigheden. Wordt u door uw gezondheid op dit moment beperkt bij deze bezigheden? Zo ja, in welke mate?

	ja, ernstig beperkt	**Ja, een beetje beperkt**	**Nee, helemaal niet beperkt**
a Forse inspanning zoals hardlopen, zware voorwerpen tillen, inspannend sporten	☐	☐	☐
b Matige inspanning zoals het verplaatsen van een tafel, stofzuigen, fietsen	☐	☐	☐
c Tillen of boodschappen dragen	☐	☐	☐
d Een paar trappen oplopen	☐	☐	☐
e Eén trap oplopen	☐	☐	☐
f Buigen, knielen of bukken	☐	☐	☐
g Meer dan een kilometer lopen	☐	☐	☐
h Een halve kilometer lopen	☐	☐	☐
i Honderd meter lopen			
j Uzelf wassen of aankleden	☐	☐	☐

4 Had u, ten gevolge van uw lichamelijke gezondheid, de afgelopen 4 weken één van de volgende problemen bij uw werk of andere dagelijkse bezigheden?

	ja	**nee**
a U heeft minder tijd kunnen besteden aan werk of andere bezigheden	☐	☐
b U heeft minder bereikt dan u zou willen	☐	☐
c U was beperkt in het soort werk of het soort bezigheden	☐	☐
d U had moeite met het werk of andere bezigheden (het kostte u bijvoorbeeld extra inspanning)	☐	☐

5 Had u, ten gevolge van een emotioneel probleem (bijvoorbeeld doordat u zich depressief of angstig voelde), de afgelopen 4 weken één van de volgende problemen bij uw werk of andere dagelijkse bezigheden?

	ja	**nee**
a U heeft minder tijd kunnen besteden aan werk of andere bezigheden	☐	☐

b U heeft minder bereikt dan u zou willen	☐	☐
c U heeft het werk of andere bezigheden niet zo zorgvuldig gedaan als u gewend bent	☐	☐

6 In hoeverre heeft uw lichamelijke gezondheid of hebben uw emotionele problemen u de afgelopen 4 weken belemmerd in uw normale sociale bezigheden met gezin, vrienden, buren of anderen?

helemaal niet	☐
enigszins	☐
nogal	☐
veel	☐
heel erg veel	☐

7 Hoeveel pijn had u de afgelopen 4 weken?

geen	☐
heel licht	☐
licht	☐
nogal	☐
ernstig	☐
heel ernstig	☐

8 In welke mate heeft pijn u de afgelopen vier weken belemmerd bij uw normale werkzaamheden (zowel werk buitenshuis als huishoudelijk werk)?

helemaal niet	☐
enigszins	☐
nogal	☐
veel	☐
heel erg veel	☐

9 Deze vragen gaan over hoe u zich de afgelopen 4 weken heeft gevoeld. Wilt u bij elke vraag het antwoord aankruisen dat het beste aansluit bij hoe u zich heeft gevoeld.

Hoe vaak gedurende de afgelopen 4 weken:

	voortdurend	**meestal**	**vaak**	**soms**	**zelden**	**nooit**
a voelde u zich levenslustig?	☐	☐	☐	☐	☐	☐
b voelde u zich erg zenuwachtig?	☐	☐	☐	☐	☐	☐
c zat u zo erg in de put dat niets u kon opvrolijken?	☐	☐	☐	☐	☐	☐
d voelde u zich kalm en rustig?	☐	☐	☐	☐	☐	☐
e voelde u zich erg energiek?	☐	☐	☐	☐	☐	☐
f voelde u zich neerslachtig en somber?	☐	☐	☐	☐	☐	☐
g voelde u zich uitgeblust?	☐	☐	☐	☐	☐	☐

h voelde u zich gelukkig?	☐	☐	☐	☐	☐	☐
i voelde u zich moe?	☐	☐	☐	☐	☐	☐

10) Hoe vaak hebben uw lichamelijke gezondheid of emotionele problemen gedurende de afgelopen 4 weken uw sociale activiteiten (zoals bezoek aan vrienden of naaste familieleden) belemmerd?

voortdurend	☐
meestal	☐
soms	☐
zelden	☐
nooit	☐

11) Wilt u het antwoord kiezen dat het beste weergeeft hoe juist of onjuist u elk van de volgende uitspraken voor uzelf vindt.

	volkomen juist	**grotendeels juist**	**weet ik niet**	**grotendeels onjuist**	**volkomen onjuist**
a Ik lijk gemakkelijker ziek te worden dan andere mensen	☐	☐	☐	☐	☐
b Ik ben net zo gezond als andere mensen die ik ken	☐	☐	☐	☐	☐
c Ik verwacht dat mijn gezondheid achteruit zal gaan	☐	☐	☐	☐	☐
d Mijn gezondheid is uitstekend	☐	☐	☐	☐	☐

12)Plaats voor elk onderstaand item een kruisje in het vak dat de beste beschrijving geeft van uw huidige toestand. Kies slechts één antwoord voor elk item.

Voorbeeld:

Ik hoest nooit	**0**	**1**	**2**	**3**	**4**	**5**	Ik hoest de hele tijd	

	VUL DE SCORES HIERONDER IN							**SCORE**
Ik hoest nooit	**0**	**1**	**2**	**3**	**4**	**5**	Ik hoest de hele tijd	
Ik hoest helemaal geen slijm op	**0**	**1**	**2**	**3**	**4**	**5**	Ik hoest zeer veel slijm op	
Ik heb helemaal geen beklemmend gevoel op mijn borst	**0**	**1**	**2**	**3**	**4**	**5**	Ik heb een zeer beklemmend gevoel op mijn borst	
Als ik een helling of een trap oploop, ben ik helemaal niet buiten adem	**0**	**1**	**2**	**3**	**4**	**5**	Als ik een helling of een trap oploop, ben ik erg buiten adem	
Ik ben helemaal niet beperkt in mijn huishoudelijke activiteiten	**0**	**1**	**2**	**3**	**4**	**5**	Ik ben zeer beperkt in mijn huiselijke activiteiten	
Ondanks mijn longaandoening voel ik me zeker wanneer ik het huis verlaat	**0**	**1**	**2**	**3**	**4**	**5**	Door mijn longaandoening voel ik me totaal niet zeker wanneer ik het huis verlaat	
Ik slaap vast	**0**	**1**	**2**	**3**	**4**	**5**	Door mijn longaandoening slaap ik niet vast	
Ik heb veel energie	**0**	**1**	**2**	**3**	**4**	**5**	Ik heb helemaal geen energie	
							TOTAAL SCORE:	

B. GEMOED

Meestal	☐
Vaak	☐
Af en toe, soms	☐

1. Ik voel me gespannen:

Helemaal niet ☐

2. Ik krijg een soort angstgevoel alsof er elk moment iets vreselijks zal gebeuren:

Heel zeker en vrij erg ☐
Ja, maar niet zo erg ☐
Een beetje, maar ik maak me er geen zorgen over ☐
Helemaal niet ☐

3. Ik maak me vaak ongerust:

Heel erg vaak ☐
Vaak ☐
Af en toe maar niet te vaak ☐
Alleen soms ☐

4. Ik kan rustig zitten en me ontspannen:

Zeker ☐
Meestal ☐
Niet vaak ☐
Helemaal niet ☐

5. Ik krijg een soort benauwd, gespannen gevoel in mijn maag:

Helemaal niet ☐
Soms ☐
Vrij vaak ☐
Heel vaak ☐

6. Ik voel me rusteloos en voel dat ik iets te doen moet hebben:

Heel erg ☐
Tamelijk veel ☐
Niet erg veel ☐
Helemaal niet ☐

7. Ik krijg plotseling gevoelens van panische angst:

Zeer vaak ☐
Tamelijk vaak ☐
Niet erg vaak ☐
Helemaal niet ☐

8. Ik geniet nog steeds van de dingen waar ik vroeger van genoot:

Zeker zo veel ☐
Niet zo veel als vroeger ☐
Weinig ☐
Haast helemaal niet ☐

9. Ik kan lachen en de dingen van de vrolijke kant zien:

Net zoveel als vroeger ☐
Niet zo goed als vroeger ☐
Beslist niet zoveel als vroeger ☐
Helemaal niet ☐

10. Ik voel me opgewekt:

Helemaal niet ☐
Niet vaak ☐
Soms ☐
Meestal ☐

11. Ik voel me alsof alles moeizamer gaat:

Bijna altijd ☐
Heel vaak ☐
Soms ☐
Helemaal niet ☐

Zeker ☐
Niet meer zoveel als ik zou moeten ☐

11. Ik heb geen interesse meer in mijn uiterlijk:	Waarschijnlijk niet zoveel	☐
	Evenveel interesse als vroeger	☐

12. Ik verheug me van tevoren al op dingen:

Net zoveel als vroeger = 0
Een beetje minder dan vroeger = 1
Zeker minder dan vroeger = 2
Bijna nooit = 3

Net zoveel als vroeger	☐
Een beetje minder dan vroeger	☐
Zeker minder dan vroeger	☐
Bijna nooit	☐

13. Ik kan van een goed boek genieten, of van een radio- of televisieprogramma:	Vaak	☐
	Soms	☐
	Niet vaak	☐
	Heel zelden	☐

C. PATIËNTENDOSSIER (PATIËNT, HUISARTS OF EQUIPE)

Patiëntnummer:_____
Volgnummer invullijst:_______
Datum:_________

Aantal opstoten/exacerbaties gehad in de afgelopen zes weken:___

Aantal geïnitieerde zorginterventies in de afgelopen zes weken:___

Door welke zorgverlener	Locatie (plaats + afdeling)	Reden	Gepland/ ongepland

Aantal hospitalisaties gehad in de afgelopen zes weken:_____

Door welke zorgverlener	Locatie (plaats + afdeling)	Reden	Duur (dagen)	Gepland/ ongepland

Is de wilsverklaring aangevraagd: Ja/nee

D. WAARGENOMEN KWALITEIT VAN ZORG (patiënt)

Met '<u>zorg en begeleiding</u>' wordt in deze vragenlijst ook de behandeling door uw (huis)arts bedoeld. Wanneer er '<u>hulpverlener</u>' staat, gaat het in dit geval over de (huis)arts, longarts, verpleegkundige, etc.

Toen ik in de afgelopen 6 maanden zorg en begeleiding kreeg voor gezondheidsproblemen die te maken hebben me ouder worden of met mijn ziekte…

		Nooit	**Zelden**	Soms	Meestal	Altijd	Niet van toepassing
1.	…werd er gevraagd naar mijn ideeën en verwachtingen tijdens het maken van een plan voor mijn zorg en begeleiding.	☐	☐	☐	☐	☐	☐
2.	…werden mij mogelijkheden voor zorg en begeleiding voorgelegd waaruit ik een keuze kon maken.	☐	☐	☐	☐	☐	☐
3.	…werd mij gevraagd of ik problemen heb gehad met medicijnen of met de (bij)werkingen ervan.	☐	☐	☐	☐	☐	☐
4.	…werd mij gevraagd of ik problemen heb gehad met de zorg en begeleiding of met mijn ervaringen daarmee.	☐	☐	☐	☐	☐	☐
5.	…werd mij (schriftelijke) informatie gegeven om gezond te blijven of mijn gezondheid te verbeteren.	☐	☐	☐	☐	☐	☐
6.	…werd mij uitgelegd hoe mijn eigen handelen of gedrag mijn gezondheid beïnvloedt.	☐	☐	☐	☐	☐	☐
7.	…werd mij gevraagd welke doelen ik zelf wil bereiken, in relatie tot mijn gezondheid.	☐	☐	☐	☐	☐	☐

Toen ik in <u>de afgelopen 6 maanden</u> zorg en begeleiding kreeg voor gezondheidsproblemen die te maken hebben me ouder worden of met mijn ziekte…

		Nooit	**Zelden**	Soms	Meestal	Altijd	Niet van toepassing
8.	…werd ik geholpen om specifieke doelen op te stellen om met de gevolgen van het ouder worden om te gaan.	☐	☐	☐	☐	☐	☐
9.	…werd ik schriftelijk geïnformeerd over de plannen voor mijn zorg en begeleiding.	☐	☐	☐	☐	☐	☐
10..	…werd ik aangemoedigd naar een cursus of (groeps-) activiteit te gaan die mij zou kunnen helpen om beter om te kunnen gaan met de gevolgen van het ouder worden.	☐	☐	☐	☐	☐	☐
11.	…werden mij schriftelijk of mondeling vragen gesteld over mijn leefstijl (roken, bewegen, eten, etc.).	☐	☐	☐	☐	☐	☐
12.	…was ik er zeker van dat mijn hulpverlener rekening hield met wat ik belangrijke waarden en normen vind.	☐	☐	☐	☐	☐	☐
13.	…werd ik geholpen een plan te maken zodat ik de voorgeschreven zorg en begeleiding in mijn dagelijkse leven kon toepassen.	☐	☐	☐	☐	☐	☐
14.	…werd ik geholpen plannen te maken voor het geval dat mijn gezondheid achteruit gaat of mijn situatie verslechtert.	☐	☐	☐	☐	☐	☐
15.	…werd mij gevraagd hoe de gevolgen van het ouder worden mijn leven beïnvloeden.	☐	☐	☐	☐	☐	☐
16.	…werd na een bezoek aan (of van) een hulpverlener, of na deelname aan een (groeps)activiteit, contact met mij opgenomen om te vragen hoe het met mij gaat.	☐	☐	☐	☐	☐	☐
17.	…werd ik aangemoedigd deel te nemen aan activiteiten in de buurt die mij zouden kunnen helpen.	☐	☐	☐	☐	☐	☐
18.	…werd ik doorverwezen naar een hulpverlener (zoals een fysiotherapeut of een maatschappelijk werker) of naar een (groeps-) activiteit.	☐	☐	☐	☐	☐	☐
19.	…werd mij uitgelegd waarom een bezoek aan een hulpverlener of deelname aan een (groeps)activiteit belangrijk is voor mij.	☐	☐	☐	☐	☐	☐
20.	…werd mij gevraagd hoe mijn bezoeken aan (of van) een hulpverlener, of deelname aan een (groeps)activiteit waren verlopen.	☐	☐	☐	☐	☐	☐

Heeft u nog aanvullende opmerkingen?

CHAPTER 6

Implementation of early-integrated palliative home care for end-stage COPD: recommendations for respiratory services[xi]

Scheerens, Charlotte Pype, Peter, Joos, Guy, Derom, Eric, Deliens, Luc , Chambaere, Kenneth

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[xi] Submitted

Background

According to the recent Global Burden of Disease study in 2015, chronic obstructive pulmonary disease (COPD) is increasing in prevalence and as a cause of death. 3.2 million deaths due to COPD were observed in 2015[1], with cardiovascular diseases and lung cancer as frequent comorbidities[2]. In the final years of life, pain, dyspnoea, low mood, anxiety, and sleeping problems occur[3]. Appropriate support is currently lacking[3]. Palliative care can offer symptom management and psychosocial support for these needs in COPD[4]. In 2002, the WHO also pledged to ensure that palliative care is integrated early in the disease course[5]. This means that well before the terminal phase, end-of-life preferences are discussed and palliative care is introduced in phases while respiratory services and medical therapy continue,[6] rather than having an undesirable switch from medical to palliative care[5]. This approach is recognized by the Global Initiative for COPD[3] and the European Respiratory Society[7]. Furthermore, the research by Higginson et al in 2014[8] was one of the first studies of integrated palliative and respiratory care for COPD which showed an improvement in breathlessness symptoms.

Still, the best way to implement this gradual approach in clinical practice for COPD is unknown, as research is still exploring it[5] and other trials show inconclusive or negative results[9]. What we do know is that COPD patients prefer to receive care and die at home[10]. This implies the need to focus on palliative home care (PHC) if the situation allows it. However, recent statistics show low[2,11] and late[12] referral to PHC. Health professionals do not see its benefits for COPD[12] and fear talking about PHC as this might take away hope for patients whom they consider not fully aware of the prognosis.[13,14] Therefore, the aim of this contribution is to address these concerns derived from recent multifaceted research[12,13,15], and give four recommendations for early integration of PHC in clinical practice for end-stage COPD. It is aimed at health professionals providing respiratory services for patients suffering from end-stage Chronic Obstructive Pulmonary Disease (COPD).

Methods

In the past four years, we have extensively researched early-integrated PHC for end-stage COPD, executing 1) A population study on the use and timing of palliative care for COPD as opposed to lung cancer in Flanders, Belgium[12]; 2) A full-population study of the use and timing of PHC in terms of medical resource use in the last month of life in Belgium (results forthcoming); 3) A focus group study with general practitioners and community nurses on perceived barriers to and facilitators of PHC[13]; 4) A Phase 0-I study for an early-integrated PHC trial, developed from the results of the focus groups, an explorative PHC trial literature search, COPD and palliative care expert consultations[15]; and 5) A phase II pilot trial with feasibility, acceptability and preliminary effectiveness results (results forthcoming). We also held numerous informal conversations with clinicians, PHC or COPD experts and researchers. These insights are used along with other literature as the empirical basis for the recommendations we formulate here.

Recommendations [Box 1]

Recommendation 1: systematically using criteria that reflect low functioning to identify end-stage COPD patients in need of early-integrated PHC. For example, for the inclusion of our phase II trial, we developed a set of criteria on low functioning (Box 2)[15]. The combination of GOLD III or IV with functionality criteria was well accepted among recruiting pulmonologists. The GOLD 2019 guidelines also recommend hospitalisation and exacerbation as PHC criteria[3], as does a previous PHC trial for COPD[16]. However, future research might also need to explore possibilities for criteria specifically for lung emphysema and for patients predominantly suffering from psychosocial distress[17]. In our pilot trial, 15.4% (6/39) of patients died within the six-month trial, while almost 1/4 (23.1%) died within one year. The WHO recommends starting palliative care well before the terminal phase, with referral based on needs and low functioning instead of prognostication, which is in line with our criteria.[6] With this approach, systematic applying criteria based on needs/functioning might actually solve the PHC barrier related to the unpredictability of death in COPD[18].

At systemic level, the Belgian legislator has recently changed eligibility for reimbursement of PHC costs to a combination of a negative answer to the surprise question, "would I [health professional] be surprised if my patient died within six to twelve months", and criteria of lower functioning. The criteria fit well with this legislation. Clinical practice can systematically use criteria reflecting low functioning during consultation or after hospitalisation when the patient is back in a stable situation, to identify patients with end-stage COPD who could benefit from early-integrated PHC.

Recommendation 2: Systematic introduction of PHC during consultations with end-stage COPD patients experiencing low functioning. If the patient fulfils the criteria for low functioning, this signals high PC needs[18]. PHC should be introduced systematically at least for those patients, as seen in the acceptance of it from pre-terminal COPD patients in our trial, those of Constatini et al[19] (who introduced it for every patient diagnosed with cancer) and a cancer trial review where routine screening for palliative care needs was an often-identified practice[20]. Adequate information will allow patients, in consultation with their health professional and informal carers, to decide if they want PHC. The introduction should be done carefully and only when a patient is in a stable situation (not during hospitalisation but afterward)[3]. When time slots during consultation are short[18], it might be more appropriate to organise an extra appointment.

While the patient's reaction to palliative care is often feared[13], our trial and that by Costantini et al[19] showed that when PHC is well-explained and benefits of early integration are clearly stated, patients do not link PHC with impending death. On the contrary: they find it helpful for care planning, support for breathing problems and practical aid (wheelchairs and mobile beds for example). Other terminology such as supportive care or extra care may be used, as long as this does not confuse patients about the content of care[19]. Conversation guides and communication tools can be used to initiate PHC[21]. If the patient consents, a first exploratory PHC consultation can assess their PHC needs.

Recommendation 3: Systematic communication for a structured integration of PHC in the extended care network of end-stage COPD patients. To improve integration, reports of PHC visits should be systematically shared with the general practitioner, pulmonologist, community nurse, and physiotherapist responsible for the patient. An understanding of everyone's role within the care network and communication mechanisms such as shared reports are considered a first step toward integration, referred to as linkage[22]. PHC nurses can provide information to other health professionals about symptom burden and management, disease insight, care planning, and psychosocial, spiritual and practical support as well as informal support from carers[16,23]. An accompanying action plan can help to sum up actions that need follow-up from the patient, PHC nurse, or other parties involved[15]. Depending on the patient's situation and preference, either the PHC nurse or others involved can coordinate this process. Being informed about the patient's situation can then facilitate conversations for the regular health professionals with their patients, for example about living will decisions and further care. It can also help with care alignment.

Reports should be short, however, and only contain a summary of the PHC visit, as pulmonologists and general practitioners especially have limited time to read and process them. Nevertheless, all health professionals should reserve the necessary time to read the reports and key conclusions in order for the integration of PHC to work. The presence of an integrated digital platform to share a patient file with information and reports will facilitate this implementation. Clinical practice can use this integrated patient file to read reports from PHC nurses and other health professionals, where specific tags can be addressed to the appropriate, responsible health care professional[24]. In the context of Flanders, Belgium, such platforms already exist for certain health professionals, but not for PHC professionals.

Recommendation 4: Establishing a network of structural multidisciplinary collaboration within and between hospital and home care settings. While evidence for this is scarce[5], we advocate the alignment and streamlining of care provided by the multitude of health professionals, while also involving the patient and informal caregiver. In cancer care, systematic integration of palliative care has shown benefits for quality of life[25,26]. Maddock et al[5] evaluated two integration models for COPD that resulted in better control of breathlessness. These models involved a hospital-based multidisciplinary team consisting of a palliative care physician, rehabilitation and respiratory services. The team chose the most appropriate clinician for follow-up, depending on the patient's situation.[5] Of course, organizing multidisciplinary teams in a decentralized home care setting or between hospital and home care settings is more challenging[13]. A

Polish intervention for COPD tested an integrated home care model, where the nurses, pulmonologists, social workers, priests, psychologists and home assistants involved all joined forces at meetings to discuss appropriate home care for the patients[10].

