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Early Integrated Palliative Care in Chronic Heart Failure (CHF) and Chronic Obstructive Pulmonary Disease (COPD): A myth or a real benefit for patient and family?

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TABLE OF CONTENTS

Abbreviations		**7**
Chapter 1	General Introduction	**9**
Chapter 2	Objectives and Specific Aims	**27**
	Part I. Theoretical Part	
Chapter 3	Integrated palliative care in Europe: a qualitative systematic literature review of empirically tested models in cancer and chronic disease.	**35**
Chapter 4	Towards integration of palliative care in patients with chronic heart failure and chronic obstructive pulmonary disease: a systematic literature review of European guidelines and pathways.	**73**
Chapter 5	Is the content of guidelines/pathways a barrier for the integration of palliative Care in Chronic Heart Failure (CHF) and chronic pulmonary obstructive disease (COPD)? A comparison with the case of cancer in Europe.	**111**
	Part II. Empirical Part	
Chapter 6	Professionals' perceptions and current practices of integrated palliative care in chronic heart failure and chronic obstructive pulmonary disease: a qualitative study in Belgium.	**135**
Chapter 7	Early Integrated Palliative Care in Chronic Heart Failure and Chronic Obstructive Pulmonary Disease: protocol of a feasibility before-after intervention study.	**159**
Chapter 8	Quality of Life and Quality of Care in patients with advanced Chronic Heart Failure (CHF) and advanced Chronic Obstructive Pulmonary Disease (COPD): Implication for Palliative Care.	**179**
Chapter 9	Lessons learned from a feasibility prospective study of Palliative Care eligible patients with Chronic Heart Failure (CHF) and Chronic Obstructive Pulmonary Disease (COPD).	**207**
Chapter 10	General Discussion	**231**
Summary		**257**
Curriculum Vitae		**261**
Acknowledgements		**267**

LIST OF FREQUENTLY USED ABBREVIATIONS

ACP: Advance Care Planning

AMED: Allied and Complementary Medicine

ASCO: American Society of Clinical Oncology

BNI: British Nursing Index

CANHELP Lite: Canadian Healthcare Evaluation Program Lite

CENTRAL: Cochrane Central Register of Controlled Trials

CHF: Chronic Heart Failure

CINAHL: Cumulative Index to Nursing and Allied Health Literature

COPD: Chronic Obstructive Pulmonary Disease

EAPC: European Association for Palliative Care

EoL: End of Life

ESMO: European Society of Medical Oncology

GOLD: Global Initiative for Chronic Obstructive Lung Disease

GPs: General Practitioners

ICSI: Institute for Clinical Systems Improvement

ICU: Intensive Care Unit

IPC: Integrated Palliative Care

LCP: Liverpool Care Pathway

MDT: Multidisciplinary Team

NCCN: National Comprehensive Cancer Network

NHS Evidence: National Health Service Evidence

NYHA: New York Heart Association

PC: Palliative Care

POS: Palliative Outcome Scale

QoL: Quality of Life

RCTs: Randomized Controlled Trials

WHO: World Health Organization

CHAPTER 1

General Introduction

General Introduction

Palliative Care (PC) is "…an approach that improves the quality of life (QoL) of patients and their families facing the problem 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" [1]. Within the PC framework, the focus is placed on three core areas: 1) symptom control and management, 2) continuous communication of treatment goals and options between physicians, patients and their families and 3) the holistic support (psychological, social and spiritual) for both patients and their families throughout the course of the illness trajectory [2].

PC is preceded by the "old type" of hospice care, i.e. supportive care for dying people, which has been practiced for hundreds of years (ie. Hospices de Beaune (Fr), Hotel Dieu since 1443). The origins of the "new type" PC can be traced back in the 50s in the UK, where Dr. Cicely Saunders systematically evaluated existing hospice care for dying patients. More attention to the topic was paid in the 60s when the US psychiatrist Elisabeth Kubler-Ross brought forward the need of a more specialized care for the dying [3]. The term "palliative care" was coined by Dr. Balfour Mount at The Royal Victoria Hospital of McGill University in Montreal, Canada. Interestingly, what motivated this new terminology was the avoidance of the negative implications associated with the term "hospice" in French [3].