However, inviting hospital-based physicians such as a pulmonologist for meetings outside the hospital is difficult, although current digital communication technologies such as Skype provide alternative options. Involving a physiotherapist for breathing and rehabilitation advice in meetings, either on Skype or in person, could also be beneficial, as physiotherapy needs for breathing and muscle weakness are high but underused in COPD[5]. PHC nurses can only provide limited respiratory aid, such as exercises in pursed lip breathing and light physical activities. In short, clinical practice could organize one or two meetings between the PHC nurse, general practitioner, community nurse, pulmonologist and physiotherapist (on Skype if necessary) at the patient's home, to align care preferences and therapies. Depending on the patient's situation, any health professional involved could initiate the meetings.

Discussion

In this position paper, we have identified four key recommendations (Box 1) to facilitate implementation of early-integrated PHC for end-stage COPD. Successful implementation will largely depend upon certain conditions. Firstly, the inter-professional trust between respiratory specialists and PHC specialists for supporting COPD should further increase[18]. Both need to know who the other specialists are, when and how they can be contacted, and particularly what they can offer the patient. Increasing the visibility of PHC professionals in the region and organising introductory meeting opportunities with pulmonologists locally can be an option. Secondly, integration with PHC specialists will require coordination mechanisms. The hospital-based palliative care support teams, general practitioners or nurses in the Respiratory Diseases Department can function as a liaison team to bring respiratory specialists into contact with PHC specialists, align therapies and thus decrease the distance between hospital and home care settings. The preferred or required role of PHC specialists in this integrated care setting, be it providing bedside care or taking on a more advisory role, will depend on the regional or country-specific culture of care and the patient's individual situation.

Lastly, although system-level changes are not within reach of respiratory specialists, they are needed too: educational programmes that integrate palliative care within specialist courses[27], PHC training for health professionals[28], COPD skills training for PHC nurses and public awareness campaigns for the general public of what palliative care entails, PHC possibilities and of the severity of, in this case, end-stage COPD[13]. This may ease the initiation of PHC conversations, change research funding systems, professional cultures and priorities in health care[29].

Box 1 Summary of recommendations with suggestions for clinical practice

1: Systematically using criteria that reflect low functioning to signal end-stage COPD patients in need of early-integrated palliative home care (PHC):
2: Systematic introduction of PHC during consultations with end-stage COPD patients experiencing low functioning.
3: Systematic communication for a structured integration of PHC.
4: Establishing a network of structural multidisciplinary collaboration within and between hospital and home care settings for a structured integration of PHC.

Box 2 Criteria for initiating early-integrated palliative home care[15]

Inclusion criteria: GOLD III (cf. GOLD 2017) and ≥ 2 or GOLD IV (cf. GOLD 2017) and ≥ 1 of the following criteria:

- Oxygen dependent
- ≥ 3 hospitalisations for COPD in the past three years
- COPD Assessment Test scale ≥25
- Medical Research Council Scale Dyspnoea 4
- Intubation in the past year
- Non-invasive ventilation in the past year
- BMI ≤18
- New York Heart Association Functional Classification (NYHA) 3

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General discussion

Inspiration for this dissertation came from the observation that early-integrated palliative home care services for end-stage COPD are recommended by health institutes, but are underexplored in literature and underused in practice[1]. Focus was in particular on the provision of specialised multidisciplinary palliative home care teams, further referred to as palliative home care.

The aims of this dissertation were fivefold:

Aim **one** explored reasons for and implications on access to specialist palliative care services and their relationship with medical resource use.

Aim **two** was to obtain knowledge on the current context and research on early-integrated palliative home care for COPD in Flanders.

Aim **three** described the development and protocol of a pilot study for early-integrated palliative home care for end-stage COPD patients in the Flemish/Belgian standard care.

Aim **four** assessed a pilot intervention of early-integrated palliative home care team for end-stage COPD patients [using the guidelines of the Medical Research Council Phase O-II] on feasibility, acceptability and preliminary effectiveness.

Aim **five** reflected on the perspective for respiratory services regarding palliative home care for end-stage COPD.

The two Parts and chapters each provide answers to one of the five Aims and research questions (Table 1).

Table 1 Overview of corresponding parts and chapters to the five aims and research questions

Aim	*Research question*	*Part*	*Chapter*
1	1.1	1	1
	1.2	1	2
2	2.1	2	3
	2.2	2	4
	2.3	2	4
3	/	2	4
4	4.1-3	2	5
5	/	2	6

General results

Part 1 provided population-based research in response to Aim one. **Chapter 1** showed that for Flemish COPD patients (n=192), when compared to lung cancer (n=251) and whose death was expected, *treatment goals in the last weeks of life were less often aimed at palliation* (60% versus 91%), *referral was lower for all palliative care services* (37.3% to 73.5%) and *palliative home care* services (7.2% versus 35.5%); median timing of referral was closer to death (6 versus 17 days). According to physicians, non-referral was mainly due to palliative care not deemed meaningful in 36% of COPD and 18% of lung cancer. Reasons for this were an unpredictable illness trajectory and a lack of understanding the need for palliative care .

Chapter 2 studied the effect of *use and timing* of the first specialised palliative home care team referral on medical resource use in the last 30 days before death. Patients died of COPD and/or cardiovascular diseases in Belgium between 2010-2015. Only 1.1% of them used specialised palliative home care earlier than 30 days before death. This (versus not using) was associated with a decreased odds ratio for hospital (0.35) and intensive care unit (0.16) admission, contact with specialists (0.58), invasive ventilation (0.13), medical imaging (0.34), RX thorax (0.34) and sedatives (0.48) and an increase of the odds ratio for home care (3.27), contact with the GP (4.65), palliative care unit admission (2.61), non-IV (2.65), gastric tube (2.15), oxygen (2.22), opioids (4.04) including morphine (5.29) in the final 30 days of life ($p<0.001$). These differences were actually largest for those receiving palliative home care closer before death (90 and 31 days) which somehow contradicted recommendations for early palliative care. Checking disease intensity, patient and care preferences was not possible.

Part 2 evolved around Aims 2-4. **Chapter 3** showed *barriers and facilitators for early-integrated palliative home care in end-stage COPD, according to general practitioners and community nurses*. Barriers were related to the disease, patients insights, lack of interprofessional collaboration and experience with palliative COPD care, insufficient continuity of care and communication. *Facilitators* were using trigger moments, such as following a hospital admission, oxygen-dependency or being forcibly housebound, positive attitudes from informal carers, advance care planning as a proxy and enhancing communication mechanisms. The results provided insights for the key components in the intervention: therapy alignment, encouragement of disease-insight, trigger moments, and training and care coordination.

Chapter 4 pertained to Aim 2-3, presenting the theory and development (phases 0-I) of the intervention. Using the *Medical Research Council Framework*[2], a phase II nurse-led care improvement programme was developed with five components: (1) pre-inclusion training on COPD care for palliative home care nurses, (2) monthly PHC visits to the home, (3) distribution of information leaflets on coping and breathing exercises to the patients, (4) a protocol (on disease insight, symptom management and support, a care and action plan) and (5) sending a report after each palliative home care visit to all healthcare professionals involved. The inclusion criteria combined end-stage lung function (GOLD III or IV) with measures of low to very low functioning.

Part 2 continued with **Chapter 5**, testing the pilot intervention (Aim 4). This six-month pilot randomised controlled phase II trial showed that 56% (39/70) of eligible patients participated, with a 20:19 intervention-control ratio. 64% completed the trial and 80% of intervention patients had 4 palliative home care visits, predominantly focused on disease insight, symptom management and care planning. All reports were sent to the involved healthcare professionals. *Qualitative post-intervention evaluation* showed that 8 out of 10 interviewed patients were pleased, referring to the ongoing support, helpful breathing exercises and care decisions. General practitioners had doubts because of the negative connotation and eligibility criteria for palliative home care in Belgium, at the time of the study; limited to 3 months life expectancy; others thought the leaflets and the report were useful.

Preliminary effectiveness analysis between baseline and week 24 showed lower hospitalisations in the control group (p=0.03), a trend of higher perceived quality of care in the intervention group (p=0.06) and more living will decisions. Other outcomes did not differ between groups for all timing points; a clinically relevant difference was observed at week 24 for health-related quality of life in favour of the control group (in-detail results: see Chapter 5). The intervention was feasible and accepted but before moving to a Phase III-trial, enhanced coordinated care, more general practitioner involvement, better trained palliative home care nurses for end-stage COPD support beyond the terminal phase, and outcomes in line with patient goals and preferences are needed.

Finally, in the **sixth Chapter** of Part 2, I presented *four recommendations for respiratory clinical practice* linked with practical implications (Aim 5): 1) Systematic use of criteria that reflect low functioning to signalise end-stage COPD patients in need of palliative home care; 2) Systematic introduction of palliative care during consultations; 3) Systematic communication mechanisms; 4) Establishment of a structural network of multidisciplinary collaboration within and between hospital and home care settings. Conditions for implementation were interprofessional trust between respiratory and palliative care specialists, coordination mechanisms between the hospital and home settings, and system-level change such as better palliative care training and more public awareness on COPD and palliative care.

Methodological considerations

This dissertation used multiple methods to explore referral and test palliative home care. Besides a number of strengths, there are unavoidably limitations in these methods which were not addressed. In the following section, I discuss the most prominent ones and give some suggestions to address them in future research.

Retrospective research design in relation to prospective design

Part 1 retrospectively assessed the care received by patients in the last two years leading up to death. This provided insights into access to palliative care services and its relation to medical resource use at a population level. While end-of-life care research often relies on retrospective methods for several reasons, there are also a number of concerns worth mentioning. I will explain these in relation with a prospective design where researchers identify patients entering the (pre)terminal phase of disease and prospectively observe their care as time passes[3]. This method was used in Chapter 5 in the context of a phase II intervention study.

Advantages of retrospective design

First, a retrospective design allows for the *selection of a population-based sample*, used in Chapter 1. It enables a random selection or an entire population sample of decedents who died of COPD (or lung cancer) in various situations[4]. Moreover, the selection of cases is not subject to the unavoidably inaccurate physician's predictions of survival[4].

Secondly, a retrospective design *can prevent burdening the respondents*, which is a concern in prospective designs for case finding, incomplete enrolment, drop-out and maximizing follow-up rate. Persons in the last phase of their life are often unable to be interviewed or complete questionnaires, due to severe illness and a high burden of symptoms. While this burden is particularly relevant when examining patient-reported outcomes[4], it can also be related to exploring care and medical resource use as is the case in Chapter 1-2. If these had used a prospective design, people who were too ill to complete a questionnaire would have been excluded, leading to substantial bias. Still, given the focus on early-integrated palliative home care, patients were still in good enough health to participate in the intervention. However, questionnaire completion happened at the patient's home instead of by mail due to high age, reduced mobility and functional status, which led to high costs.

Thirdly, a retrospective design is in general *more efficient and less expensive than prospective* cohort studies[5]. The latter need a very extensive follow-up period since a few patients will still live for many years, while the former can measure outcomes up to death for a large sample. Especially when using administrative resources as in Chapter 2, a prospective design is not possible, as the databases collect health data after the event took place. In the intervention study, patients were followed for only six months in total. Of the two methods, the retrospective design allows for the greatest amount of useful data[6].

Disadvantages of retrospective design

First, this design might ignore the fact that resources could have been provided in a context where the health professional did not realise that the patient was entering the end-of-life phase[7]. Because medicine is practiced prospectively, a retrospective study may analyse resources in a biased way[3]. This is relevant for COPD given the unpredictable prognosis[8]. In those cases, care leading up to death would not have had an end-of-life intent. Therefore, the longer patients are examined before death, the more this can occur[9]. As a result, retrospective designs are best used when analysing care in periods very close to death, such as a few months, or when deaths were predicted.

Chapter 2 only analysed medical resources in the final month of life, but did examine palliative home care services up to two years before death. Although controlled for covariates (such as socio-demographic, care intensity and disease severity variables), the variance never surpassed 10%. This suggests that other variables, such as care preferences of patients or health professionals, might also explain the results. In contrast, the patients from the intervention were included in the current clinical practice setting. This enabled a more realistic view on their end-of-life care.

Secondly, it is often a proxy respondent who provides the data in retrospective studies. In Chapter 1, this was the health professional who signed the patient's death certificate or the treating physician. Using proxy respondents is a recurrent event in the field of palliative care research[10] and has been considered reliable (i.e. in line with the patient's judgement) for quality of services and care, functioning, physical health and cognitive status. It is less reliable for judging psychological wellbeing, such as emotional distress and low mood.[11,12] Therefore, Chapter 1 explored palliative care services and Chapter 2 medical resource use, for which the patient's judgement was not necessary.

Thirdly – and this is only relevant for the study in Chapter 1 – memory or recall biases may exist when using retrospective design[13]. These are cognitive biases influencing the content of a recalled memory or the way a memory is recalled. Physicians might not remember all care given in the final phase of life, or could have forgotten reasons for non-referral. An event such as death may trigger distortion[13] and influence how this is recalled. There is also ambiguity as to whether a memory can be recalled, especially when the event happened a long time ago. Therefore, it is advisable to ask questions shortly after the event took place, or let the respondents use memory supports such as notes[12]. There was a certain delay (maximum three months) between death and the questionnaire for the physician in Chapter 1. They may not have been able to reconstruct the full care trajectory due to a lack of knowledge on care given in other settings. To mitigate this, physicians were instructed to consult the patient's medical file.

Retrospective and prospective designs seem complementary

End-of-life care is complex and difficult to study but is important to identify deficiencies in care quality and areas of improvement. Prospective and retrospective methods identify different groups of patients and serve different goals. The prospective design is best used for research about the care given to patients who can readily be identified as having a life-limiting illness and in need of palliative care, for assessing health outcomes as done in the intervention. The retrospective approach is optimal for asking "what happens shortly before death to patients who will die?", which was done in Chapter 1-2. Both designs are complementary. Secure assessment of biases should however be explored through sensitivity analysis (secondary analysis restricting or expanding the study population) and the relative limitations of each approach should be acknowledged during reporting.[3]

Using administrative databases for analysing use of care and medical resources

Chapter 2 gave the results of a population study using administrative databases. I will reflect on this for using with a retrospective design. Firstly, by using nationwide administrative data from health insurance on all deaths over four years, the findings could be generalised to the full Belgian population. Experimental studies and surveys are more often prone to difficulties in reaching underrepresented groups and may lack the strength necessary for generalisation[14].

Secondly, the process of linking several databases enabled analysis of medical resource use while also taking into account socio-demographical confounders. This led to relevant information for designing health policy concerning access and lack of access to palliative care services in COPD.

Thirdly, when compared to data collection in intervention studies and large surveys, using administrative databases is a relatively inexpensive way to collect data for a large population without potentially causing a burden on vulnerable and sick people.[14,15] In Belgium, health insurance is obligatory and claims to provide information on 99% of the population's healthcare use[14].

There are some downsides too. First, this approach cannot analyse the relationship between specific patients or health professional preferences for the use and type of care. For example, a desire to die at home experienced by both the patient and the informal caregivers is an important predictor of home death[16]. The study in Chapter 1 also showed the influence of attitudes of health professionals to provide or refer to palliative care[17].

Secondly, end-of-life care might also be influenced by the level of severity of the disease, the intensity of care or the number of exacerbations. However, due to a lack of diagnostic information available in these databases, assessing this was impossible nor was the reason why someone was reimbursed. Belgian health insurance cannot provide information on the frequency of specialist palliative home care visits. These limitations could partly be overcome by checking a wide range of co-variates.

Lastly, to identify the cause of death in administrative databases, intermediate or associated causes of death indicated on the death certificates were used as well as a validated algorithm to identify those patients. However, it was impossible to determine the specific level of the disease from the data, since dispensing data is often the only available data in these databases and not prescription data. Although there is no standard validated algorithm, the use of pharmacy data to identify COPD patients in administrative databases was found adequate in previous studies[18].

Medical Research Council Framework for complex interventions: what is the added value?

In Part 2 (Chapter 4-5), the Medical Research Council Framework was used for developing and testing the intervention. Published in 2000[2], it has since been used for a variety of treatments, services and public health interventions[19]. It is recommended for palliative care programs[20], and has been tested for several trials [21,22]. It follows five Phases in an iterative manner (Figure 1).[22]

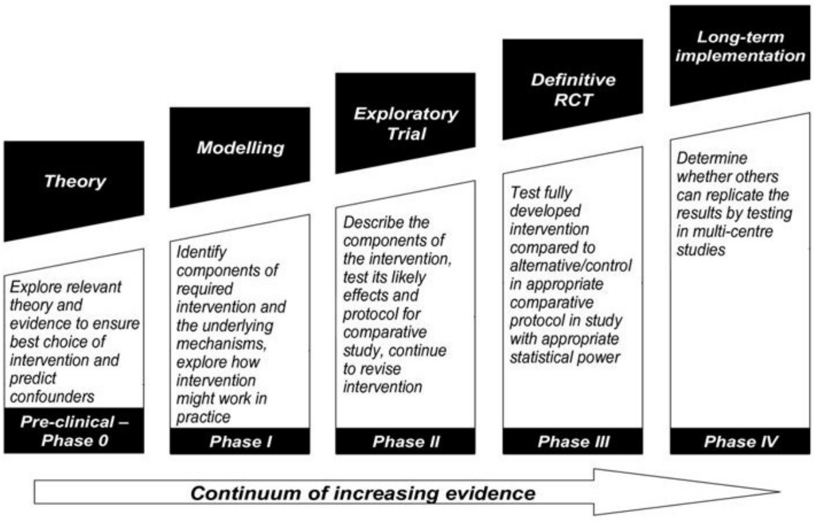


Figure 1 The Medical Research Council Framework for complex interventions[22]

Advantages of the Framework

The overall advantage was the systematic approach with a strong rationale for design and for the explicit reporting of the development process[23]. Firstly, the modelling phase provided valuable information on the detail of the structures and processes, which aided in tackling several barriers in the components; Secondly, there was an opportunity for a wide range of (international) disciplines, to feed into the design of the service. This probably helped to improve the roles of involved health professionals[22], although the integration results showed room for improvement; Thirdly, consulting Flemish experts and health professionals helped to identify local needs and determine the precise modelling within the Flemish healthcare context.

Fourthly, embarking on a preliminary evaluation in Phase II was more cost-effective than directly attempting a definitive stage III randomised controlled trial. The explorative Phase II trial allowed testing of the feasibility of the components and trial methods. This can aid selection of design, measures and calculation of sample sizes for a larger trial should this be appropriate. The results actually showed that re-evaluating components and chosen outcomes is needed.

In contrast, Tilling et al[20] advanced directly to a Phase III trial after developing a family support service, therefore potentially risking adverse effects because of the limited theoretical development. Ultimately, their Phase III did not result in the hypothesized effects. Given the number of palliative care trials that experience serious problems with recruitment, attrition and contamination[24], a detailed phase II study is thus warranted. In the development of drugs, Phase I and II studies are often given considerable attention, and findings are published in high-impact journals. It is time, perhaps, for such attention to be given to palliative service developments at Phase I and II[22].

Remarks on the Framework

In Chapter 4, the quality of the three methods used for in Phase 0 can be questioned. An explorative literature search method evaluated COPD trials and protocols. Therefore, this was only a general overview of used components and not a systematic quality evaluation. This could have biased the results. A systematic literature search as done by De Vleminck et al[0] seems preferred. Furthermore, evaluating other studies on palliative home care than trials, such as observational studies, might have enriched the results of Phase 0 too. Neither were patient's and informal carer's perspectives assessed, whereas this may have aided in fitting the intervention better to the patient's capabilities. In this light, considering explanatory qualitative research (reflecting on results from previous studies) rather than using solely exploratory interviews (exploring a hypothesis) may be an interesting option for analysing the results of the literature search.

This volatile use of methods is related to the lack of operational guidance in the five Phases. There is no fixed process on how to move from the evidence found in Phase 0 to a fully-modelled intervention in Phase I. As a consequence, the choices made in Phase I depend predominantly on the insights and the ideas of the researchers, rather than fixed guidelines. The quality of the intervention modelling Phase is thus not assured. Operationalisation of result analysis is also lacking. *Feasibility* and *acceptability* are both terms for which the literature has not yet given a consensus-based definition and strategy[25]. For example, feasibility can be assessed at program, study or site levels[26], while acceptability partly relies on the quality standards of conducting interviews with participants. As a result, studies use a variety of operational methods and strategies, which leads to unclear reporting on the quality of the intervention[27]. This is especially true for palliative home care interventions, for which successful components and outcomes are still explored[28].

Possible alternative

An alternative method is participatory action research. Hockley et al[29] have explored this relatively new method in the field of palliative care. It allows for patients, informal caregivers and practitioners to be involved in the design and set-up of an intervention. During execution, continuous feedback loops are possible, and continuous adjustments can solve practical problems. In traditional randomised controlled trials, adjustments to the design are not allowed, because of the effect it can have on the outcome results. Participatory research leaves this strict process and focuses on quality improvement and organisational change[29] instead.

Methods for the perspective article

In the last Chapter of Part 2, I presented recommendations for respiratory physicians and services. The method used was an analysis of the results of my previously conducted studies, other literature, and informal conversations with relevant stakeholders in the field of palliative home care. It was a perspective article in a series of perspective articles about integrating of palliative care[30,31].

The advantage of using this is that it allows the authors to contribute viewpoints on the interpretation of recent findings in any research area, the value of methods used, and the weaknesses and strengths of any scientific hypothesis[32]. The method also enables constructive criticism backed by evidence[32]. By doing this, it was possible to raise awareness and promote discussion on current issues concerning the topic[33] without executing another observational study.

Still, the strength of the recommendations could have been higher if we had used systematic methods that allow experts to reach consensus in a structured way. The Delphi consensus process method for guidelines is a good example[34], also applied in white papers for palliative care[35]. It allows investigators to work at a distance with a variety of target group representatives[34] and permits opinions to be consolidated into a manageable number of precise statements. It also ensures that all have an equal voice regardless of peer pressure, social status, seniority, personality, and interpersonal dynamics[34].

However, the recommendations in Chapter 6 need to be distinguished from papers with standardised guidelines as the goal was *to reflect on the relevant results of the previous studies for implementing palliative home care in clinical practice.* Developing fixed guidelines was not the intent as the evidence from the previous studies did not justify the value of fixed guidelines. Therefore, an unstructured method was sufficient in combination with statements backed by evidence.

Discussion of the results in relation to the state of affairs

Here, the results of the six studies of this dissertation will be discussed in relation to the state of affairs within existing research, policy and practice. I distinguish six overarching themes about palliative home care: low and late referral, effects on quality of life and symptoms, effects on care quality, referral criteria, mechanisms for modelling interventions, and integration of care.

Low access and late timing of specialist palliative care in Belgium

Low access to palliative care for COPD

A first important finding in Chapter 2 was that in Belgium, between 2010-2015, specialised palliative care use was low (3.0-7.2%) and was installed late (predominantly in the last two weeks of life). In Flanders, 37.3% COPD patients used palliative care services in 2012, but only those whose death was expected by the health professionals.

These results were in line with other studies on palliative care access for COPD in several countries[36–40]. A 2018 Canadian population study by Gershon et al[40] authors did see an increase of formal palliative care services from 5.3% in 2004 to 14.3% in 2014, but could not explain this evolution. They also argued that their study population were patients who previously have gotten hospitalised for COPD (and thus more access to specialised services), who were also older, predominantly female and used palliative care up until twelve months before death. The use of opioids and long-term oxygen was higher[40] than in previous studies[41], suggesting different strategies towards end-of-life care depending on the country and perhaps the view of health professionals.

Lung cancer patients receive more palliative care

When comparing with lung cancer, although both diseases exhibit a similar symptom burden at the end of life[42], referral in Chapter 1 was much lower for COPD for palliative care services (37.3% versus 73.5%) and for palliative home care (7.2% versus 35.5%). These findings again confirmed previous studies executed in the UK[42] and Canada[36]. Claessens et al[43] described in 2000 that COPD patients were more likely to die with aggressive medical interventions – as opposed to palliative care – than lung cancer patients. Our investigation in Chapter 1 also showed that treatment in the last week of life aimed at comfort and palliation was much lower for COPD (59.1% versus 92.1%).

Timing of palliative care is late

Chapter one also showed that the median *timing* of referral for COPD was six days prior to death and 17 days for lung cancer. This is low for both diseases. In Chapter 2, 63.2% of those COPD patients using palliative home care, received it merely in the last month of life. This suggests that referral to the palliative home care teams might still be seen as a comfort measure in the terminal phase, when curative and standard medical treatment are no longer appropriate[44]. This older model of palliative care focused solely on symptom-control without addressing the quality and viability of the remaining life[45].

Possible explanations

These retrospective results (Chapter 1-2 and the abovementioned literature) could not determine which patients required palliative care and left out COPD patients who died of lung cancer. Still, they seem to confirm existing evidence that palliative care largely remains associated with cancer[46]. While institutions such as The World Health Organisation[47] and GOLD[8] have been emphasizing its benefits for chronic disease such as COPD, clinical practice seems to shy away from it.

The main reasons for low and late use pointed out in the introduction were largely confirmed in the studies of Chapter 1 and 3. The majority were related to access: health professionals believe palliative home care is not meaningful for COPD, needs can be addressed in standard care providing generalist palliative care[48], lack of time or unpredictable prognosis hampers introduction or conversation on palliative home care[31]. Additionally, some reasons were connected with the patient who might not want palliative home care or is not aware of this care option[31], and has a perceived lower insight in the disease[49]. While these can explain to a large extent the low care use for COPD, it is necessary to also address system-level issues. Increasing skills and knowledge about palliative care in educational programs for health professionals and informing the public about COPD and palliative care through public awareness campaigns are often mentioned solutions[50].

The effect of early-integrated palliative home care on health-related outcomes

Chapter 5 prospectively assessed whether early-integrated palliative home care teams can affect health-related quality of life, anxiety, mood and COPD symptom-burden with an *intervention* (Box 1 and Chapter 4-5). The preliminary effectiveness results showed no overall differences with the control group. At week 24, a not-significant but clinically relevant trend in increased health-related quality of life was in favour of the control group. This is in line with inconclusive results from previous COPD pilot interventions[51–53]. Only integrated respiratory and palliative care interventions[54,55] improved patient-reported breathlessness mastery (a quality of life domain in the CRD-Questionnaire). Kavalieratos et al[56] associated specialised palliative care services with improved symptom burden, quality of life, and reduced health-care use for cancer (69.7%) and a minority for heart failure. In contrast, COPD data to assess this association are lacking. Here, I will elaborate on the briefly described reasons in Chapter 5. I distinguish five plausible explanations.

The disease fluctuates over time

Relatively stable periods are interrupted by exacerbations, impacting on symptom burden[8]. As a result, health-related quality of life or symptom burden might strongly alternate. This could explain the fluctuating results between baseline, 6, 12, 18 and 24 weeks in the intervention and the worse results at week 24. Apparently, restorative-oriented care will remain important up until death for COPD patients[53].

Health-related quality of life might be too general

Beneficial effects might depend on the individual care trajectory, context and symptom burden[52]. Still, most early palliative care trials choose this as primary outcome[52,57–60] because it is interrelated with the definition of palliative care[60]. In contrast, a recent review[28] showed that symptom burden and participant experiences were more often a primary outcome in palliative home care interventions. Symptoms can vary across COPD due to the different phenotypes[52]. As a consequence, improvement may thus be expected for specific symptoms instead of general symptom burden or health-related quality of life. Depending on the symptom, different (non-) pharmacological treatments are needed[61]. Symptom-targeting intervention have proven more successful in COPD[54,62]. Finally, there is evidence that quality of life can be mediated by the critical positivity ratio or the degree of positivity of the individual[63] showing the impact of a positive attitude.

The care improvement program did not impact enough on the patient's health outcomes

The interviews revealed that patients understood the purpose of the intervention and were actually happy to receive home visits. Drop-out rates were also low. Still, patients who are aware of the prognosis often worry about the manner of their death, and being scared of dying of breathlessness or suffocation[64]. Palliative home care nurses were ill-prepared for non-terminal COPD care and often raised concerns[52,53]. The focus of palliative care is still on cancer support[65] while COPD might require another approach. Cancer suddenly clearly worsens, whereas COPD evolves slowly[66], causing patients to adapt to their situation[66] and not fully realising the risks[67].

Hospitalisation is associated with lower health-related quality of life

Four intervention and uncontrolled patients were hospitalised between week 18 and 24. Esteban et al[68] found that hospitalisations for exacerbations of COPD impact independently and negatively on health-related quality of life. Qualitative patient interviews confirm this[69]. This can explain the lower mean of hospitalised interventions patients in week 24 and why basic physical and mental quality of life was lower for the higher amount of hospitalised control patients (physical 21.8 versus 26.5 and mental: 34.4 versus 37.2).

Quantitative scales and measurements might not assess the subtleties of improvement

Besides complaints on the amount of questionnaires, the SF-36-scale, assessing health-related quality of life, has been criticised on accuracy and validity issues for COPD[70]. Some items assessed unrealistic physical goals such as 'walking 100 meters' for the often immobile COPD patient[8]. Answering questions about the past is also difficult in this older and sick population[8] due to memory recall bias. Similar concerns are applicable for the HADS in COPD. Qualitative methods might be more suitable to assess complex and subtle improvements as well as individual context[51].

Box 1 Intervention components linked with Phase 0 results

COMPONENT 1: TRAINING IN CARE FOR PEOPLE WITH SEVERE COPD FOR PHC TEAM

Explanation of the component	***Barriers and facilitators from Chapter 3-4, addressed by the component****
Before the start of the patient inclusions, a two hour training was organised for the PHC team. The first part was given by a pulmonologist and a physiotherapist specialised in respiratory rehabilitation to inform the PHC team on care, symptom relief and support for end-stage COPD. The second part, given by the researcher (CS), taught the PHC team to work with the information leaflets (component 3) and the care protocol (component 4).	No experience in clinical practice with palliative care for COPD (focus group - barrier) Not enough focus on knowledge and advantages of palliative care for COPD in basic and continuing education (focus group-barrier) More focus on early-integrated PHC for COPD and concrete implementation in clinical practice in education for professionals (focus group facilitator) Training professionals in early identification of patients in need of palliative care and structuring advance care planning (literature)

COMPONENT 2: MONTHLY HOME VISITS BY A PHC NURSE

Explanation of the component	***Barriers and facilitators from Chapter 3-4, addressed by the component****
After the GP was brought into contact with the PHC nurse and the patient was discharged at least two weeks from hospital (if the inclusion happened during hospitalisation), the patient met the PHC nurse during a first home visit where the nurse introduced himself/herself and explained what the PHC team can do for the patient during the intervention. Following this introductory visit, the PHC nurse planned structured home visits at least once a month for a period of six months in total, the length of the study. If more adequate follow-up was needed, a higher frequency of visits could be given.	Specialised palliative care integrated with standard care (literature) Palliative status for PHC is based on prognosis in Belgium (focus group-barrier) Palliative reimbursement of PHC is restricted to 3 months (focus group-barrier) Not enough time during consultations to discuss palliative care and further care (focus group-barrier) Not discussing palliative care during consultations (focus group-barrier) Health professionals fear PHC because of the patient's reaction (focus group-barrier) Difficulties for health professionals to discuss palliative care needs with their end-stage COPD patients (focus group-barrier)

COMPONENT 3: INFORMATION LEAFLETS

Explanation of the component	***Barriers and facilitators from Chapter 3-4, addressed by the component****
During home visits, PHC nurses gave and explained the patients two information leaflets for self-management improvement derived from *the Canadian Living Well with COPD project*[71] (Dutch version used) which is part of a learning method for patients and their families. They included information on the disease and its causes, on use of medication, breathing exercises, panic distress. Titles are 'Preventing and coping with complaints' and 'Breathing and saving energy'.	Educating patients with COPD (literature) Self-management of patients with COPD (literature) Not understanding the severity of the disease or realising the possibility of death (focus group-barrier) Denial of the severity of the disease (focus group-barrier) Inform patients clearly and firmly on disease and future (focus group-facilitator) Knowledge and disease insight (expert consultations)

COMPONENT 4: CARE PROTOCOL DURING HOME VISITS

Explanation of the component	***Barriers and facilitators from Chapter 3-4, addressed by the component****
PHC nurses used a written care protocol during home visits based on a combination of components of interventions[59,72,73]. Several areas of care assessment were included: disease-insight and coping, symptom management (flagged by completing an Edmonton Symptom Assessment Scale [ESAS] and a visual representation of the human body to indicate symptom burden), care planning, support for informal carers, psychosocial support, existential/spiritual support, other non-predefined support e.g. financial, practical and administrative. A care plan containing an overview of all involved healthcare professionals. A summary of the focus areas discussed, agreed actions and the time spent on	Healthcare professional-patient communication (focus group– barrier): Not discussing palliative care (needs) during consultations Difficulties for professionals to discuss end-of-life preferences and palliative care needs Patient-relative relationship can prevent palliative care Fear of bringing up palliative care due to patient's reaction Increase knowledge about advantages of PHC for relatives of patients with COPD (focus group- facilitator) Start advance care planning as a standard procedure (focus group - facilitator) Communication between professional and patient (focus group– facilitator) Discussing practical matters to introduce palliative care Better explanation of the term PHC can help acceptance by patient Advance care planning as a part of palliative care (literature)

discussing it during the home visit could be reported in the protocol. An action plan tailored to the needs of the patient: PHC nurses defined actions during each visit for the next month, e.g. practising breathing exercises. They noted down the type of action and the relevant healthcare professional. At the next visit the nurse checked whether actions had been completed.	Self-management of patients with COPD (literature) Advance care planning as a component of palliative care (expert consultations) Psychosocial support (expert consultations) Symptom control (expert consultations) Involvement of those close to the patient (expert consultations)
COMPONENT 5: INTEGRATION OF CARE BETWEEN INVOLVED HEALTH PROFESSIONALS	
Explanation of the component	***Barriers and facilitators from Chapter 3-4, addressed by the component****
The completed protocol was sent to the pulmonologist, GP and if necessary other healthcare professionals after each visit. If the ESAS reported a symptom burden higher than 4 out of 10, PHC nurses were encouraged to seek help for symptom management from GPs or others. During visits, the PHC nurse decided with the patient if any other actions were needed and, if necessary, assigned these to others involved, with the patient's consent.	Lack of a coherent and proactive care plan (focus group barriers) No cooperation between professionals involved at home Conflicting therapy and treatment between professionals Interprofessional communication Not knowing each other well enough for proper communication Unclear who takes initiative to introduce PHC to the patient Not understanding each other's messages Communication between professionals: appoint a care coordinator who facilitates the care transition to PHC (focus group– facilitator)

*PHC: palliative home care; GP: GP; *For barriers and facilitators see Chapter 3; An overview of expert consultation information in Chapter 4, Table 3-4 and Appendix 4; An overview of the analysed intervention papers and protocols in Chapter 4, Figure 2 Appendix 2 and 3*

Inconclusive results on care quality and place of death: do we measure wrong outcomes?

Medical resource use in the final month of life

Chapter 2 showed that palliative home care was associated with less hospitalisations and extensive medical procedures and with more primary care contacts and comfort medication in the last month of life. Home or nursing home death occurred more. These results confirm a similar study for all kinds of life-limiting diseases (Maetens et al[14]), and a review of palliative home care services by Gomes et al[74] associated with a doubling of home deaths, although this was mainly for cancer. Our results also align with increased appropriate (e.g. general practitioner contact) and decreased inappropriate (e.g. chest radiograph and hospitalisations) end-of-life care[75]. More detailed results can be consulted in Chapter 2.

Earlier referral to palliative home care less impactful than expected?

In Chapter 2 however, referral to palliative home care later (90-31 days before death) showed even less extensive resource use in the last 30 days of life than earlier referral (one to two years before death). This contradicts somewhat with recommendations for earlier initiation[8,76]. Still, 'later' referral may reflect a direct transition towards symptom-only palliative care[45] for comfort measures (high opioid use). As a result, it may have been appropriate, although the database lacks data to confirm this. On the contrary, in Chapter 5, perceived care quality was higher but hospitalisations, primary care and home death did not differ between groups. Hospitalisations even occurred less in the control group. It may be that early referral associated with short periods of restorative palliative care (with a life-prolonging intent) while standard therapies are further provided[45]. This may result in a sudden unexpected death at the hospital with less comfort measures[45]. The earliest referral in Chapter 2 had more hospital deaths than those who did not receive palliative care, while the intervention patients also died more often at the hospital.

Did we measure the wrong aspects or are palliative home care nurses incapable to impact on care before (or during) the terminal phase in COPD? Some reasons are here explicated here.

Hospitalisations are too complex to assess appropriateness

The impact on hospitalisations is well-explained in Chapter 5. To sum up, the nurses were ill-prepared to provide COPD-specific support, benefits might only materialise when palliative home care was given more frequently and even earlier[77], intervention patients had unplanned life-threatening exacerbations and one entered a coma between week 18 and 24, all difficult to resolve at home[52,78] as it requires intensive treatment[78]. Moreover, lacking care alignment prevented hospital-home care collaboration whereas this is crucial during care transitions[79]. In a similar trial[51], patients often relied on the emergency room during escalating symptoms or decreased capacity to cope. Finally, in contrast with cancer[80], informal caregivers are often physically and emotionally exhausted from years of COPD-support[81]. Staying at home might then even be impossible or undesirable[80]. Of the interviewed intervention patients, many had a severely ill or immobile partner.

Patient care preferences fluctuate over time

The dynamic or unstable nature of patient preferences should not be underestimated either and is in fact a normal aspect of life[61]. In stable outpatients with end-stage COPD, about a third change their preference for life-sustaining treatments within 1 year, and two-thirds change their willingness to accept these treatments[82]. There is a tension between preferring home care and home death on the one hand[83] and being hospitalised when survival chance is high on the other hand[82]. The indicators for (in-)appropriate[75] care do not include reasons for care, which leaves room for interpretation. COPD patients often display a myriad of comorbidities[8]. It might thus be more valuable to explore the appropriateness when reasons for care are known[43], and assess the care preferences of patients[84] instead measuring quality of care without context information[51].

Oscillatory standard and palliative home care is needed before the terminal phase

Standard medical interventions and shifting care preferences will occur more often in an earlier disease phase. That is why early-integrated care interventions[59–61,85] test standard and palliative care given simultaneously. The 2000 SUPPORT-study[43] may suggest that life-sustaining interventions should remain possible until death for COPD compared to a cancer trajectory. Severe dyspnea and pain last until the final days for COPD, often worse than for lung cancer[43]. A more pharmacological implementation of palliative treatments is advised to temper these symptoms[43]. Figure 2 portrays the final years of a comorbid COPD patient, adapted from Sercu et al[45]. This shows a complex story with admissions for either COPD or comorbidities even up until death, confirming the SUPPORT-findings[43] and the hypothesis explained abovementioned. It also identifies the tensions between life-sustaining therapies and (predominantly medical) palliative care, which can occur differently depending on the patient's situation[45].

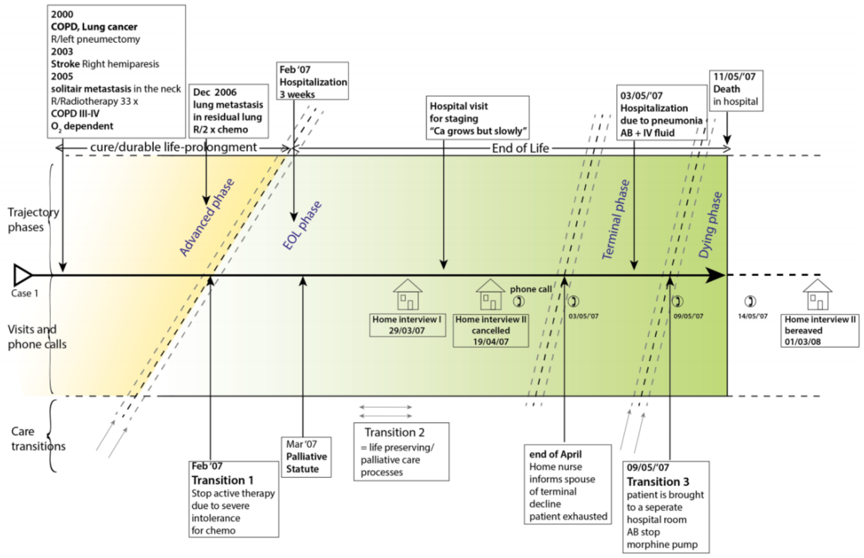


Figure 2 Phases and care transitions of the advanced-terminal illness trajectory; Case 1, male, age 77 years at the time of death, Sercu et al(2018)[45]

There is criticism that the mechanisms of early palliative care alongside standard care to streamline the transition from restorative into symptom-oriented only care[45], are not understood in the models of Lynn and Adamson[44] and Boyd[86], and barely investigated[27,45]. As a result, Sercu et al[45] concluded that the terms standard medical care (i.e. life-prolonging-oriented) and palliative do not adequately capture end-of-life care pathways due to their conceptual ambiguity. Conversely, the concept of end-of-life medical care encompassing three palliative care modalities (life-prolonging palliative therapy, restorative palliative care, and symptom-oriented [only] palliative care), each harbouring a different blend of life-prolonging and symptom-comforting aspects, proved to capture the reality of end-of-life medical care and the subtle gradations of the notion "palliative" more clearly according to the authors. Hence, they proposed a "Layered" model of (Figure 3) where care evolves in three phases. The first phase is named *life-prolonging palliative therapy*, focusing on disease-specific treatments to gain short-term life prolongation; The second is *restorative palliative care* that prioritises the function, viability, and quality of the remaining life; The third is *symptom-oriented (only) palliative care* which acknowledges death and concentrates on comfort to minimise suffering up until death.[38] These phases can run serially, simultaneously and alternatingly, depending on the patient's situation and wishes, the complexity of their chronic disease (COPD) and on the treating physicians' caring attitude. This might reflect better the clinical reality and may result in better quality of care outcomes[87]. In practice however, both health professionals and patient/family often stick to the restorative approach (seen in the Chapter 2 results where 40.9% of COPD patients received curative care in the last week of life) which may explain the Chapter 5 results. This may ultimately lead for some to preferred outcomes, but for others to inappropriate care[45]. As a result, early palliative care may function as a gatekeeper for aligning these care transitions and choosing a palliative approach which fits the patient's individual needs and context.[45] This is a challenging task for the palliative home care nurses.

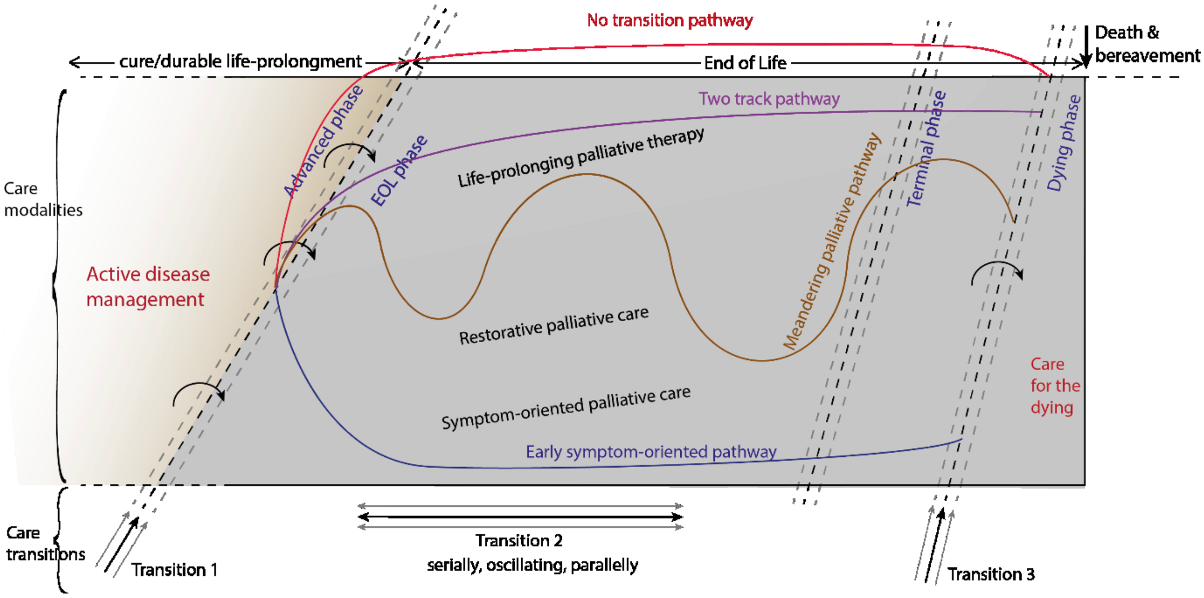


Figure 3 The "Layered" Model of End-of-Life care and the different end-of-life care pathways, Sercu et al(2018)[45]

The timing of palliative home care: Which referral criteria are needed and useful?