In its early stages, PC has been more or less synonymous to old style hospice care and almost exclusively concerned patients with cancer at the end-of-life (EoL) stage. In other words, the application of PC was limited to the last hours of life and marked the stop of the (curative and palliative) treatment [4-5]. The reason behind this operating model was twofold: i) patients with malignant disease had high mortality and their terminal phase could be prognosticated and ii) owing to its hospice care roots, PC was already associated

with death and was considered a separate type of care and not a complimentary one to the curative treatment [6].

Despite the rather limited initial scope of PC, a considerable number of empirical studies after 2000 have shown that PC has clearly measurable benefits on the QoL of the patients with malignant disease [7-8]. These results have not only grown awareness on the topic but have also served as the basis for the evolution and transformation of PC. As a consequence and as reflected from the WHO definition on PC, modern PC promotes its initiation earlier in the disease trajectory and concurrently with curative treatment [6, 9-10] and its application to an increasing list of non-malignant diseases such as Chronic Heart Failure (CHF), Chronic Obstructive Pulmonary Disease (COPD), Dementia and other types of neurological disease, HIV etc. [11-14].

From PC to integrated PC

The combination of an aging population with the increase of survival rates of patients with malignant and non-malignant disease has posed new challenges on PC [15-16]. Owing to these factors, the frequencies of eligible PC patients have increased and are expected to continuously do so while their PC needs have become substantially more complex. A sustainable response to this reality requires a more systematic and integrated approach to the provision of high quality and patient-focused care.

A (unifying) possible solution to these challenges can be offered by the concept of integrated PC. Although a unanimous agreed description does not exist, the essence of what is commonly understood as integrated PC is captured in the following consensus based definition:

Integrated PC involves bringing together administrative, organizational, clinical and service aspects in order to achieve continuity of care between all those involved in the

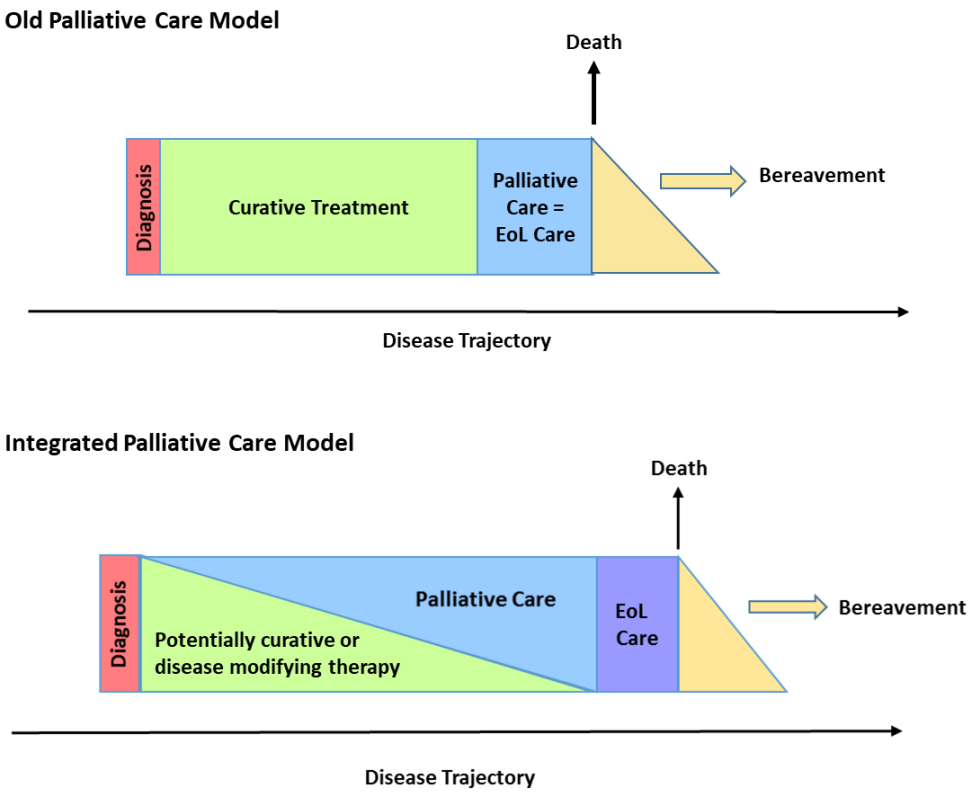
patient's care network. It aims to achieve quality of life and a well-supported dying process for the patient and the family in collaboration with all the care givers (paid and unpaid) [19].