An important issue is identifying when and for whom palliative home care can be introduced. In Chapter 2-5, inclusion criteria (Box 1) combining GOLD III or IV with physical functionality items were well-accepted among recruiting pulmonologists. Similar criteria have been used in other research[51,73,88,89]. One similar tool (PRoPAL-COPD) for COPD was made by Duenk et al[53] who gave variable weight to different criteria (ranging from the surprise question, markers of COPD severity and co-morbidities) to predict mortality within one year during admission for an exacerbation. This one-year death prediction was used as a proxy for the potential need of palliative care and was deemed promising. The NECPAL[90] and the PICT[91] use a similar approach and distinguish frailty criteria with disease-specific indications besides emphasis on physical functioning. These tools seem valid for COPD too and it was beyond the scope of this dissertation to compare and prioritise certain tools.

Our criteria resulted in 15.4% deaths within six months and 23.1% within one year, while similar trials had lower[52] or higher[51] death rates. Our criteria thus captured a population that was not on the verge of dying, in line with recommendations for palliative care to start from diagnosis of the end-stage onwards[92]. However, the intervention only tested this for a small intervention study; attention should be made when generalising these findings for the entire COPD population. Furthermore, the World Health Organisation[92] and peer-reviewed studies[93] suggest that referral should be based on needs and low functioning instead of prognostication, which the used criteria allowed to a certain extent (although the amount of items to identify low functioning was rather low). This can solve the barrier of unpredictable death in COPD, which impedes referral according to health professionals[94].

Box 2 Inclusion and exclusion criteria

Inclusion criteria
FEV1/FVC<70% with GOLD III (FEV1 30-50% predicted[8]) and ≥ 2 or
GOLD IV (FEV1<30% predicted[8]) and ≥ 1 of the following criteria:
Oxygen-dependent[95]
≥ 3 hospitalisations for COPD in the past three years
COPD Assessment Test-scale ≥25[96]
Medical Research Council Scale Dyspnea 4
Intubation in the past year
Non-invasive ventilation in the past year
BMI ≤18
New York Heart Association Functional Classification (NYHA) 3
Exclusion criteria
Patients living outside the region Ghent-Eeklo, Flanders
Patients in the last days of life (bedbound and/or semi-comatose and/or taking only fluid and/or no longer able to take oral drugs[73])
Patients with cognitive impairment: Mini Mental Status Examination ≤23 on the day of inclusion of patients[97]
Lung cancer diagnosis
Patients with active cancer
Patients who are no longer living at home
Patients with no knowledge of Dutch
Patients with a GP already involved in this study for an intervention/control group patient

Still, these methods might be subject to criticism.[78] For example, dyspnea is not necessarily correlated to FEV_1: a patient with a predicted FEV_1 >30% can have a higher symptom burden than a patient having more severe airways obstruction[98]. Another study found that COPD patients on long-term oxygen who have never previously required intensive care admission show similar health and cognitive function as those six months after discharge for respiratory failure requiring mechanical ventilation.[99] Furthermore, physical activity and hospitalisation for an exacerbation (used in the criteria) seem effective[78], as they strongly affect mortality rates in COPD[100]. GOLD adds that palliative care should not be introduced during hospitalisation when the patient is back in a stable position[8]. Further research should dig into this deeper for COPD.

Another problem was seen in the criteria being less sensitive for identifying lung emphysema (indicated by interviewed pulmonologists), psychosocial distress[1], existential needs, and pain[65,101]. Depression for example is not associated with severity of airflow obstruction, which shows that the latter alone cannot predict palliative care needs[102]. I could not find palliative care interventions for COPD using psychosocial scales for inclusion whereas a psycho-educational trial targeting anxiety in COPD did[62]. Our criteria from the pilot intervention therefore need some adaptations.[78]

At national policy level, the Belgian legislator has recently changed eligibility for reimbursement of palliative home care costs to the PICT-scale[103]. This scale uses a negative answer on the surprise question, "would I be surprised if my patient died within six to twelve months", and criteria on the severity of frailty and disease-specific indications of palliative care needs, such as long-term oxygen or severe dyspnea for COPD[103]. Although I think the surprise question may not be relevant in the COPD population, some disease-specific criteria (focused on dyspnea) seem in line with ours. The Belgian legislator also included a list[91] to identify palliative care needs. This list encompasses besides physical needs, several psychosocial and social needs: anxiety, depression, existential disorder, psychiatric pathologies and social isolation. They may be useful to capture psychosocial distress in COPD and should be further tested.

Modelling early-integrated palliative home care: re-thinking the components?

The Phase II complex intervention in Chapter 4-5 applied specialised palliative home care (with teams experienced in terminal cancer care in Belgium) early on in end-stage COPD. Added to the arrival of the teams were reporting mechanisms with general practitioners and pulmonologists and other elements (training, leaflets, care protocol) to improve COPD-support. Modelling the intervention was difficult however. Effective palliative care models for COPD are still under debate[61] and intervention-testing is scarce[73,83]. Moreover, what "early palliative care" exactly does mean is still not clearly understood. Runacres et al[104] pointed that "early palliative care has created its own grey zone" and Yoong et al[27] noticed that a clear description of its intentions and key elements does not exist[27]. In this earlier phase, palliative care seems to be a merger between helping patients to live as actively as possible until death; while also preparing them and family for death, which demands an anticipating attitude of care[105]. The previous paragraphs showed that expecting benefits with this model for COPD is a challenge.

Five core components (Box 1) tried to address these concerns, resulting in a complex intervention structure[106]. In fact, palliative home care interventions use a variety of components: accessibility of healthcare, caregiver support, individualised care, multidisciplinary care and quality improvement[28]. Primary outcomes vary from symptom burden, resource use, reported experiences, cost analysis to a combination of all[28]. Quality of reporting the results is also moderate. This impedes generalisation whereas practice and future research need this[28]. Below, I will discuss which components were crucial, which should be re-evaluated and which were possibly lacking for effective palliative home care for COPD.

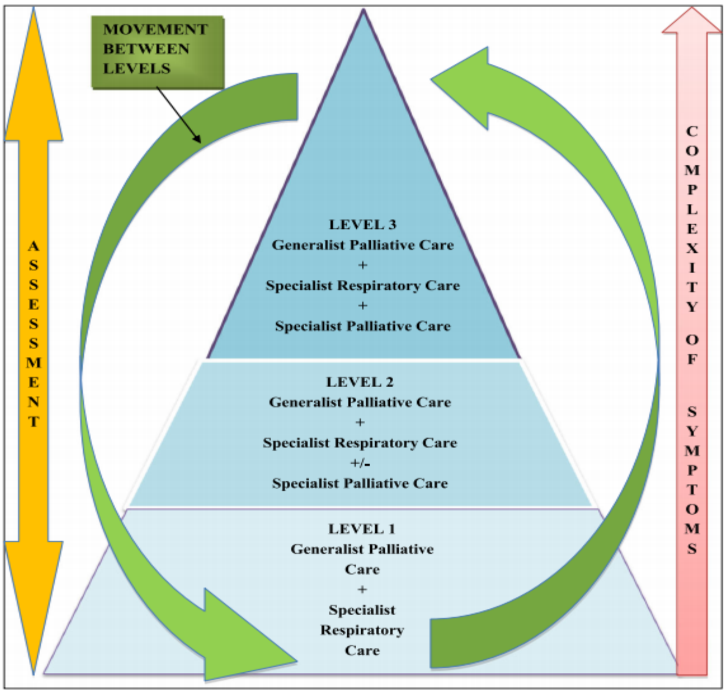
Training health professionals for early specialised and generalist palliative care

Training palliative care nurses and specialists[28] is needed as symptom-detection, disease-support, and discussing care preferences requires another approach in an earlier disease phase[53,59,107]. This can also enhance skills in non-cancer support[65], which was a barrier in the Chapter 3 results. COPD patients, often unaware about disease severity[31], may prefer different symptom management[67] or change care preferences often[108] when the last days of life are not yet in sight. The two hour training in our intervention (component 1, Box 1) was too short to skill the nurses for this. Installing several trainings and feedback moments is better[67].

Health professionals in standard care should also be trained on knowledge and skills about palliative home care, understand its effectiveness for symptom control[104] and advance care planning[109]. This seems valid for general practitioners[110] and for pulmonologists[48]. In the intervention, both accepted early palliative care but seemed unaware of palliative care options and guidelines (see Chapter 5). This was similar with Dutch findings[48]. They should thus be trained for this patient-centered approach[111]. As a consequence, 'generalist' palliative care may be explored for COPD[93], whereas current trials focus solely on specialised palliative care next to standard care[61,85]. Including both generalist and specialist palliative care can increase integrated care and impact on outcomes[112]. Veigh et al[93] proposed a model (Figure 4) where both co-interact to introduce palliative care within primary or specialist respiratory care; and refer to specialised palliative care for complex management of symptoms and needs. This model however needs further feasibility testing.

Structured and systematic palliative home care visits to allow adequate follow-up

Structural and systematic (specialist) palliative home care increases accessibility[28]. This was applied in successful trials for cancer[59,113,114], for COPD[52,53] and in our intervention (component 2, Box 1). Structured visits early in the disease trajectory give patients and their carers the opportunity to develop a long-standing relationship with palliative home care nurses as opposed to introduction in the final weeks of life[59]. Building trust requires ample time to facilitate prognostic or care discussions on patient preferences[77]. Our mean of 3.5 patient visits in six months may have been insufficient. In contrast, the nurses thought four visits sufficed for stable patients whereas the general practitioners said this was up to the patient. It might be an option to provide structured 'short-term' palliative care only when the patient needs extra support[61]. This can re-intensify and be set on hold, which is a realistic pattern in a unpredictable disease trajectory[45].



Level 1	A holistic approach to care should be introduced from diagnosis, and delivered by both generalist palliative care and specialist respiratory care providers.
Level 2	As symptom complexities increase, generalist palliative care and specialist respiratory care providers must continue to provide holistic care. However, they must also assess the need for referral to specialist palliative care providers if they feel they need support or guidance in managing the patient's symptoms.
Level 3	If the patient develops complex symptoms that generalist palliative care and specialist respiratory care providers perceive they are no longer able to effectively manage, then timely referral to specialist palliative care services is required.

Figure 4 Model of generalist and specialised palliative care for COPD, adapted with permission from Veigh et al(2018)[93]

Individualised care to address a multitude of needs in COPD

An individualised approach can address particular COPD needs and coping skills[28,52,59,72]: leaflets for disease insight[51], a care protocol prioritising symptom burden[52] and an action plan[72] to defined individual goals were tested as part of a holistic approach in Chapter 5 (component 3-4, Box 1). In contrast, other research targets particular populations with one symptom and design components to address this symptom. This happened within COPD for those with refractory breathlessness (for these interventions, see Table 2)[54] and those with anxiety[62] where cognitive-behaviour therapy[8] was applied in a home-based psycho-educative intervention. They proved successful for symptom relief[61]. However, the strength of a holistic approach, addressing multiple symptoms, is that it is applicable to all kinds of patients and can prioritise needs.[59] Ultimately, what matters are the individual goals and patients' preferences[111]. Research should explore whether symptom-targeting or holistic assessment is most effective for this.

Documentation and standardisation to improve quality of care

Quality improvement[28] can be achieved using documentation or standardised tools. In the intervention, a protocol assessed several care aspects in a standardised way (component 4, Box 1). This structured the visits by enabling a multitude of focus areas linked with concrete actions. It was a first step towards goal-oriented care[84], where patient's goals are prioritised. The added ESAS-scale also enabled conversations about anxiety, as scoring symptom burden made patients and nurses realise the impact of it.

Still, quality improvement may have been higher when all involved health professionals would have used this document[28] as seen in other interventions[51,72]. In our intervention, they solely received it afterwards as a way of information update. This also applies to the action plan, a self-management tool in COPD[72], which was less used because the nurses did not discuss actions with others involved. It was seen as a burden due to practical issues and ambiguity on the definition of an action. Documentation can only be effective when it is user-friendly, easy to implement and with understandable content for all involved[115]. It should also have a more systematic follow-up[72] via telehealth solutions, which patients accept[116].

Multidisciplinary care approach to align therapy

Finally, multidisciplinary care provision[28] can improve care integration[61]. Close collaboration between palliative home care nurses and general practitioners (for general home care and coordination)[21], respiratory services[54] and pulmonologists[61] (for lung function and standard medical care), psychologists (for lowering anxiety and depression)[59,62] or physiotherapists (for breathing and muscle exercises[28], pulmonary rehabilitation, as a part of restorative care if the patient[117]) seems promising in COPD. In Belgium, the existing community health centres could apply this approach, including a palliative care nurse. In contrast, our intervention was limited to a 'one-way' communication. Besides the recruiting pulmonologists, no other health professionals were actively involved.

Multidisciplinary functioning is difficult in Flemish home care, with the exception of Community health centers using primary care teams[118]. Testing if adding a palliative home care nurses in such primary care team is effective is an option. Recently, an Australian interdisciplinary primary care team tested a home-based prevention and rehabilitation approach for COPD[119], but reported implementation issues. Another solution lies in ad-hoc multidisciplinary consultations (at the hospital or at home) each time a serious deterioration of functioning occurs (which happened twice in the intervention). This model exists in oncology care in Belgium. An ultimate option is using telecommunication to deliberate care options while still working in separate care silo's. Integrated care is discussed in-detail in the following part.

Table 2 Intervention components of integrated care services for COPD adapted with permission from Maddocks et al(2017)[61]

	King's College Hospital Breathlessness Support Service	Cambridge Breathlessness Intervention Service
Staffing	Clinical specialist physiotherapist; clinical specialist occupational therapist; palliative care nurse; palliative care social worker; respiratory medicine consultant; palliative medical consultant	Clinical specialist occupational therapist (clinical coordinator or joint clinical lead with consultant); clinical specialist physiotherapists (one of whom also works as part of respiratory medicine department t days per week); palliative medical consultant; access to specialist psychologist
Patients seen	Patients with advanced disease that is refractory to optimal medical management and with breathlessness on exertion or at rest	Patients with any disease and who have any diagnosed cause of breathlessness who could benefit from a self-management programme
Referrals	From respiratory medicine, cardiac medicine, physiotherapy, palliative care, or primary care by an electronic record system or by letter	From any clinician in hospital or community by an electronic record system, by letter, or by phoned (if urgent)
First appointment	Typically 2–4 weeks	Typically 3–4 weeks, telephone advice might be given before first appointment
Face-to-face contacts	Two clinic visits, one home visit	Two to four home visits
Phone contacts (patient plus other care providers)	Three to four	Three to four
Average length of service contact	4 weeks	4–8 weeks
Service outcomes	Mastery of breathlessness (assessed by Chronic Respiratory Questionnaire), breathlessness severity (by Borg and Visual Analogue Scale), palliative care needs and symptoms (by Palliative Care outcome Scale and London Chest Activity of Daily Living Scale), functional exercise performance (by 6 min walk test), and carer burden (by Zarit Burden Inventory)	Anxiety, breathlessness, satisfaction with service (assessed by Numerical Rating Scales), self-report of improvement in specific areas nominated by patient
First stage or contact interventions	Respiratory medicine doctor—explore the symptom of breathlessness and its triggers, establish underlying cause of breathlessness, optimise disease-orientated management (check medications used correctly, appropriate treatments), review previous investigations, verbal and hand-written handover of notes from respiratory doctor to palliative medicine doctor to ensure patients do not have to repeat information; palliative medicine doctor—experience of breathlessness, development of crises plan, burden on patient and family, symptom burden (other than breathlessness), with recommendations to patients and the general practitioner of any appropriate treatments, psychosocial and spiritual issues, introduction of non-pharmacological measures such as the hand-held fan and water spray; other interventions include a breathlessness pack with information leaflets on managing breathlessness, a poem and chart of positions to ease breathlessness (laminated, to put up in the house and to read and follow when in acute breathlessness), fan or water spray	Multidisciplinary team decides most appropriate clinician to see patient or carer, or both—Breathing, Thinking, Functioning[60] drivers to breathlessness are prioritised after comprehensive assessment and used to set goals (initial medical assessment more common with patients with cancer or complex medical problems) and additional intervention is prioritised in line with the Breathing, Thinking, Functioning assessment or as indicated: explanation and reassurance (always); psychological support (always); hand-held fan (always); information fact sheets (subject prioritised by Breathing, Thinking, Functioning assessment); anxiety management; emergency plan; positioning to reduce work of breathing (rest, recovery, and activity); breathing control; education to patient and carer; pacing and lifestyle adjustment; assessment for and provision of mobility aids; individualised exercise plan (eg, walking with pedometer); relaxation and visualisation; airway clearance techniques; advice for nutrition and hydration; support to family and patient to use education and self-management programmes; resources to help build social contacts; advice to carer about importance of looking after their own health; sleep hygiene (always assessed); smoking cessation prompt; brief cognitive therapy; pharmacological review; wellbeing intervention; hypnosis; mindfulness CD; other resilience-building options (eg, Five Ways To Wellbeing framework)[56]
Follow-up interventions (based on the patient's need, as assessed or following review of first stage interventions)	Physiotherapist—positions to ease breathlessness, walking aid, breathing control techniques, anxiety-panic cycle aids, education on management of exacerbations, home-based programme of exercise (DVD, personalised sheet), cough minimisation techniques, pacing and fatigue management, sputum clearance techniques, ambulatory oxygen assessments; occupational therapist—assessment of daily living activities, mobility and transfers, assessment for aids and minor adoptions and referral for provision of equipment, wheelchair prescription, education on planning, pacing, and energy conservation techniques to patients and carers; social worker—carer assessment including understanding disease and symptoms, information needs and coping strategies; palliative medicine doctor—re-evaluation of breathlessness and other symptoms, check use of fan, spray, pack, DVD, and further guidance given, change recommended drugs if required with contact to doctor regarding future planned treatments if necessary, provide information on drop-in patient and family information centre for further resources	Palliative medicine consultant—further pharmacological review (eg, low-dose opioids, anti-depressants, anxiolytics); all team members—monitoring of extent to which goals set at first meeting are attained, implementation of new strategies depending on need

Documentation includes individualised letter addressed to patient (to reinforce self-management) summarising progress made, further recommendations and plan. A copy is sent to the referring clinicians and the general practitioner. The patient receives a summary of any outpatient consultation with medical consultant, the referrer receives a discharge summary with copies to the general practitioner, the specialist services the patient was already in contact with (eg, respiratory physicians), and other involved health-care professionals (eg, district nurses, nursing-home care staff). Onward referrals include pulmonary, cardiac, community or hospice rehabilitation services, specialist dietetic or psychological services, hospice day services or breathlessness services, and third-sector support services (eg, Maggie's Centres, Breathe Easy).

Table 2: Structure and components of integrated palliative care and respiratory services for patients affected by breathlessness

Do reporting and communication mechanisms represent care integration?

Linkage within an autonomous care network

In the intervention, integration was construed (component 5 in Box 1). This did not ensure advanced integration[61] as communication and collaboration was not obligatory (except sending reports). Focus was thus on information flows and reporting, the so-called first step of integration, namely *'linkage'*[120] (see Figure 3[112]). This linkage entails a basic and common understanding of the various skills of all involved professionals[121]. It means that patients are cared for in a planned system, based on an understanding of their needs, while standard and palliative home care is given simultaneously and oscillatory[121]. Still, merely adding palliative home care to standard care within a well-understood network does not assure integration.

Coordination of care to align care pathways

What is needed is the *second step of integration, 'coordination' of care* (Figure 5), defined here as "the deliberate organisation of patient care activities between health professionals care to facilitate appropriate delivery of health care services"[122]. Evidence suggests that this contributes to enhanced quality of care and efficiency performance[123]. Although some elements of the integration component (Box 1) tried to install this, this did not happen. Reasons were time constraints, technical barriers and unwillingness to collaborate. Hospital-home care interaction is also demanding[52,94] due to the physical distance[123], the lack of a common documentation system[124], unequal power distribution[123] and different care approaches[94].

A *facilitating care coordinator* was suggested in Chapter 3 and is recommended for care integration[118]; severely ill COPD patients also want this for adequate follow-up within integrated care[116] as they are most affected by insufficient cooperation due to their more comprehensive use of healthcare services[116,125]. In contrast, the intervention did not systematically implement this. Palliative home care nurses were however implicitly assigned (contacting GPs if the ESAS-scale >4), but only one installed multidisciplinary meetings with a general practitioner and community nurse to discuss future hospitalisations. In community models, nurses may play a crucial role in coordinating, delivering, and overseeing care in the home and community by working indirectly with lay community health workers[126,127].

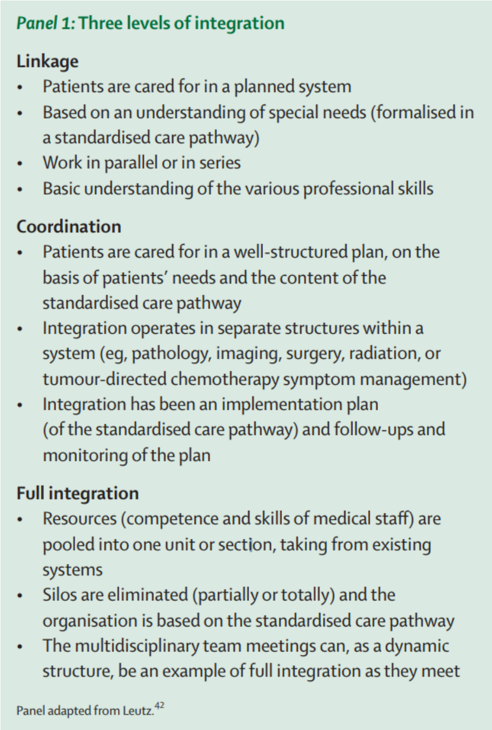
Still, palliative home care nurses operate in Belgium on a secondary care level and care for patients within a large region[128]. This can impede a liaison function in a complex COPD care network[118]. General practitioners[118] or community nurses[127] might be more realistic coordinators as they provide daily follow-up for the patient[118]. Patient preferences for one health professional, interprofessional dynamics and a regional-specific culture of care can influence the decision who the preferred coordinator is too[112]. In the context of inter-setting integration the hospital-based palliative care support teams or nurses in the Respiratory Diseases Department might also bring involved people in contact, align therapies and thus decrease the distance between hospital and home care settings.

General practitioners were not involved in the set-up phase of the trial. Collaboration thus depended on their willingness and good interaction with the palliative home care nurse. Collaboration with pulmonologists was even harder: nurses could hardly reach them, patients had shifting pulmonologists (within a team of several specialists) and pulmonologists said that collaboration between primary and palliative care is more meaningful. Community nurse collaboration was as usual, but this was already quite well established said the interviewees.

Furthermore, the sent reports did not allow for care alignment. It even resulted in a care conflict: while reading the report, a pulmonologist did not approve the wheelchair ordered by the palliative nurse for a housebound patient. The pulmonologist reasoned that this would weaken muscles and increase symptom burden, while the nurse wanted to improve mobility. Proactively discussing views for the mobility issue should have taken place[61,112]. This also shows that inter-professional trust needs improvement[94]. Increasing the visibility of palliative home care teams in the region and organising local introductory meetings (to get to know each other) with pulmonologists can be an option.

Multidisciplinary teams as the epitome of integration

Currently, although health care provision is considered a collective work, organisations tend to work autonomously in 'distinct silos'[79]. The unequal distribution of power among them is an obstacle to collaboration. Hospitals, providing most health care services and receiving most of the resources, enjoy a privileged position[123]. Primary and home care organisations depend on hospitals for many aspects of care provision; they are typically given much less resources to provide follow-up[79]. Therefore, vertical integration while care silos remain, as seen in the second level[118] may be insufficient too. When moving on to *the most complete level, 'full integration'* (Figure 5), care should be completely reorganised in a horizontal way, eliminating silos and implementing multidisciplinary teams and people-centered services[118] over different care settings[61]. Future research should test this an obligatory part of an integrated care[112].



***Panel 1:* Three levels of integration**

Linkage

- Patients are cared for in a planned system
- Based on an understanding of special needs (formalised in a standardised care pathway)
- Work in parallel or in series
- Basic understanding of the various professional skills

Coordination

- Patients are cared for in a well-structured plan, on the basis of patients' needs and the content of the standardised care pathway
- Integration operates in separate structures within a system (eg, pathology, imaging, surgery, radiation, or tumour-directed chemotherapy symptom management)
- Integration has been an implementation plan (of the standardised care pathway) and follow-ups and monitoring of the plan

Full integration

- Resources (competence and skills of medical staff) are pooled into one unit or section, taking from existing systems
- Silos are eliminated (partially or totally) and the organisation is based on the standardised care pathway
- The multidisciplinary team meetings can, as a dynamic structure, be an example of full integration as they meet

Panel adapted from Leutz.[42]

Figure 5 Three levels of integration as adapted by Kaasa et al[112] (2018) from Leutz et al[129] (1999)

Overlooked within integrated care: a goal-oriented approach?

This dissertation explored tested specialised palliative care early in the course of COPD. This was accepted, feasible and improved perceived quality of care. However, the intervention did not alter health-related outcomes and care when compared with the control group, while less hospitalisations were actually observed in the latter. Full-integration was difficult too[118]. Discussing these findings in relation to methodological limitations, barriers and facilitators, choice of outcomes and components, and the views of patients and health professionals did not render solid conclusions. The question remains: is something being overlooked in this dissertation? Or is complex COPD simply unmanageable to even expect positive outcomes?

Shifting towards an underlying goal-oriented approach

Reflecting further on possible gaps, I have identified one missing link to be the implementation of a goal-oriented care approach within the continuum of regular and palliative home care[61]. It is relevant for end-stage chronic ill and multimorbid COPD patients living at home until death[84]. In such complex situations, the classical biomedical, disease-oriented model with evidence-based guidelines on biomedical targets for clinical practice does not fit [84].

Despite admonitions of the World Health Organization[118] and others[84,130,131], the current health care system operates under the assumption that health represents the absence of health problems or symptom burden. While this has led to incredible advances in medical science[131], it may now negatively affect health care and drive up costs, while not leading to more quality or achievement of the life-goals of the patient[84]. It is less well suited to the management of chronic disease (such as COPD) and important life events (such as death and dying)[111]. It does not fully align with an interdisciplinary team approach and tends to shift control of health away from the patient and toward the health professional[131].

Redefining health in terms of patient-relevant goals

If health were redefined in terms of achieving patient-relevant goals related to function and social participation (“what matters to the patient”), emphasis would be more on prevention, meaningful activities, advance directives, personal growth and development, even in the final years or months of life. The role of patients would be elevated to goal-oriented therapeutic clinician-patient relationships (and not solely biomedical target-oriented). Reframing health in terms of achieving life-goals and directing the health care system to help people achieve them, could both improve quality and reduce costs[111]. In the process, it could also make health care less mechanic and more humane. It is more compatible with a multidisciplinary team approach[111], which is the ultimate form of integrated care[112].

Palliative care implicitly addresses patient goals

The patient-centered palliative care concept actually embodies goal-oriented care as it focuses on the (last) wishes and preferences in the ultimate stages of life instead of trying to cure the disease[92]. For example, one nurse successfully showed an intervention patient how to climb a staircase without being out of breath, using pursed-lip breathing exercises. The patient perceived this as positive, as her goal to move more freely in her own house was now within reach. Furthermore, the practice of advance care planning, where care for the future according to the patient's wishes is defined, also aligns with the approach of targeting the patient's goals[132].

The idea of goal-oriented care may have been implicitly present in our intervention given the leaflets - where goals could be noted - structured care protocol and action plan. It was also measured as goal-setting within perceived quality of care. However, it was not structurally implemented, not agreed upon with those involved professionals nor defined as an important outcome. The example (mentioned in the section on integration) about the care conflict between a pulmonologist and palliative home care nurse for ordering a wheelchair, showed that patient goals were not discussed or agreed upon. Physicians tend to focus critical choice conversations on procedures (e.g. resuscitation or feeding tube insertion) rather than on the goals, values and wishes[109].

Patient empowerment and shared health records

Standard or palliative symptom management (highly needed in the COPD population[43]) does not oppose goal-oriented care[84]. It should be used to empower the patient in reaching their individual goals instead of solely resulting in the absence of health problems[111]. De Sutter et al[84] explains that for COPD the biomedical target is an optimal FEV1. However, if the patient simply wants enough breath to be able to walk to the supermarket, reaching an optimal FEV1 might not be the primary goal.

Patient empowerment is a prerequisite for goal-oriented care[109]. Only informed and confident patients will readily elicit their personal goals[109]. This is a challenge for the older and vulnerable COPD population, who is less used to an emancipatory healthcare approach[133] and may not be able to define clear 'goals'[134] in life.

For example, Boeckxstaens et al[171] qualitatively assessed whether COPD patients are able to define their goals. The results showed that patients do not naturally present their goals. Their goals were difficult to elicit, even when different interviewing techniques were used. Four underlying hypotheses were given as possible explanations: (1) patients cannot identify with the concept of goal-setting; (2) goal-setting is reduced due to acceptation; (3) actual stressors predominate over personal goal-setting; and (4) patients may consider personal goals as selfish. Health literacy in this population is said to be lower, but it is for the general public also not easy to know which type of care is the best option[133]. Therefore, Boeckxstaens et al see a responsibility for health professionals to aid in defining goals[171] which is in particular relevant towards the end-of-life. Recognising patients as partners, and being accountable for relevant patient outcomes are important principles for health professionals.[135] Within such interaction, personal needs and context are defined, turned into objectives (one or multiple per goal) and through shared decision making, these are prioritised. Next, appropriate care is selected within the range of preventive, standard/chronic care, rehabilitation, and palliative approaches to realise the objectives. For this, tools such as action plans and certain time frames can be developed. Follow-up is assured via feedback-loops[130].

Besides needed deliberation and face-to-face communication between health professionals to structure discussions using this approach, a shared health record file with goals as the central focus is needed too[130]. Ideally, information is accessible for all involved and is shared with one singular classification system[136]. The International Classification of Functioning seems most eligible as patients and context are its central coding base[136]. It has proven valuable for COPD[136], for inter-setting communication[137], while core-sets (a summary or relevant codes) are being developed for geriatric patients[138].

Refocusing palliative care research?

While the explicit testing of the theoretical concept of goal-oriented care is quite new in the field of early-integrated palliative care, I suggest to implement it in COPD models. Within this approach, palliative home care can provide an excellent opportunity to coordinate care, decrease acute care visits, decrease cost, reduce hospital stay, and care for those with serious COPD in need of chronic disease management. An intervention can focus on the patient's goals and their relationship with care (based on available and for the patient acceptable evidence[139]) provided by standard and palliative care. Trial outcomes can assess whether the patient has achieved the goals via the intervention while knowing that preferred goals may change over time. Finally, exploring if this ultimately leads to increased health-related quality of life (the epitome of palliative care[92]) for COPD is needed.

Suggestions for future research

The findings in this dissertation highlight the necessity for more research exploring access, timing and outcomes of palliative home care models for end-stage COPD. I have several research suggestions which I will address here.

Explore reasons for low and late palliative home care in COPD

Given the low and late use of palliative home care found in Chapter 1-2, I suggest more trend analysis such as those of Gershon et al[40] for COPD in Canada and Maetens et al[14] to detect the evolution of PC access. Retrospective methods prove to be the best method. Furthermore, the reasons of use, timing and effects on medical resource use need more extensive study. The predicted variance of the results in Chapter 1-2 was low, suggesting undiscovered explaining variables. An explanatory approach, analysing retrospective population or prospective results[52] is an option. Qualitative interview studies with involved health professionals, patients and informal caregivers can further explore disease severity, context information, certain care preferences and goals of care next to newly explored reasons.

Explore the mechanisms of effective early-integrated palliative home care

The variety of components in palliative home care interventions is high[28]. Effective mechanisms are yet to be further developed[140] and tested[141], while previous reviews of respiratory interventions[142] and palliative home care trials[143] assessed outcome effectiveness but not component mechanisms. As a result, many key questions remain: How is care alignment installed within and between hospital-home care settings?[79] How may a generalist interprofessional team (general practitioners, respiratory care, physiotherapists, psychologists, social workers) integrate more effectively with specialised palliative care?[45,144] Who is the preferred care coordinator?[112,116] How is goal-oriented care implemented along the entire care pathway?[111] When goals become the primary focus of all involved in COPD care, what are the most effective symptom management options to achieve these goals?[140] Are models of palliative care for cancer applicable to COPD and other chronic illness if goal-oriented care is implemented? [45,144]

Qualitative methods with involved healthcare professionals and patients can address these questions. Next to this, there is a high demand for interventions testing novel approaches for COPD[140]. Compared with randomised controlled trials, participatory research methods that assess what works for whom and in which circumstances [29] may be a better way to test the added value of new models.

Explore the role and burden of informal caregivers within palliative care for COPD

COPD patients prefer to be cared for at home[83] and healthcare systems are shifting towards home care to limit costs and assure quality of life[81]. At home, patients rely to a great extent on informal caregivers for practical help and emotional support[81]. On the one hand, caregivers can be overprotective which may even lead to symptoms of anxiety, depression, social isolation and a changed relationship with the patient.[145] On the other hand, informal caregivers also suffer from years of COPD support and need more help[81].

The intervention in Chapter 4-5 was not designed using informal caregiver's input and the evaluation insufficiently assessed impact on them, with only a number of them included in the qualitative assessment. There is no evidence of lower caregiver burden for COPD associated with this model[51] in contrast with other care interventions for COPD[146,147] and increased caregiver satisfaction for cancer patients due to palliative care[148].

Relevant interventions should design and test components for supporting informal caregivers[149]. Both the patient and the informal caregiver should be included in the intervention through participation from the start, even in the design of the study[146]. The qualitative study of Wodskou et al[116] on integrated care from the patient and informal caregivers' perspective can serve as a basis to design these components while self-conducted interviews can assess country-specific context.

Test different care therapies for COPD and its cost-effectiveness

Finally, the impact, cost-effectiveness and safety of pharmacological and symptomatic therapies needs examination in interventions and population-based cohort studies. Our intervention and previous research[61,89,150] have identified multiple gaps to alleviate symptoms such as breathlessness within end-of-life and palliative care. [61]. This is on the one hand important for standard and palliative care specialists as pain and dyspnea tend to remain a burden until death in COPD[43]. On the other hand, knowing which therapies are appropriate for the individual context of the patient should be explored too.

Policy implications

COPD is a major cause of morbidity and mortality throughout the world[151]. Its prevalence is expected to increase in the coming decades[152], due to the ageing population, the continued exposure to known COPD risk factors (although smoking cessation is rising further), and disease-specific life-enhancing treatments[151]. Palliative care is not often given whereas needs are high[65]. Therefore, the societal and economic burden of COPD may increase.[81] Policy implications related to the societal burden of COPD and access to palliative care services can alter this expected evolution.

Elevate awareness about the benefits of early-integrated palliative care

As shown, access to palliative care is still low and is installed late in Belgium, this is similar to other countries[38,40,65]. Patients may not be fully aware of the severity of COPD and may not know what (early-integrated) palliative care can offer[31,153]. This seems compounded by the public's general lack of awareness of these palliative care services[154]. A more accurate public awareness of palliative care can aid in clarifying misperceptions on this type of care and on reducing its stigma about dying.[154] The World Health Organisation[50], The European Health Committee[155] and the United States Institute of Medicine[156] all advocate for appropriate public awareness campaigns. Our intervention and those of Costantini et al[114], actually showed that patients understand and accept early palliative if its purpose is well-explained.

Beside media campaigns, possibilities lie within meticulously designed websites. For example, the Center to Advance Palliative Care explains different aspects of palliative care on *https://www.getpalliativecare.org*. They also have a YouTube channel that hosts videos providing lay explanations on palliative care, how to access services, and patient narratives on their experiences receiving care. In San Francisco, researchers have developed another website to facilitate advance care planning decisions for patients: *https://prepareforyourcare.org/welcome.* Although no study has assessed those initiatives' impact on improving awareness, dispelling misconceptions, or increasing demand for services[154], transferability to other countries, such as Belgium, should be explored. This is a key task for administrators and politicians responsible for health affairs[50].

Address disease insight and access to care in COPD

A disproportionate burden of COPD occurs in people of low socioeconomic status[157] due to differences in health behaviours, socio-political factors, social and structural environmental exposure[8]. Not only does socioeconomic status affect the risk of developing COPD, it is also associated with worsened COPD health outcomes at the end of life[158]. In Chapter 3, health professionals indicated that some patients are less aware about the severity of COPD or do not fully realise the possibility of death. Besides increasing efforts to prevent this disease, policy makers should help to address these health inequities in low socioeconomic groups by educating the public and those involved in health care provision about COPD via multimedia resources and education programmes[159]. It is likely that the proportion of people with low health literacy is relatively high in the COPD population as they are older and have a lower socioeconomic status[133]. As a consequence, educating the public about COPD should be done in layman's terms[133].

Policy makers should also facilitate access to cost-effective and affordable health care[8]. Hospital-based care is often a burden for immobile COPD patients living in semi-urban or rural areas or for those who are financially vulnerable[118]. In contrast, increasing access to palliative (home) care can reduce unnecessary costs at the end-of-life for COPD[160] and other diseases[14], which benefits both (vulnerable) patients and overall healthcare expenses for society.

Facilitate coordinated care

The World Health Organisation has advocated a needs-based continuum of care throughout the life of chronically ill people, such as COPD[161]. Effective care coordination is however difficult[118] as currently, the organisation of the health system is still one of independent care silo's[112]. Policymakers recognise this, and are increasingly tinkering with mechanisms to integrate care activities[79]. Still, these mechanisms are not well understood[162] and "rarely identified in relevant policies"[163].

An option within the current setting is *installing an interprofessional electronic health record*[130] to facilitate information within different primary and secondary care[124]. Policy makers should enable the design and implement a patient- and goal-oriented, integrated electronic patient file[164]. However, ICT communication can also create tensions between organisations and accentuate power asymmetry in favor of secondary care[79]. As a consequence, patient health records may use one classification system (such as the ICF[137]) that is used by all involved[136]. This can allow care alignment which is important in an earlier disease phase[43].

The geographical re-organisation of primary care in 'primary care zones' in Flanders provides another opportunity to merge different care settings and improve communication with palliative home care[165]. Each primary care zone could make one (or two) palliative home care nurses responsible for this zone. Finally, the possibility to support interprofessional care teams, such as Community Health Centres in Flanders, by a palliative nurse should be explored too.

Increase palliative care skills within basic and continuing education

Basic and continuing education for health professionals should give more information and teach skills for advanced communication and palliative care[61]. A worldwide shortfall of 6000-18000 specialised palliative care nurses and physicians to meet existing palliative care demands has been estimated[166]. Due to the aging population and increased prevalence of COPD and other non-communicable diseases, this could increase with 25-47% by 2040.[152] Therefore, basic educational programmes that integrate generalist palliative care within specialist courses, i.e. for respiratory diseases, would constitute a necessary step forward[112]. Further education can offer training to increase awareness about palliative home care[50]. Emphasis should be on attitude change as palliative care is still linked with terminal care preventing early conversations about future care[112].

Increase resources for needed services

Finally, resources for palliative (home) care and research should further increase[166]. While palliative home care in Belgium is financed per capita and not consultation-based, early integration will not be encouraged under this type of financing. However, palliative care is one of the fastest growing subspecialties in medicine, and is predicted to rise when integrated models will be implemented[166]; more personnel is thus needed.

Policy makers should invest in supporting these teams while also providing adequate resources and infrastructure for better integration of it in regular (primary) care[121]. Research shows that investing in this care for chronic diseases is cost-efficient[126] and thus interesting for health policy. The Flemish and Belgian legislator could allocate resources based on value from the perspective of society and patients for a given cost (value for money) instead of providing care to reduce costs[172].

Practice implications

As briefly touched upon in the introduction of this dissertation, the future for health professionals is to provide a continuum of care from prevention to palliation[161]. This will need secure communication and coordination across the different care settings. Here, I address implications for general practitioners, respiratory professionals, community nurses and specialised palliative home care nurses, who were protagonists in this work. Implications for other health professionals are just as important, but beyond the scope of this dissertation.

Criteria of low functioning can aid palliative care referral

Clinical practice can systematically use criteria of low physical functioning developed in this dissertation to signal patients in need for early palliative home care. With these criteria, introducing palliative care options during consultation, or after hospitalisation when the patient is back in a stable situation[8] is possible. If a general practitioner has access to the clinical parameters, they can use these criteria too. In collaboration with advice from community nurses (who visit home-bound patients daily), severe deterioration can be signalised. There are several options; starting generalist palliative care themselves or arranging an introductory consultation with the specialised palliative home or hospital-based care teams. This can eliminate palliative home care use before the terminal phase and avoid the barrier of unpredictable prognosis in COPD experienced by health professionals[94].

Other, well-developed tools such as the general NECPAL[90] and the COPD-specific PRoPAL-COPD[167] may be even more sensitive for capturing lung emphysema patients, and those with more psychological or spiritual needs. It was however beyond the scope of this dissertation to compare all existing tools and knowing which one is best should be further explored. The PICT-criteria for palliative home care referral defined by the Belgian legislator in 2018 represent another tool to identify patients with low functioning and physical and psychosocial needs[103]. The surprise question in these criteria however should be interpreted allegorically: as a signalisation that the final year of life may occur in the patient[103]. An overall attention point is to not use these criteria as merely a way of ticking boxes. The patient's individual context, goals, wishes and care preferences should always be taken into account when suggesting different care pathways[84].

Apply systematic palliative home care

As discussed in this dissertation, a systematic approach of early palliative home care may be preferred above care on demand. This was applied in successful palliative care (mainly hospital-based) trials for cancer[59,113,114], for COPD[52,53] and applied by specialised nurses in our intervention. Structured and repeated generalist or specialised palliative care consultations from end-stage COPD diagnosis enable patient-health professional relationship building[59] and trust for discussions about care preferences[77]. It should be possible to also provide structured 'short-term' generalist or specialised palliative care when the patient needs extra support[61]. This can re-intensify during critical moments and be set on hold in stable periods, which is a realistic pattern in the unpredictable COPD trajectory[45].

This approach is also useful for other chronic diseases such as heart failure, following a similar disease trajectory as COPD[44]. Among the long list of comorbid conditions seen in people with COPD, cardiovascular diseases are generally perceived to be the most important[168] and are associated with an increased risk of death[169]. The typical COPD patient is just as likely to die from a cardiovascular cause as they are from a respiratory one.[170]

Let generalist and specialised palliative care interact

Appropriate and integrated standard and palliative care cannot be provided within independent care organisations[118]. Pulmonologists, general practitioners and others involved can start generalist palliative care when the patient enters an end-stage COPD phase. Simultaneously or fluctuating, specialised palliative care services, insofar as they have expertise in COPD-specific care needs, can be consulted initially for specific symptom management or complex palliative care situations[45,144]. Ultimately, this may lead to symptom-only palliative care in the last days of life[84]. All involved should embrace this interactive process according to the patient's possibilities[84].