Integrated PC requires not only a well-orchestrated coordination of all the health care professionals and continuity of care, but also the initiation of these practices early in the disease trajectory, in order to increase the efficiency of the PC practices and the benefits for the patients and their families. In this respect integrated PC abandons its initial "end-of-life care" character and assumes a new patient centered role aiming to optimize both QoL and quality of care. Figure 1 illustrates a comparison between the old PC model and the new integrated PC one [6].

Even though integrated PC is a relatively new concept, it has attracted a lot of attention from both academia and health care organizations. Literature has experienced a substantial growth of integrated PC studies that have aimed to empirically investigate its benefits and potential. Collectively, these studies show that integrated PC improves indeed the QoL of the patients and their families, reduces patients' physical and psychological symptoms, reduces the number of unnecessary hospitalizations, it is overall cost effective for the health care system [20-24]. This growing evidence in favor of integrated PC has prompted health care organizations and medical societies to issue explicit recommendations for the "early" integration of PC in the illness trajectory. Such health care organizations include, but not limited to the World Health Organization (WHO), the European Society of Medical Oncology (ESMO), the American Society of Clinical Oncology (ASCO), the National Comprehensive Cancer Network (NCCN), the European Association for Palliative Care EAPC and the Institute for Clinical Systems Improvement (ICSI) [1, 25-29]. For example, the EAPC advocates that PC should be fully integrated in primary care systems internationally so that all patients have early access to a palliative care services in every setting (homecare, hospice, residential home facilities)

[30]. Along the same line, the most recent WHO definition of PC explicitly promotes an early integrated approach to PC [1].

Figure 1. Comparison between the old PC model and the integrated PC model. Modified from [6], permission for use received from BMJ journal.



Integrated PC in Chronic Heart Failure and Chronic Pulmonary Disease

CHF and COPD are two prominent life-threatening chronic diseases (see definitions in table 1). Although their prevalence rates are difficult to assess precisely, previous studies have conservatively estimated the worldwide prevalence for CHF and COPD to be 26 and 64 million patients respectively [31-32]. More importantly, the WHO reports that CHF and COPD constitute the leading and third cause of death worldwide [33]. In Europe, the

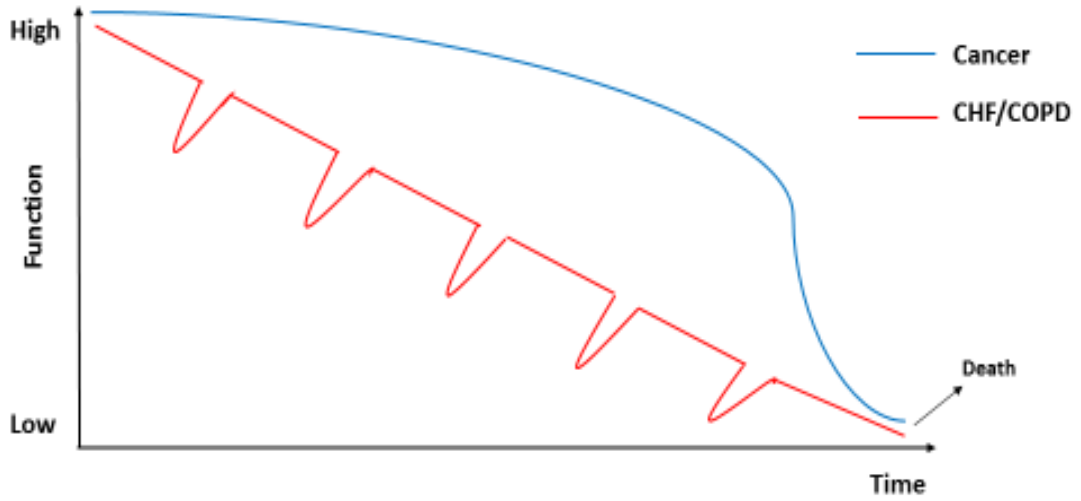
yearly health care cost for CHF and COPD (for both in- and outpatient settings) is estimated to be approximately 30 billion and 38.7 billion euros respectively [34-35].

Table 1. Definitions of CHF and COPD.