For this to work, interprofessional trust should increase, for instance by installing introduction meetings between involved regular and palliative care teams within one region. Further steps are systematically sharing patient information, ad-hoc multidisciplinary meetings (with all involved) when a serious deterioration occurs, as done within oncology care in Belgium. This can be at the hospital if respiratory services (or other specialised services for comorbidities) need consultation, or at the patient's home (to discuss home care). Tele-solutions such as Skype can solve barriers such as time constraints and physical distance between health professionals.

Person-centered integrated care addressing needs and goals

As mentioned above, I suggest a paradigm shift towards an underlying approach of needs-based, goal-oriented person-centered care within the entire continuum of care[111]. This can tailor care more to patients' needs[84] although this will be a challenge in the older COPD population who is not used to an emancipatory care approach[134]. It should be embodied by the involved health professionals and not just merely used in shared electronic health records[130]. Multidisciplinary deliberation and care alignment between health professionals, and if possible, with the presence of the patient and informal caregiver, should be directed towards achieving personal goals future care wishes. Therapies should be selected to fulfil these individual preferences, if the situation allows it.

Finally, this dissertation and other research[114] shows that the term early-integrated "palliative care" is well-understood by the patient when explained in detail. As a consequence, reframing it as supportive care is not advised as this will ultimately lead to the same negative connotation with dying[114]. Still, when health professionals start thinking in terms of needs and goals, they may leave the current cut-offs that divide support into separate blocks of preventive, standard, and palliative care. As a result, healthcare professionals may need to use the term "palliative care" only to explain it as an appropriate approach to address certain goals and needs. These goals and needs will require different therapies, where goals at the end of life will of course be more met with a palliative approach. This would in a certain sense constitute the ultimate integration of palliative care into standard healthcare.

General conclusion

This dissertation departed from the need to explore early-integrated palliative home care for end-stage COPD in the Belgium healthcare setting and to develop a standard model for practice implementation. The population data in Part 1 revealed that Flemish and Belgian end-stage COPD patients do not use palliative care often and if they do, only very close to death, which confirms previous studies in various countries. The developed and pilot-tested intervention model in Part 2 showed that end-stage COPD patients appreciated the model of early-integrated palliative home care while most involved health professional thought it was feasible. Still, the preliminary effectiveness analysis did not render clear benefits in favour of the intervention group.

In the general discussion, reflections were made that adding COPD-specific care elements to a palliative home care model initially developed for terminal and cancer care might not fully suffice for the end-stage COPD population. A better approach might lie in starting from the patient perspective, its goals and needs, and then testing a fit-for-purpose model in line with the patient's needs.

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SUMMARIES

English summary

General introduction

This dissertation departs from the need to explore early-integrated palliative home care into standard care for end-stage Chronic Obstructive Pulmonary Disease (COPD) in Belgium. Here, the *end-stage* reflects a (very) low lung function (GOLD III or IV[1]) with high physical and psychosocial symptom burden. This high symptom burden is often unmet solely by standard medical care[2] and may lead to reduced health-outcomes in the final years of life[3.] Early-integrated palliative home care (meaning: specialised services) can provide an extra layer of support for this slow-evolving, chronic disease[4–6]. Still, COPD patients do not use palliative care often and if they do, only very close to death[7]. A standard model for practice implementation (pathway) is also lacking[4]. Here, I will try to address these issues by 1) exploring palliative home care referral in Belgium and 2) developing and testing a model for early-integrated palliative home care into standard care to increase quality of life and care for COPD.

Symptom burden for end-stage COPD patients include low mood, anxiety, sleeping disorders, dyspnoea and pain. Integrated palliative home care can offer support for these symptoms. The World Health Organisation defined palliative care in 2002 as '*An approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems of physical, psychosocial and spiritual*[8]. They emphasize the early-incorporation of it in standard care. This was based on the Trajectory Model of Lynn and Adamson[9] developed for chronic and slowly-evolving diseases such as COPD. Debate persists as to whether these models truly reflect reality. Boyd et al[10] and Sercu et al[9] suggested alterations to this model. Currently a new definition of palliative care[11] is under scrutiny for identifying health-related suffering separately from life-limiting disease as referral criterion[12].

Likewise, effective models of integrated palliative care are more often found for cancer[13–16], whereas, for COPD, results remain inconclusive[17] and effective models are under debate[4]. Palliative home care, is the preferred care for end-stage COPD patients[18] and for health systems to limit costs and improve quality of life[19]. Still, only a handful of interventions have tested early application of it for COPD, and they did not find benefits on outcomes such as quality of life and symptom-burden[20,21]. More testing is urgently needed.

Following the advice of several institutions[1,22,23] and evidence for palliative care benefits in cancer and non-cancer populations, the rationale of this dissertation is to explore early-integrated palliative home care in standard care for end-stage COPD in Belgium. With palliative home care, the specialised multidisciplinary palliative home care teams in Belgium are meant. There are five aims to answer specific research questions, which are presented below.

Aim **one** explores the reasons for and implications of access to specialist palliative care services and their relationship with medical resource use, with the following research questions:

1. What is the use and timing of palliative home care services for COPD versus lung cancer patients in Flanders? [using quantitative multivariate analysis on Flemish End-of-Life Decision data, 2013]
2. What is the effect of use and timing of palliative home care teams for COPD on medical resource use in the Belgian patient's last thirty days of life? [using quantitative multivariate analysis on Belgian Inter Mutualistic Agency population data between 2010 and 2015]

Aim **two** obtain knowledge about the current context and research on early integrated palliative home care for COPD in Flanders, with the corresponding research questions:

1. What are the barriers and facilitators for earl integration of palliative home care for end-stage COPD, according to general practitioners and community nurses? [using a qualitative method of focus group conversations]
2. What are the successful components of interventions on palliative home care and COPD? [using an explorative literature search method of palliative care interventions and protocols]
3. What are the views of experts in COPD and/or palliative care on early-integrated palliative home care for end-stage COPD? [using a qualitative method of semi-structured expert consultations]

Aim **three** describes the development of and protocol for a pilot study for early-integrated palliative home care for end-stage COPD patients in Belgian standard care.

Aim **four** assesses a pilot intervention of early-integrated palliative home care team for end-stage COPD patients [using the guidelines of the Medical Research Council Phase O-II], with the following research questions:

1. What is the feasibility of early-integrated palliative home care for end-stage COPD patients and their health professionals?
2. What is the acceptability of early-integrated palliative home care for end-stage COPD patients and their health professionals?
3. What is the preliminary effectiveness of early-integrated palliative home care on health-related quality of life and quality of care for end-stage COPD patients?

Aim **five** reflected on the perspective for respiratory services regarding palliative home care for end-stage COPD.

These aims were addressed in two Parts, the first on Population research (including Chapter 1-2), and the second on the Development and testing of an integration model (Chapter 3-6), see Table 1. The results of these Chapters are described below.

Table 1 Overview of corresponding parts and chapters to the five aims and research questions

Aim	*Research question*	*Part*	*Chapter*
1	1.1	1	1
	1.2	1	2
2	2.1	2	3
	2.2	2	4
	2.3	2	4
3	/	2	4
4	4.1-3	2	5
5	/	2	6

Part 1 Population research

Chapter 1 Comparing the use and timing of palliative care services in chronic obstructive pulmonary disease (COPD) and lung cancer: a population-based survey

Chapter 1 described *treatment goals in the last phase of life, use and timing of specialist palliative care services and reasons for non-referral in COPD and lung cancer*. It used a representative sample of deaths in 2013 (n=6871) in Flanders, Belgium of which we selected deaths from COPD (n=251) and lung cancer (n=192). For COPD, treatment goals in the last weeks of life were less often aimed at palliation and patients were less often referred to palliative care services (37.3% to 73.5%). The median timing of referral for COPD was six days prior to death and 17 days for lung cancer. Physicians whose patients had not been referred cited palliative care as not being meaningful in 36% of COPD and 18% of lung cancer cases. We concluded that while palliative care services are perceived terminal care in both diseases, there is less and later palliative care service use for COPD. This is likely to be due to the unpredictable illness trajectory and to a lack of understanding of the need for palliative care. We recommend informing the benefits of palliative care for COPD and its value in the pre-terminal phase for both diseases.

Chapter 2 Does use and timing of palliative home care have an effect on medical resource use in the last thirty days before death in COPD? A full-population retrospective study

In Chapter 2, we studied the effect of *the use and timing* of the first palliative home care referral on medical resource use in the last 30 days before death for COPD patients in Belgium. This retrospective study covered all Belgian decedents in 2010-2015 who died with COPD and had a primary cause of death of COPD or of cardiovascular diseases. With regard to the timing the results showed that 644 patients (1.1% of all people with COPD) used specialised palliative home care earlier than 30 days before death. Using palliative home care services at least once (versus not using) decreased the odds ratios for hospital (0.35) and intensive care unit (0.16) admission, contact with specialists (0.58), invasive ventilation (0.13), medical imaging (0.34), RX thorax (0.34) and sedatives (0.48) and increased the odds ratios for home care (3.27), contact with the GP (4.65), palliative care unit admission (2.61), non-IV (2.65), gastric tube (2.15), oxygen (2.22), opioids (4.04) including morphine (5.29) in the final 30 days of life ($p<0.001$). These differences were not larger for the subgroup receiving palliative home care > 360 days before death for the first time, and were actually largest for those receiving palliative home care between 90 and 31 days before death. We concluded that, for COPD, palliative home care use is strongly associated with less extensive standard medical resource use in the last 30 days before death. No clear timing effect was found, although less extensive medical resource use was mostly seen when starting up palliative home care in the final two or three months before death. We suggested that health policy and services should focus on increasing palliative home care access for COPD, while research should further explore the effect of early initiation of palliative home care for COPD.

Part 2 Developing and testing a pilot intervention

Chapter 3 “A palliative end-stage COPD patient does not exist": a qualitative study of barriers to and facilitators for early-integrated palliative home care for end-stage COPD

Chapter 3 answered showed *barriers and facilitators for early integration of palliative home care for end-stage COPD, according to general practitioners and community nurses*. The results from three focus groups with general practitioners (n=28) and four with community nurses (n=28) showed that *barriers* were related to 1) the unpredictability of COPD, 2) a perceived lack of disease insight and resistance towards care on behalf of the patient? the patient, 3) to a perceived lower insight into the complexity of the disease of some patients due to unknown reasons, 4) a certain amount of resistance towards further care of the patient, 4) lack of experience and cooperation with palliative home care on behalf of the healthcare professionals, 5) lack of education about early integration of palliative home care, 6) insufficient continuity of care from hospital to home and 7) lack of deliberation about palliative home care between professional caregivers and the person with end-stage COPD. *Facilitators* were 1) the use of trigger moments for early integration of palliative home care, such as after a hospital admission or when the person becomes oxygen-dependent or housebound, 2) positive attitudes towards palliative home care in informal carers, 3) more focus on early-integrated palliative home care in professional education, 4) implementing advance care planning in healthcare systems, and 5) enhancing communication about palliative home care. The results of this study provided insights for clinical practice and for developing key components for a phase 0-2 early-integrated palliative home care model for end-stage COPD. These are improvement of care integration, encouragement of disease-insight for a COPD person w and training of palliative home care nurses in the care for end-stage COPD.

Chapter 4 Development of a complex intervention for early-integrated palliative home care in standard care for end-stage COPD patients: A Phase 0–I study

Chapter 4 presented an overview of the theory and development (phases 0-I) of a pilot intervention on early-integrated palliative home care. Using the *Medical Research Council Framework* (ref)for the development of complex interventions, we identified core components and inclusion criteria for the intervention in phase O. This was done through an explorative literature search of interventions, expert consultations and through the seven focus groups with general practitioners and community nurses on perceived barriers to and facilitators of early integrated palliative home care for COPD (Chapter 3). In phase 1, the intervention itself, the *inclusion criteria and components* were developed and further refined by an expert panel and two expert opinions. This resulted in an intervention in form of a nurse-led care improvement programme consisting of five core components: (1) pre-inclusion training on COPD care for palliative home care nurses, (2) monthly palliative home care visits to the home, (3) distribution to the patients of information leaflets on coping and breathing exercises, (4) a protocol (on disease insight, symptom management and support, a care and action plan) and (5) a report sent to the healthcare professionals involved after each palliative home care visit. The inclusion criteria for the patients were focused on a combination of end-stage lung function (GOLD III or IV) with criteria representing low to very low functioning.

Chapter 5 Early Integrated Palliative home care and standard care for end-stage COPD patients (EPIC): A Phase II pilot RCT testing feasibility, acceptability and preliminary effectiveness

Chapter 5 presented *the feasibility, acceptability and preliminary effectiveness results* of the care improvement programme of early-integrated palliative home care for end-stage COPD (Aim 4, research question 4.1-3). During this six-month pilot randomised controlled phase II trial, we assessed health-related quality of life, quality of care and other patient-reported outcomes every six weeks. Intervention patients, informal carers, general practitioners, pulmonologists and palliative home care nurses were interviewed for a post-intervention evaluation. The results showed that 56% (39/70) of eligible patients participated, with a 20:19 intervention-control ratio. 64% completed the trial and 80% of intervention patients had 4 palliative home care visits, predominantly focusing on disease insight, symptom management and care planning.

All reports were sent to the involved healthcare professionals. Qualitative post-intervention evaluation showed that 8 out of 10 interviewed patients were pleased about the intervention, referring to the ongoing support, helpful breathing exercises and care decisions. General practitioners had doubts about integrating palliative home care early, while pulmonologists and palliative home care nurses responded positively, in particular about the leaflets and the sent report, and to a lesser account about the protocol. Preliminary effectiveness analysis showed less hospitalisations in the control group and higher perceived quality of care in the intervention group at week 24. No overall differences on other outcomes were found. This pilot study showed that an early-integrated palliative home care intervention for end-stage COPD is feasible and accepted, but did not favour outcomes for intervention group. Exploring whether palliative home care can actually benefit health-related outcomes, and re-evaluating trial design, component optimisation, measures and general practitioner involvement are needed before a phase III-trial.

Chapter 6 Implementation of early-integrated palliative home care for end-stage COPD: recommendations for respiratory services

Finally, in the sixth Chapter of Part 2, I presented *recommendations for respiratory clinical practice* regarding early-integrated palliative home care to answer aim 5. The methodology for this study was to reflect on and bring together the results of 1) all five previous studies in this dissertation, 2) informal conversations with palliative care and health professionals, patients, informal caregivers and policy workers, 3) p international literature on this topic, and 4) critical discussions with the project group consisting of sociologists, pulmonologists, and general practitioners. This resulted in four recommendations: 1) systematic use of criteria that reflect low functioning to signalize end-stage COPD patients in need of early integrated palliative home care; 2) systematic introduction of palliative home care during consultations with low functioning end-stage COPD patients; 3) systematic communication mechanisms for a structured integration of palliative home care; 4) establishment of a structural network of multidisciplinary collaboration within and between hospital and home care settings for a structured integration of palliative home care. Each recommendation was linked to practical implications. The chapter was concluded by reflecting on the conditions needed to facilitate implementation of the recommendations in practice: interprofessional trust between respiratory and palliative care specialists, coordination mechanisms between the hospital and home settings, and system-level change such as better palliative care training for health professionals and more public awareness about the severity of COPD and the advantages of palliative care.

General discussion

The final and third part of this dissertation presents a general discussion with methodological considerations, a reflection on the results and implication for research, policy and practice.

Methodological considerations

Retrospective research design in relation to prospective design

Part 1 retrospectively assessed care in the last two years leading up to death. I will explain these in relation with a prospective design[24] used in Chapter 5. Advantages are 1) it allows for the *selection of a population-based sample*; 2) *it removes the burden from the respondents*, which is a concern in prospective designs for case finding, incomplete enrolment, drop-out and maximizing follow-up rate; 3) it is in general *more efficient and less expensive than prospective* cohort studies[25]. Disadvantages are 1) that this might ignore the fact that resources could have been provided in a context where the health professional did not realise that the patient was entering the end-of-life phase[26]; 2) it is often a proxy respondent who provides the data in retrospective studies; 3) memory or recall biases may exist when using retrospective design[27]. To conclude, the prospective design is best used for research about the care given to patients who can readily be identified as having a life-limiting illness. The retrospective approach is optimal for asking "what happens shortly before death to patients who will die?"

Using administrative databases for analysing use of care and medical resources

The advantages are 1) the findings could be generalised to the full Belgian population; and 2) that it enabled analysis of medical resource use while also taking into account socio-demographical confounders. Disadvantages are 1) this could not analyse the relationship that might develop between specific patient or health professional preferences for the use and type of care; 2) end-of-life care might also be influenced by the level of severity of the disease, the intensity of care or the number of exacerbations; and 3) it was impossible to determine the specific level of the disease from the data.

Medical Research Council Framework for complex interventions: what is the added value?

The overall advantage was the systematic approach with a strong rationale for design and for the explicit reporting of the development process[28]. Firstly, the modelling phase provided information on the detail of the structures and processes; Secondly, a wide range of (international) disciplines feed into the design of the service. Thirdly, consulting Flemish experts and health professionals helped to identify local needs within the Flemish healthcare context. Fourthly, embarking on a preliminary evaluation in Phase II was more cost-effective. Disadvantages are 1) the quality of the three methods used for in Phase 0 can be questioned; and 2) There is no fixed process on how to move from the evidence found in Phase 0 to a fully-modelled intervention in Phase I. Possible alternatives are the use of participatory action research[29].

Methods for the perspective article

In the last Chapter of Part 2, I presented recommendations for respiratory physicians and services. It was a perspective article[30,31]. The advantage is that it allows to contribute viewpoints on the interpretation of recent findings in any research area[32]. It enables constructive criticism backed by evidence[32] without executing another observational study.[33] Still, the strength could have been higher if we had used systematic methods that allow experts to reach consensus in a structured way such as The Delphi consensus process method[34]. However, the goal was *to reflect on the relevant results of the previous studies for implementing palliative home care in clinical practice.*

Discussion of the results in relation to the state of affairs

Low access and late timing of specialist palliative care in Belgium

These results were in line with other studies on palliative care access for COPD in several countries[35–39]. Lung cancer patients received more palliative care. These findings again confirmed previous studies carried out in the UK[40] and Canada[35]. Timing of palliative care is late. This suggests that referral to the palliative home care teams might still be seen as a comfort measure in the terminal phase, when curative and standard medical treatment are no longer appropriate[9]. Possible explanations are that health professionals think palliative home care is not meaningful for COPD, needs can be addressed in standard care providing generalist palliative care[41], lack of time or unpredictable prognosis hampers introduction or conversation on palliative home care[31]. Additionally some reasons were connected with the patient who might not want palliative home care or is not aware of this care option[31],and has a perceived lower insight in the disease[42]. Increasing skills and knowledge about palliative care in educational programs for health professionals and informing the public about COPD and palliative care through public awareness campaigns are often mentioned solutions[43].

The effect of early-integrated palliative home care on health-related outcomes: unforeseen results

Here, I will elaborate on the briefly described reasons in Chapter 5 for the inconclusive results of the intervention between intervention and control group on health-related outcomes: 1)The disease fluctuates over time. Relatively stable periods are interrupted by exacerbations, impacting on symptom burden[1]. As a result, health-related quality of life or symptom burden might strongly alternate; 2) Health-related quality of life might be too general. Beneficial effects might depend on the individual care trajectory, context and symptom burden[21]; 3) The care improvement program did not impact enough on the patient's health outcomes; 4) Four intervention and uncontrolled patients were hospitalised between week 18 and 24. Esteban et al[44] found that hospitalisations for exacerbations of COPD impact independently and negatively on health-related quality of life; and 5) Qualitative methods might be more suitable to assess complex and subtle improvements as well as individual context[20].

Inconclusive results on care quality and place of death: do we measure wrong outcomes?

Chapter 2 showed that palliative home care was associated with less hospitalisations and extensive medical procedures and with more primary care contacts and comfort medication in the last month of life, in line with Maetens et al[45] and Gomes et al[46]. In

Chapter 2 however, referral to palliative home care later (90-31 days before death) showed even less extensive resource use in the last 30 days of life than earlier referral (one to two years before death). Did we measure the wrong aspects or are palliative home care nurses incapable to impact on care before (or during) the terminal phase in COPD? Some reasons are here explicated here: 1) Hospitalisations are too complex to assess appropriateness; 2) Patient care preferences fluctuate and it may be more appropriate to assess reasons of care instead of care as such; 3) Standard and palliative home care before the terminal phase is needed, where standard care (such as hospitalisations) can remain important for the patient.

The timing of palliative home care: Which referral criteria are needed and useful?

An important issue is identifying when and for whom palliative home care can be introduced. In Chapter 2-5, inclusion criteria combining GOLD III or IV with physical functionality items were well-accepted among recruiting pulmonologists. The NECPAL[47] and the PICT[48] use a more elaborate approach and distinguish frailty criteria with disease-specific indications besides emphasis on physical functioning. Still, The World Health Organisation[8] and research[49] suggest that referral should be based on needs and low functioning instead of prognostication, which our criteria allowed to a certain extent. The criteria were for example less sensitive for identifying lung emphysema (indicated by interviewed pulmonologists), psychosocial distress[50], existential needs, and pain[2,51]. At national policy level, the Belgian legislator has recently changed eligibility for reimbursement of palliative home care costs to the PICT-scale[52] and included a list[48] to identify palliative care needs. This list encompasses besides physical needs, several psychosocial and social needs: anxiety, depression, existential disorder, psychiatric pathologies and social isolation. They may be useful to capture psychosocial distress in COPD and should be further tested.

Modelling early-integrated palliative home care: re-thinking the components?

Effective palliative care models for COPD are still under debate[4] and intervention-testing is scarce[18,53]. Moreover, what "early palliative care" means is still not clearly understood. Five core components (Chapter 5) tried to address these concerns, resulting in a complex intervention structure[54]. Following core elements seem important to include in components on early-integrated palliative home care: 1) Training health professionals for early specialised and generalist palliative care; 2) Structured and systematic palliative home care visits to allow adequate follow-up; 3) Individualised care to address a multitude of needs in COPD; 4) Documentation and standardisation to improve quality of care, and 5) Multidisciplinary care approach to align therapy.

Do reporting and communication mechanisms represent care integration?

In the intervention, integration was construed (component 5 in Box 1). This did not ensure advanced integration[4] as communication and collaboration was not obligatory (except sending reports). Focus was thus on information flows and reporting, the so-called first step of integration, namely *'linkage'*[55]. What is needed is the *second step of integration, 'coordination' of care*, defined here as "the deliberate organisation of patient care activities between health professionals care to facilitate appropriate delivery of health care services"[56]. A *facilitating care coordinator* was suggested in Chapter 3 and is recommended for care integration[57]. In contrast, the intervention did not systematically implement this. Palliative home care nurses were however implicitly assigned (contacting GPs if the ESAS-scale >4), but only two multidisciplinary meetings with a general practitioner and community nurse took place to discuss future hospitalisations. Still, palliative home care nurses operate in Belgium on a secondary care level and care for patients within a large region[58]. This can impede a liaison function in a complex COPD care network[57]. Still, vertical integration while care silos remain, as seen in the second level[57] may be insufficient too. When moving on to *the most complete level, 'full integration'*, care should be completely re-organised in a horizontal way, eliminating silos and implementing multidisciplinary teams and people-centred services[57] over different care settings[4]. Future research should test this an obligatory part of an integrated care[59].

Overlooked within integrated care: a goal-oriented approach?

I have identified one missing link to be the implementation of a goal-oriented care approach within the continuum of regular and palliative home care[4]. It is relevant for end-stage chronic ill and multimorbid COPD patients living at home until death[60]. In such complex situations, the classical biomedical, disease-oriented model with evidence-based guidelines on biomedical targets for clinical practice does not fit [60]. The patient-centred palliative care concept actually embodies goal-oriented care as it focuses on the (last) wishes and preferences in the ultimate stages of life instead of trying to cure the disease[8]. I suggest to implement it in COPD models. Within this approach, palliative home care can provide an excellent opportunity to coordinate care, decrease acute care visits, decrease cost, reduce hospital stay, and care for those with serious COPD in need of chronic disease management.

Suggestions for future research

Explore reasons for low and late palliative home care in COPD

Explore the mechanisms of effective early-integrated palliative home care

Explore the role and burden of informal caregivers within palliative care for COPD

Test different care therapies for COPD and its cost-effectiveness

Policy implications

Elevate awareness about the benefits of early-integrated palliative care

Address disease insight and access to care in COPD

Facilitate coordinated care

Increase palliative care skills within basic and continuing education

Increase resources for needed services

Practice implications

Criteria of low functioning can aid palliative care referral

Apply systematic palliative home care

Let generalist and specialised palliative care interact

Person-centred integrated care addressing needs and goals

Nederlandstalige samenvatting

Algemene inleiding

Dit proefschrift ging uit van de noodzaak om vroegtijdig geïntegreerde palliatieve thuiszorg te onderzoeken in de standaardzorg bij vergevorderd chronisch obstructief longlijden (COPD) in België. *Vergevorderd* weerspiegelt hier een (zeer) lage longfunctie (GOLD III of IV[1]) met een zware fysieke en psychosociale symptoombelasting. Deze zware symptoomlast kan in de laatste levensjaren leiden tot verminderde gezondheidsuitkomsten[2] en wordt door medische zorg alleen onvoldoende ondersteund[3]. Vroeg geïntegreerde palliatieve thuiszorg (d.w.z.: gespecialiseerde diensten) kan een extra laag van ondersteuning bieden voor deze langzaam evoluerende, chronische ziekte[4-6]. Toch maken COPD patiënten niet vaak gebruik van palliatieve zorg en als ze dat wel doen, is het heel dichtbij de dood[7]. Ook ontbreekt een standaardmodel voor de toepassing in de praktijk[4]. In dit doctoraat probeer ik deze problemen aan te pakken door 1) het onderzoeken van palliatieve thuiszorg in België en 2) het ontwikkelen en testen van een model voor vroeg geïntegreerde palliatieve thuiszorg in de standaardzorg om de kwaliteit van leven en zorg voor COPD te verhogen.

De symptomen van patiënten in het eindstadium van COPD zijn onder meer een zwaar gemoed, angst, slaapstoornissen, ademhalingsproblemen en pijn. Geïntegreerde palliatieve thuiszorg kan ondersteuning bieden voor deze symptomen. De Wereldgezondheidsorganisatie definieerde palliatieve zorg in 2002 als *'Een aanpak die de levenskwaliteit van patiënten en hun families met levensbedreigende ziekten verbetert door het voorkomen en verlichten van lijden door middel van vroegtijdige identificatie en een onberispelijke beoordeling en behandeling van pijn en andere problemen van fysieke, psychosociale en spirituele'*[8]. Zij leggen de nadruk op de vroege integratie ervan in de standaardzorg. Dit was gebaseerd op het Trajectiemodel van Lynn en Adamson[9] dat werd ontwikkeld voor chronische en langzaam ontwikkelende ziekten zoals COPD. Toch blijft het debat over de vraag of deze modellen de werkelijkheid werkelijk weerspiegelen. Boyd et al[10] en Sercu et al[9] stelden wijzigingen in dit model voor, terwijl een nieuwe definitie van palliatieve zorg[11] onder vuur ligt gezien het lijden in plaats van levensbedreigende ziekten als verwijzingscriterium gebruikt[12].

Ook worden er vaker effectieve modellen van geïntegreerde palliatieve zorg uitgewerkt voor kanker[13-16], terwijl de resultaten voor COPD onduidelijk blijven[17] en effectieve modellen nog niet gevonden zijn[4]. (Palliatieve) thuiszorg geniet de voorkeur van patiënten met vergevorderde COPD[18] terwijl gezondheidszorgsystemen dit verkiezen om de kosten te beperken en de kwaliteit van leven te verbeteren[19]. Toch heeft slechts een handvol interventies de vroege toepassing ervan voor COPD getest en geen grote voordelen gevonden op levenskwaliteit en symptoombelasting[20,21]. Er is dringend behoefte aan meer onderzoek om dit verder uit te werken.

Volgens het advies van verschillende instellingen[1,22,23] en aangetoonde effectiviteit van palliatieve zorg bij kanker- en niet-kankerpopulaties, wordt hier vroeg geïntegreerde palliatieve thuiszorg in de standaardzorg voor eindstadium COPD in België onderzocht. Met palliatieve thuiszorg worden de gespecialiseerde multidisciplinaire palliatieve thuiszorgteams in België bedoeld. Dit proefschrift heeft vijf doelstellingen om specifieke onderzoeksvragen te beantwoorden, die hieronder worden gepresenteerd.

Doelstelling één onderzoekt de redenen en implicaties van toegang tot gespecialiseerde palliatieve zorgdiensten en hun relatie met het gebruik van medische hulpmiddelen, met de volgende onderzoeksvragen:

> 1) Wat is het nut en de timing van palliatieve thuiszorg voor COPD versus longkankerpatiënten in Vlaanderen? [gebruikmakend van kwantitatieve multivariate analyse bij Vlaamse gegevens over het einde van het leven, 2013].
>
> 2) Wat is het effect van het gebruik en de timing van palliatieve thuiszorgteams voor COPD op het gebruik van medische hulpmiddelen in de laatste dertig dagen van het leven van de Belgische COPD-patiënt? [met behulp van kwantitatieve multivariate analyse van de bevolkingsgegevens van het Belgische InterMutualistisch Agentschap tussen 2010 en 2015].

Doelstelling twee is kennis verwerven over de huidige context en onderzoek naar vroege geïntegreerde palliatieve thuiszorg voor COPD in Vlaanderen, met de bijbehorende onderzoeksvragen:

> 1) Wat zijn de drempels en kansen voor de vroege integratie van palliatieve thuiszorg in de eindfase van COPD, volgens huisartsen en buurtverpleegkundigen? [met behulp van een kwalitatieve methode van focusgroepgesprekken].
>
> 2) Wat zijn de succesvolle componenten van interventies over palliatieve thuiszorg en COPD? [Met behulp van een verkennende literatuurstudiemethode van palliatieve zorginterventies en -protocollen].
>
> 3) Wat zijn de opvattingen van deskundigen op het gebied van COPD en/of palliatieve zorg over vroeg geïntegreerde palliatieve thuiszorg voor COPD in het eindstadium? [met behulp van een kwalitatieve semi-gestructureerde interviews met deskundigen].

Doelstelling drie beschrijft de ontwikkeling van en het protocol voor een pilootstudie voor vroeg geïntegreerde palliatieve thuiszorg in de Belgische standaardzorg voor vergevorderde COPD-patiënten

Doelstelling vier beoordeelt een pilootinterventie van een vroeg geïntegreerd palliatief thuiszorgteam voor vergevorderde COPD-patiënten [volgens de richtlijnen van de Medical Research Council Phase O-II], met de volgende onderzoeksvragen:

1) Wat is de haalbaarheid van vroeg geïntegreerde palliatieve thuiszorg voor vergevorderde COPD patiënten en de betrokken zorgverleners?

2) Wat is de aanvaardbaarheid van vroeg geïntegreerde palliatieve thuiszorg voor vergevorderde COPD patiënten en de betrokken zorgverleners?

3) Wat is de inleidende doeltreffendheid van vroeg geïntegreerde palliatieve thuiszorg op gezondheidsgerelateerde levenskwaliteit en kwaliteit van zorg voor vergevorderde COPD patiënten?

Doelstelling vijf ontwikkelde doelstellingen over palliatieve thuiszorg voor vergevorderde COPD voor longdiensten.

Deze doelstellingen worden behandeld in twee delen, het eerste over bevolkingsonderzoek (inclusief hoofdstuk 1-2), en het tweede over de ontwikkeling en het testen van een integratiemodel (hoofdstuk 3-6), zie tabel 1. De resultaten van deze hoofdstukken worden hieronder beschreven.

Tabel 1 Overzicht van de onderdelen en hoofdstukken van de vijf doelstellingen en onderzoeksvragen

Aim	*Research question*	*Part*	*Chapter*
1	1.1	1	1
	1.2	1	2
2	2.1	2	3
	2.2	2	4
	2.3	2	4
3	/	2	4
4	4.1-3	2	5
5	/	2	6

Deel 1 populatieonderzoek

Hoofdstuk 1 Vergelijking van het gebruik en de timing van palliatieve zorg bij COPD en longkanker: een bevolkingsonderzoek

Hoofdstuk 1 beschrijft de behandelingsdoelen in de laatste levensfase, het gebruik en de timing van gespecialiseerde palliatieve zorg en de redenen voor niet-verwijzing bij COPD en longkanker. Dit was op basis van een representatieve steekproef van sterfgevallen in 2013 (n=6871) in Vlaanderen, België, waarvan we sterfgevallen door COPD (n=251) en longkanker (n=192) hebben geselecteerd. Voor COPD waren de behandelingsdoelen in de laatste weken van het leven minder vaak gericht op palliatie en werden patiënten minder vaak doorverwezen naar palliatieve zorgdiensten (37,3% versus 73,5%). De mediane timing van de verwijzing voor COPD was zes dagen voor het overlijden en 17 dagen voor longkanker. Bij 36% COPD en 18% longkanker patiënten die niet werden doorverwezen, was dat omdat palliatieve zorg door artsen niet als zinvol werd beschouwd. Eindconclusie van deze studie was dat palliatieve zorg laat werd ingeschakeld bij beide ziekten, maar veel minder en nog later bij COPD. Dit zal waarschijnlijk toe te schrijven zijn aan het onvoorspelbaar ziekteverloop en aan een gebrek aan kennis over de noodzaak van palliatieve zorg bij COPD. Wij adviseren kennisverhoging van de voordelen van palliatieve zorg voor COPD en haar waarde in de pre-terminale fase voor beide ziekten.

Hoofdstuk 2 Heeft het gebruik en de timing van palliatieve thuiszorg een effect op het gebruik van medische zorg in de laatste dertig dagen voor de dood bij COPD? Een retrospectief bevolkingsonderzoek

In hoofdstuk 2 bestudeerden we het effect van het gebruik en de timing van palliatieve thuiszorg op het medische zorg in de laatste 30 dagen voor het overlijden van COPD patiënten in België. Deze retrospectieve studie had betrekking op alle Belgische overlijdens in 2010-2015 die stierven met COPD en een primaire doodsoorzaak van COPD of hart- en vaatziekten hadden. Met betrekking tot de timing toonden de resultaten aan dat 644 patiënten (1,1% van alle mensen met COPD) eerder dan 30 dagen voor hun overlijden gespecialiseerde palliatieve thuiszorg kregen. Het gebruik van palliatieve thuiszorg (versus niet gebruiken) verminderde de kans op opname in het ziekenhuis (0,35) en intensieve zorg (0,16), contact met specialisten (0,58), invasieve ventilatie (0,13), medische beeldvorming (0,34), RX thorax (0,34).34) en kalmerende middelen (0,48) en verhoogden de kans voor thuiszorg (3,27), contact met de huisarts (4,65), palliatieve zorgopname (2,61), niet-invasieve ventilatie (2,65), maagsonde (2,15), zuurstof (2,22), opioïden (4,04) inclusief morfine (5,29) in de laatste 30 dagen van het leven ($p<0{,}001$). Deze verschillen waren niet groter voor de subgroep die voor het eerst palliatieve thuiszorg meer dan 360 dagen voor overlijden kreeg, en waren eigenlijk het grootst voor degenen die palliatieve thuiszorg kregen tussen 90 en 31 dagen voor overlijden (de latere groep). We concludeerden dat het gebruik van palliatieve thuiszorg bij COPD sterk geassocieerd wordt met minder gebruik van agressieve medische hulpmiddelen in de laatste 30 dagen voor de dood. Wij stellen voor dat het gezondheidsbeleid en de diensten zich zouden moeten concentreren op het vergroten van de toegang tot palliatieve thuiszorg voor COPD, terwijl onderzoek het effect van vroege initiatie van palliatieve thuiszorg voor COPD verder zou moeten exploreren.

Deel 2 Ontwikkelen en testen van een piloot interventie

Hoofdstuk 3 "Een palliatieve eindfase COPD-patiënt bestaat niet": een kwalitatief onderzoek naar drempels en kansen voor vroeg geïntegreerde palliatieve thuiszorg voor vergevorderde COPD.

Hoofdstuk 3 toonde drempels en kansen voor vroege integratie van palliatieve thuiszorg voor vergevorderd COPD, volgens huisartsen en thuisverpleegkundigen. De resultaten van drie focusgroepen met huisartsen (n=28) en vier met thuisverpleegkundigen (n=28) toonden aan dat drempels te maken hadden met 1) de onvoorspelbaarheid van COPD, 2) een gepercipieerd gebrek aan inzicht in de ziekte, 3) een zekere mate van weerstand tegen verdere zorg voor de patiënt, 4) gebrek aan ervaring en samenwerking met palliatieve thuiszorg namens de zorgprofessionals, 5) gebrek aan opleiding over kennis over vroege integratie van palliatieve thuiszorg, 6) onvoldoende continuïteit tussen ziekenhuis- en thuiszorg en 7) gebrek aan overleg over palliatieve thuiszorg tussen professionele zorgverleners en de COPD patiënt. Kansen waren 1) het gebruik van triggermomenten voor vroege integratie van palliatieve thuiszorg, zoals na een ziekenhuisopname of wanneer de persoon zuurstofafhankelijk of huisgebonden wordt, 2) een positieve houding ten opzichte van palliatieve thuiszorg bij mantelzorgers, 3) meer aandacht voor vroeg geïntegreerde palliatieve thuiszorg in het onderwijs, 4) het implementeren van voortijdige zorgplanning, en 5) het verbeteren van de communicatie over palliatieve thuiszorg. De resultaten van dit onderzoek gaven inzicht in de klinische praktijk en voor het ontwikkelen van belangrijke componenten voor een fase 0-2 vroegtijdig geïntegreerd palliatief thuiszorgmodel voor vergevorderd COPD: verbetering van zorgintegratie, aanmoediging van ziekte-inzicht voor een COPD en opleiding van palliatieve thuisverpleegkundigen in de zorg voor vergevorderd COPD.

Hoofdstuk 4 Ontwikkeling van een complexe interventie voor vroeg geïntegreerde palliatieve thuiszorg in de standaardzorg voor patiënten met vergevorderd COPD: een Fase 0-I studie

In hoofdstuk 4 werd een overzicht gegeven van de theorie en ontwikkeling (fase 0-I) van een pilootinterventie rond vroeg geïntegreerde palliatieve thuiszorg. Aan de hand van het Medical Research Council Framework voor de ontwikkeling van complexe interventies hebben we de kerncomponenten en inclusiecriteria voor de interventie in fase O geïdentificeerd. Dit gebeurde door middel van een verkennend literatuuronderzoek naar interventies, consultaties van deskundigen en via de zeven focusgroepen met huisartsen en buurtverpleegkundigen over de gepercipieerde drempels voor en kansen van vroeg geïntegreerde palliatieve thuiszorg voor COPD (hoofdstuk 3). In fase 1 is de interventie zelf, de inclusiecriteria en componenten ontwikkeld en verder verfijnd door een experten panel en twee experts.

Dit resulteerde in een interventie in de vorm van een zorgverbeteringsprogramma onder leiding van een verpleegkundige, bestaande uit vijf kerncomponenten: (1) pre-inclusie training over COPD zorg voor palliatieve thuisverpleegkundigen, (2) maandelijkse palliatieve thuiszorgbezoeken aan huis, (3) informatiebrochures over coping en ademhalingsoefeningen, (4) een protocol (over ziekte-inzicht, symptoommanagement en psychosociale ondersteuning, een zorg- en actieplan) en (5) een rapport dat na elk palliatief thuiszorgbezoek naar de betrokken zorgprofessionals wordt gestuurd. De inclusiecriteria voor de patiënten waren gericht op een combinatie van een longfunctie in het eindstadium (GOLD III of IV) en laag tot zeer laag functioneren.

Hoofdstuk 5 Vroege Geïntegreerde Palliatieve thuiszorg en standaard zorg voor patiënten in het eindstadium COPD (EPIC): Een Fase II pilot RCT testen haalbaarheid, aanvaardbaarheid en voorlopige effectiviteit

Hoofdstuk 5 presenteerde de haalbaarheid, aanvaardbaarheid en voorlopige resultaten van het zorgverbeteringsprogramma van vroegtijdig geïntegreerde palliatieve thuiszorg voor vergevorderd COPD (doelstelling 4, onderzoeksvraag 4.1-3). Tijdens deze gerandomiseerde fase II-studie van zes maanden beoordeelden we elke zes weken de gezondheidsgerelateerde levenskwaliteit, de kwaliteit van de zorg en andere patiënt-gerapporteerde resultaten. Interventiepatiënten, mantelzorgers, huisartsen, longartsen en palliatieve thuisverpleegkundigen werden geïnterviewd voor een post-interventie evaluatie. Uit de resultaten bleek dat 56% (39/70) van de in aanmerking komende patiënten deelnam, met een 20:19-interventie-controle verhouding. 64% voltooide het onderzoek en 80% van de interventiepatiënten had 4 palliatieve thuiszorgbezoeken, voornamelijk gericht op ziekte-inzicht, symptoommanagement en zorgplanning. Alle verslagen werden naar de betrokken zorgprofessionals gestuurd.

Kwalitatieve post-interventie evaluatie toonde aan dat 8 van de 10 geïnterviewde patiënten tevreden waren over de interventie, verwijzend naar de voortdurende ondersteuning, nuttige ademhalingsoefeningen en toekomstige zorgbeslissingen. Huisartsen hadden twijfels over de vroege integratie van palliatieve thuiszorg, terwijl longartsen en palliatieve thuisverpleegkundigen vooral positief waren over de informatiebrochures en het verspreiden van het verslag, en in mindere mate over het semi-gestructureerde protocol. Voorlopige effectiviteitsanalyse toonde minder ziekenhuisopnames in de controlegroep en een hogere kwaliteit van zorg in de interventiegroep in week 24. Er werden geen verschillen gevonden op andere uitkomsten. Deze pilootstudie toonde aan dat een vroeg geïntegreerde palliatieve thuiszorginterventie voor vergevorderd COPD haalbaar en geaccepteerd is, maar toonde geen grote voordelen voor de interventiegroep. Nagaan of palliatieve thuiszorg daadwerkelijk uitkomsten kan verbeteren, her-evalueren van proefopzet, componentoptimalisatie, maatregelen en betrokkenheid van de huisarts is nodig voor een fase III-interventie.

Hoofdstuk 6 Implementatie van vroeg-geïntegreerde palliatieve thuiszorg voor eindstadium COPD: aanbevelingen voor ademhalingsdiensten

Tot slot heb ik in het zesde hoofdstuk van deel 2 aanbevelingen ontwikkeld voor longdiensten met betrekking tot vroeg geïntegreerde palliatieve thuiszorg. De input daarvoor waren resultaten van 1) alle vijf andere studies in dit proefschrift, 2) informele gesprekken met palliatieve zorg en gezondheidswerkers, patiënten, mantelzorgers en beleidsmedewerkers, 3) internationale literatuur over dit onderwerp, en 4) kritische discussies met de projectgroep bestaande uit sociologen, longartsen en huisartsen. Dit resulteerde in vier aanbevelingen: 1) systematisch gebruik van criteria die een afspiegeling zijn van het lage functioneren van COPD patiënten die behoefte hebben aan vroege geïntegreerde palliatieve thuiszorg; 2) systematische introductie van palliatieve thuiszorg tijdens consultaties met COPD patiënten; 3) systematische communicatie voor een gestructureerde integratie van palliatieve thuiszorg; 4) opzetten van een structureel netwerk van multidisciplinaire samenwerking tussen ziekenhuizen en thuiszorginstellingen voor een gestructureerde integratie van palliatieve thuiszorg.

Elke aanbeveling werd gekoppeld aan praktische implicaties. Het hoofdstuk werd afgesloten met een reflectie op de nodige randvoorwaarden zijn om de aanbevelingen in de praktijk te kunnen uitvoeren: interprofessioneel vertrouwen tussen longspecialisten en palliatieve zorg, coördinatiemechanismen tussen het ziekenhuis en de thuiszorg, en systeemveranderingen, zoals een betere opleiding in de palliatieve zorg voor gezondheidswerkers en een groter publiek bewustzijn van de ernst van COPD en de voordelen van palliatieve zorg.

Algemene discussie

In het laatste en derde deel van dit proefschrift presenteer ik een algemene discussie met methodologische overwegingen, een reflectie op de resultaten en implicaties voor onderzoek, beleid en praktijk.

Methodologische overwegingen

Retrospectief onderzoeksdesign in relatie tot prospectief design

Deel 1 beoordeelde de zorg in de laatste twee jaar voor de dood met terugwerkende kracht. Ik zal deze toelichten in relatie tot een prospectief design[24] dat in hoofdstuk 5 wordt gebruikt. De voordelen zijn 1) het maakt het mogelijk om een steekproef op basis van een populatie te selecteren; 2) het neemt de last van de deelnemers weg, wat een probleem is bij prospectief design voor het vinden van deelnemers, onvolledige inschrijvingen, drop-out en follow-up; 3) het is in het algemeen efficiënter en goedkoper dan prospectieve cohortstudies[25]. Nadelen zijn 1) dat hierdoor het feit kan worden genegeerd dat zorg was verstrekt waarin de zorgprofessional zich niet realiseerde dat de patiënt de levenseindefase[26] inging; 2) het is vaak een proxy respondent die de gegevens in retrospectieve studies verstrekt; 3) er kunnen geheugen- of terugroepingsvooroordelen bestaan bij het gebruik van retrospectief ontwerp[27]. In conclusie kan het prospectief ontwerp het best worden gebruikt voor onderzoek naar zorg die wordt verleend aan patiënten die gemakkelijk kunnen worden geïdentificeerd als patiënten met een levensbedreigende ziekte. De retrospectieve benadering is optimaal om te vragen "wat gebeurt er kort voor de dood van patiënten die zullen sterven?"

Gebruik van administratieve databanken voor het analyseren van zorggebruik en medische zorg

De voordelen zijn 1) de bevindingen kunnen worden veralgemeend naar de volledige Belgische bevolking; en 2) dat het een analyse van het gebruik van medische zorg mogelijk maakte, rekening houdend met socio-demografische factoren. Nadelen zijn 1) de onmogelijkheid om de relatie tussen specifieke voorkeuren van patiënten of gezondheidswerkers voor het gebruik en het type zorg na te gaan; 2) de ernst van de ziekte, de intensiteit van de zorg die onmogelijk te achterhalen is;

Medical Research Council Framework voor complexe interventies: wat is de toegevoegde waarde?

Het algemene voordeel was de systematische aanpak met een sterke onderbouwing van het ontwerp en de expliciete rapportage van het ontwikkelingsproces[28]. In de eerste plaats leverde de modelleringsfase informatie op over de details van de structuren en processen; in de tweede plaats leverde een breed scala aan (internationale) disciplines input voor het ontwerp. Ten derde hielp de raadpleging van Vlaamse deskundigen en gezondheidswerkers om de lokale behoeften binnen de Vlaamse gezondheidscontext in kaart te brengen. Ten vierde was het testen van een voorlopige fase II evaluatie kosten effectiever. Nadelen zijn 1) de kwaliteit van de drie methoden die in fase 0 worden gebruikt kan in twijfel worden getrokken; en 2) er is geen vast proces voor de overgang van fase 0 naar een volledig gemodelleerde interventie in fase I. Mogelijke alternatieven zijn het gebruik van participatief actieonderzoek[29].

Methoden voor het perspectief artikel

In het laatste hoofdstuk van deel 2 heb ik aanbevelingen gedaan voor longdiensten. Het was een perspectiefartikel[30,31]. Het voordeel is dat het de mogelijkheid biedt om standpunten over de interpretatie van recente bevindingen op elk onderzoeksgebied te brengen[32]. Het maakt constructieve kritiek mogelijk[32] zonder dat er nog een observationele studie moet worden uitgevoerd.[33] Toch had de impact groter kunnen zijn geweest als we systematische methoden hadden gebruikt die experts in staat stellen om op een gestructureerde manier tot een consensus te komen, zoals de Delphi-consensusprocesmethode[34]. Het doel was echter om na te denken over de relevante resultaten van de eerdere studies voor de implementatie van palliatieve thuiszorg in de klinische praktijk.

Bespreking van de resultaten in relatie tot de stand van zaken

Lage toegang tot en late timing van gespecialiseerde palliatieve zorg in België

Deze resultaten waren in overeenstemming met andere studies naar de toegang tot palliatieve zorg voor COPD in verschillende landen[35-39]. Longkankerpatiënten kregen meer palliatieve zorg. Deze bevindingen bevestigden opnieuw eerdere studies die in het Verenigd Koninkrijk[40] en Canada[35] werden uitgevoerd. De timing van de palliatieve zorg is echter laat. Dit suggereert dat verwijzing naar de palliatieve thuiszorgteams nog steeds gezien kan worden als een comfortmaatregel in de terminale fase, wanneer curatieve en standaard medische behandeling niet langer geschikt zijn[9]. Mogelijke verklaringen zijn dat zorgverleners denken dat palliatieve thuiszorg niet zinvol is voor COPD, dat de behoeften kunnen worden aangepakt in de standaardzorg die generalistische palliatieve zorg biedt[41] , dat gebrek aan tijd of onvoorspelbare prognose de introductie of conversatie over palliatieve thuiszorg belemmert[31]. Daarnaast waren er een aantal redenen die verband hielden met de patiënt die misschien geen palliatieve thuiszorg wil of zich niet bewust is van deze zorgoptie[31] en een minder goed inzicht in de ziekte heeft[42]. Het vergroten van vaardigheden en kennis over palliatieve zorg in educatieve programma's voor zorgverleners en het informeren van het publiek over COPD en palliatieve zorg door middel van bewustwordingscampagnes worden vaak genoemd[43].

Het effect van vroeg geïntegreerde palliatieve thuiszorg op gezondheidsgerelateerde resultaten: onvoorziene resultaten

Hier zal ik ingaan op de kort beschreven redenen in hoofdstuk 5 voor de niet overtuigende resultaten van de interventie tussen interventie- en controlegroep over resultaten: 1) De ziekte fluctueert in de tijd. Relatief stabiele periodes worden onderbroken door exacerbaties, die van invloed zijn op de symptoomlast[1]. Als gevolg hiervan kan de levenskwaliteit of symptoomlast sterk wisselen; 2) De levenskwaliteit kan te algemeen zijn als uitkomstmaat. De gunstige effecten kunnen afhangen van het individuele zorgtraject, de context en de belasting van de symptomen[21]; 3) Het zorgverbeteringsprogramma had onvoldoende invloed op de gezondheidsresultaten van de patiënt; 4) Vier interventies patiënten werden tussen week 18 en 24 in het ziekenhuis opgenomen. Esteban et al[44] ontdekten dat ziekenhuisopnames voor exacerbaties onafhankelijk van elkaar een negatieve invloed hebben op de kwaliteit van leven; en 5) Kwalitatieve methoden zouden geschikter kunnen zijn om complexe en subtiele verbeteringen en individuele contexten te beoordelen[20].

Resultaten voor zorgkwaliteit en plaats van overlijden: meten we verkeerde uitkomsten?

Hoofdstuk 2 liet zien dat palliatieve thuiszorg in de laatste levensmaand geassocieerd was met minder ziekenhuisopnames, uitgebreide medische procedures en met meer primaire zorgcontacten en comfortmedicati, in lijn met Maetens et al[45] en Gomes et al[46]. In hoofdstuk 2 was duidelijk dat de verwijzing naar palliatieve thuiszorg 90-31 dagen voor overlijden geassocieerd was met nog minder intensief gebruik van zorg in de laatste 30 dagen van het leven dan eerdere verwijzing (één tot twee jaar voor overlijden). Hebben we de verkeerde aspecten gemeten of zijn palliatieve thuisverpleegkundigen niet in staat om invloed uit te oefenen op de zorg voor (of tijdens) de terminale fase in COPD? Enkele redenen worden hier toegelicht: 1) Ziekenhuisopnames zijn te complex om de gepastheid ervan te kunnen beoordelen; 2) De voorkeuren van de patiënt fluctueren en het lijkt beter om redenen van zorg in plaats van zorg als zodanig te beoordelen; 3) Afwisselende standaard en palliatieve thuiszorg voor de terminale fase kan belangrijk blijven voor de patiënt.

De timing van palliatieve thuiszorg: Welke verwijzingscriteria zijn nodig en nuttig?

Een belangrijke vraag is wanneer en voor wie palliatieve thuiszorg kan worden gestart. In hoofdstuk 2-5 werden inclusiecriteria die GOLD III of IV combineren met fysieke functionaliteit, goed geaccepteerd onder rekruterende longartsen. De NECPAL[47] en de PICT[48] hanteren een uitgebreidere aanpak en onderscheiden frailty criteria met ziekte specifieke criteria naast fysiek functioneren. Toch suggereren de Wereldgezondheidsorganisatie[8] en onderzoek[49] dat verwijzing gebaseerd moet zijn op behoeften en laag functioneren in plaats van op prognose, wat onze criteria tot op zekere hoogte toestonden. De criteria waren bijvoorbeeld minder gevoelig voor het identificeren van longemfyseem (aangegeven door geïnterviewde longartsen), psychosociale nood[50] , existentiële behoeften en pijn[2,51]. Op nationaal beleidsniveau heeft de Belgische wetgever onlangs de vergoeding van palliatieve thuiszorgkosten gekoppeld aan de PICT-schaal[52] en een lijst[48] opgenomen om de palliatieve zorgbehoeften te identificeren. Deze lijst omvat naast fysieke behoeften ook verschillende psychosociale en sociale behoeften: angst, depressie, existentiële stoornis, psychiatrische pathologie en sociaal isolement. Ze kunnen nuttig zijn om psychosociale nood in COPD vast te leggen en moeten verder worden getest.

Ontwikkelen van vroeg geïntegreerde palliatieve thuiszorgmodellen: heroverweging van de componenten?

Over effectieve palliatieve zorgmodellen voor COPD wordt nog steeds gediscussieerd[4] en interventies zijn schaars1[8,53]. Bovendien is nog steeds niet duidelijk wat "vroege palliatieve zorg" betekent. Vijf kerncomponenten (hoofdstuk 5) probeerden deze zorgen aan te pakken, wat resulteerde in een complexe interventiestructuur[54]. De volgende kernelementen lijken belangrijk om in de componenten van de vroeg geïntegreerde palliatieve thuiszorg op te nemen: 1) opleiding van zorgverleners voor vroegtijdige gespecialiseerde en generalistische palliatieve zorg; 2) gestructureerde en systematische palliatieve thuiszorgbezoeken om een adequate follow-up mogelijk te maken; 3) geïndividualiseerde zorg om tegemoet te komen aan een veelheid van behoeften in COPD; 4) documentatie en standaardisatie om de kwaliteit van de zorg te verbeteren, en 5) multidisciplinaire zorgaanpak om de therapie op elkaar af te stemmen.

Zijn rapportage- en communicatiemechanismen een vorm van zorgintegratie?

In de interventie werd integratie geïnterpreteerd (component 5). Dit zorgde niet voor een vergevorderde integratie[4], aangezien communicatie en samenwerking niet verplicht was (behalve het verzenden van verslagen). De nadruk lag dus op informatiestromen en rapportage, de zogenaamde eerste stap van integratie, namelijk "koppeling "[55] .

Wat nodig is, is de tweede stap van integratie, "coördinatie" van de zorg, hier gedefinieerd als "de doelbewuste organisatie van patiëntenzorgactiviteiten tussen zorgprofessionals om een goede dienstverlening in de gezondheidszorg mogelijk te maken"[56]. In hoofdstuk 3 is een faciliterende zorgcoördinator gesuggereerd en aanbevolen voor zorgintegratie[57]. De interventie heeft dit echter niet systematisch geïmplementeerd. Palliatieve thuisverpleegkundigen werden wel impliciet toegewezen (contact opnemen met huisartsen als de ESAS-schaal >4), maar er vonden slechts twee multidisciplinaire bijeenkomsten met een huisarts en thuisverpleegkundige plaats om toekomstige ziekenhuisopnames te bespreken. Palliatieve thuisverpleegkundigen in België werken echter op de tweede lijn[58]. Dit kan een verbindingsfunctie in een complex COPD-zorgnetwerk[57] belemmeren. Ook blijkt verticale integratie, onafhankelijke zorgsilo's die communiceren, zoals in het tweede niveau[57], onvoldoende. Bij de overgang naar het meest complete niveau, 'volledige integratie', moet de zorg volledig worden gereorganiseerd op een horizontale manier, waarbij de silo's worden geëlimineerd en multidisciplinaire teams en persoonsgerichte diensten[57] worden geïmplementeerd over verschillende zorgsettings[4]. Toekomstig onderzoek zou dit als een verplicht onderdeel van geïntegreerde zorg moeten testen[59].

Over het hoofd gezien binnen geïntegreerde zorg: een doelgerichte aanpak?

Een ontbrekende schakel lijkt de implementatie van doelgerichte zorgaanpak binnen het continuüm van reguliere en palliatieve thuiszorg[4]. Het is relevant voor vergevorderde chronisch zieke en multimorbide COPD patiënten die thuis wonen tot aan de dood[60]. In zulke complexe situaties past het klassieke biomedische, ziektegerichte model met *evidence-based* richtlijnen voor biomedische doelen voor de klinische praktijk niet[60]. Het patiëntgerichte palliatieve zorgconcept belichaamt in feite doelgerichte zorg, omdat het zich richt op de (laatste) wensen en voorkeuren in de laatste levensfasen in plaats van te proberen de ziekte te genezen[8]. Ik stel voor om het te implementeren in COPD-modellen. Binnen deze benadering kan de palliatieve thuiszorg een uitstekende kans bieden om zorg te coördineren, aggresieve zorg te verminderen, kosten te verlagen, het ziekenhuisverblijf te verminderen.

Suggesties voor toekomstig onderzoek

Onderzoek redenen voor lage en late palliatieve thuiszorg bij COPD

Verken de mechanismen van effectieve vroeg geïntegreerde palliatieve thuiszorg

Onderzoek de rol en de last van informele zorgverleners binnen de palliatieve zorg voor COPD

Test verschillende zorgtherapieën voor COPD en de kosteneffectiviteit ervan

Implicaties voor het beleid

Verhoogt het bewustzijn over vroeg geïntegreerde palliatieve zorg

Verhoog inzicht in de ziekte en toegang tot zorg bij COPD

Faciliteer Gecoördineerde zorg

Vergroot palliatieve zorgvaardigheden binnen het basis- en voortgezet onderwijs

Voorzie meer middelen voor de benodigde diensten

Implicaties voor de praktijk

Criteria van laag functioneren kunnen helpen bij doorverwijzing van palliatieve zorg

Pas systematische palliatieve thuiszorg toe

Laat generalistische en gespecialiseerde palliatieve zorg op elkaar inwerken

Installeer persoonsgerichte geïntegreerde zorg gericht op de behoeften en persoonlijke doelen

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CURRICULUM VITAE AND LIST OF PUBLICATIONS

Curriculum Vitae

°25/06/1989 – Tielt, Belgium
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Education

2012- 2014	Master Management of Government Organisations, Ghent University, Belgium(distinction) *Thesis: Human resource Management in Taiwanese public sector (self-organised research study in Taipei, Taiwan)*
2011-2012	Master Sociology, Ghent University, Belgium(great distinction) *Thesis: Does action for land lead to action for political rights? A study on the association between the organisational structure of the Movimiento dos trabalhadores Sem Terra and political consciousness of her members (self-organised research study in Fortaleza, Brazil)*
2008-2011	Bachelor Sociology, Ghent University, Belgium (distinction) with an erasmus exchange at Universade Nova de Lisboa, Lisbon, Portugal

Professional

2019	Consultant to the World Health Organisation on equity gauges within data monitoring of human resources for health
2015-present	Junior researcher, End-of-Life Care Research Group, Ghent University & Vrije Universiteit Brussel (VUB), Belgium. PhD title: Early Integration of Palliative home care into standard care for people with end-stage COPD
2014	Scientific researcher, Department of family Medicine and Primary Health Care, Ghent University, Belgium. Project title: ICF (International Classification of Functioning) and the integration of registration systems in health and welfare sector, Flanders, Belgium.

Awards and fellowships

2019	Belgian American Educational Foundation Post-doctoral Fellowship 2019-2020

Memberships

2019	Member of European Association of Palliative Care
2018	Member of the European Respiratory Society
2018	Member of the Council for Sustainable policy of Ghent University, Ghent, Belgium
2018	Member of Generation T, The Shift, Belgium
2018	Member of The Belgian Association for Pulmonology, Belgium
2015-2018	Member of Climate Coalition, Belgium

Academic and courses and experience

2018-2019	Palliative care for clinicians and masters (PALM), Wemmel, Belgium
2018	Member of the Council for Sustainable policy of Ghent University
2018	Let's talk science: scientific communication, Leuven, Belgium
2018	Meeting Skills, Ghent, Belgium
2015&2018	Taught an exercise in inter-professional care strategies for 2nd bach. Medicine students
2015&2018	Supervised thesis's of Master students in Health care organisation
2017	Project Management, Ghent, Belgium
2017	Univariate and bivariate Statistical Analysis using SPSS, Ghent, Belgium
2017	Presentation skills, Ghent, Belgium
2016	Effective scientific communication course, Ghent, Belgium

Language

Dutch	Native	Portuguese	Good
English	Fluent	Spanish	Average
French	Fluent	German	Average

List of publications

International peer-reviewed journals

Scheerens C, Chambaere K, Pardon K, Derom E, Van Belle S, Joos G, Pype, P, Deliens, L. (2018) Development of a complex intervention for early integration of palliative home care into standard care for end-stage COPD patients: A Phase 0–I study. PLOS ONE 13(9): e0203326. https://doi.org/10.1371/journal.pone.0203326 [2017 SCI impact factor 2,766 ; ranking n°15/64 multidisciplinary science, journal ranking Q1]

Scheerens C, Deliens L, Van Belle S, Joos G, Pype P, Chambaere K. "A palliative end-stage COPD patient does not exist": a qualitative study of barriers to and facilitators for early integration of palliative home care for end-stage COPD. npj Prim Care Respir Med. 2018;28(1):23. doi:10.1038/s41533-018-0091-9. [2017 SCI impact factor 2,485; ranking n°4/20 primary health care, journal ranking Q1]

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Scheerens C, Faes, K, Beernaert K, Pype P, Cohen J, Derom E., Joos G., Deliens L, Chambaere K. (2019) Does use and timing of palliative home care have an effect on medical resource use in the last thirty days before death in COPD? A full-population retrospective study. Submitted

Scheerens C, Vancauwenberg J, Eecloo, K, Vanbutsele G, Derom E, Van Belle S, Joos G, Pype, P, Chambaere K Deliens, L. (2019): Early Integrated Palliative home care and standard care for end-stage COPD patients (EPIC): A Phase II pilot RCT testing feasibility, acceptability and preliminary effectiveness. Submitted.

Submitted: Scheerens C, Pype P, Derom E, Joos G, Chambaere K, Deliens, L. Implementation of early integrated palliative home care for end-stage COPD: recommendations for respiratory services. Submitted

Other publications

Scheerens C, Deliens L, Van Belle S, Joos G, Pype P, Chambaere, K. Wanneer palliatieve zorg starten voor patiënten met vergevorderd chronisch longlijden? (2019) Huisartsen nu, België.

Scheerens, C., Beernaert, K., Brusselle, G., Cohen, J., Deliens, L., & Chambaere, K. (2017). Comparing the use and onset of palliative care services in chronic obstructive pulmonary disease (COPD) and lung cancer : a population-based mortality follow-back survey. *Respiratory Medicine 2017:*132;271–271. Published abstract.

Scheerens, Ch., De Maeseneer, J., de Sutter, A. (2015). Naar een geïntegreerd registratie- en classificatiesysteem in de gezondheids- en welzijnssector? https://steunpuntwvg.be/images/rapporten-en-werknotas/swvg-2-rapport-43-1a2-registratiesystemen

Oral and poster presentations

Early Integration of Palliative Care in standard care for end-stage COPD patients (EPIC): feasibility, acceptability and preliminary effectiveness of a Phase II pilot randomised controlled trial, 16th World Congress of the European Association for Palliative Care, Berlin, Germany. May 2019.

Does use and timing of palliative home care have an effect on resource use in the last month of life in COPD? A full-population retrospective study, 16th World Congress of the European Association for Palliative Care, Berlin, Germany. May 2019.

Timely introduction of palliative care for end-stage COPD in clinical practice. Congress of Society of Belgian pulmonology nurses, Brussels, Belgium. December 2018.

Are use and timing of palliative home care associated with appropriate end-of-life care for end-stage COPD patients? 1st International Seminar of EAPC RN and the EAPC Reference Group on Public Health and Palliative Care, Brussels, Belgium, 2018.

Barriers and facilitators on early integration of palliative home care for people with severe COPD: a focus group study. 22nd International Congress on Palliative Care, Montréal, Canada. October 2018.

Barriers and facilitators on early integration of palliative home care for severe COPD : a focus group study. 10th World Research Congress of the European Association for Palliative Care, Bern, Switzerland. May 2018.

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