Definitions	
Chronic Heart Failure (CHF)	"CHF is a clinical syndrome characterized by typical symptoms (e.g. breathlessness, ankle swelling and fatigue) that may be accompanied by signs (e.g. elevated jugular venous pressure, pulmonary crackles and peripheral oedema) caused by a structural and/or functional cardiac abnormality, resulting in a reduced cardiac output and/or elevated intracardiac pressures at rest or during stress" [36].
Chronic Obstructive Pulmonary Disease (COPD)	"COPD is a lung disease characterized by chronic obstruction of lung airflow that interferes with normal breathing and is not fully reversible. The more familiar terms 'chronic bronchitis' and 'emphysema' are no longer used, but are now included within the COPD diagnosis. COPD is not simply a "smoker's cough" but an under-diagnosed, life-threatening lung disease" [37].

Long-term prognosis for both CHF and COPD remains poor, however, the trajectories for both diseases are substantially more complex than that of cancer. Patients with CHF/COPD experience a gradual decline in their health status accompanied with recurring and progressively intensified exacerbations and more and more uncompleted recoveries (Fig. 2). This is in contrast with the classical cancer trajectory that begins with a gradual, albeit steady, decline followed by a more rapid one during the end-of-life stage. Throughout the disease trajectory, CHF/COPD patients face heavy physical and psychosocial burdens, have frequent hospital admissions and it is common for them to be readmitted, sometimes even within a month, following their last discharge [38]. Moreover, it has been found that the majority of these patients suffer from other comorbidities that affect negatively their health condition [39-40]. In fact, the overall symptom burden of these patients is comparable to the one of cancer patients and it is experienced throughout the whole duration of the chronic disease span [41].

Figure 2. Cancer vs CHF/COPD disease trajectories. Modified from [42]. Permission for use received from BMJ journal.



Treatment options for CHF/COPD are currently non-curative but focus on symptom

control and life-prolongation. Although the non-curative character of the treatment options still persists, the corresponding efficacy has improved with time. Consequently, survival rates of this population have increased [43]. However, the increase of survival rates is not necessarily associated with improvements in the QoL of these patients and recent studies have shown that indeed the QoL of CHF/COPD patients has been not markedly improved QoL [44].

The overall characteristics of CHF and COPD patients hint that they are amenable to PC services. However, it is due to the same characteristics that their PC needs are complex and require a more integrated and patient-centred approach [43]. The eligibility of CHF/COPD patients to PC services has been recognised by both PC and non-PC experts who strongly advocate for integration of PC early in the disease trajectory, as opposed to the traditional EoL model[1] [45-46]. Nevertheless, a review of the literature on PC in CHF and COPD reveals two core issues:

i) CHF/COPD patients are unlikely to receive PC at all. Typically less than 25% of these patients have access to PC services with the actual percentage oftentimes being lower than 10%. On the other hand, the corresponding percentage for cancer patients that receive PC is more than 50%, which reveals a notable inequity in PC access [47-51].

ii) CHF/COPD patients, who do receive PC, receive it mainly in their last hours of living [45, 52] or for a duration that is typically less than the one of cancer patients [50-51]. By confining PC in the terminal phase of the disease the patients can only receive the absolute minimum of the benefits that PC can offer.

[1] The end of life model is hard to use in these populations, because the judgement that such patient is in that phase is to some extend a self-fulfilling prophecy. The survival of these patients largely depends on the use of critical care during every disease exacerbation. If that is withheld, the patient is likely to die. Therefore, the end of life is more a result of advance medical orders for life sustaining treatment.

The poor record of PC in CHF/COPD, both in terms of access to services and level of integration, has motivated ongoing investigations for the identification of the barriers that imped the PC application in these two diseases. A synthesis of the findings of relevant studies results in the following barriers.

- PC Misconceptions. PC is frequently still perceived by healthcare professionals, patients and their families as an EoL care, especially designed for cancer patients. It is synonymous to death and dying and a "last call solution" when nothing else can work [53-54]. At the professional level, these misconceptions have been associated with lack of PC education [54].
- Public image of CHF and COPD. Correctly or not, patients and their families do not consider CHF or COPD as a terminal or life-threatening disease, but rather as a chronic disease that requires adjustments in their lifestyle. For these patients, PC related conversations with specialists can be surprising and confronting, because they contradict the fundamental understanding of their disease and challenge their coping mechanisms [55-56].
- Difficulties in prognostication. Even though prognosis in CHF and COPD is poor, prognostication is challenging and quite inaccurate. The complexity and unpredictability of the trajectories for both diseases, comprising periods of stability followed by sudden relapses and partial improvements and the frequent occurrences of sudden deaths, render the timing of the patient's referral to PC services difficult for the specialists to assess [53-54]. This also affects discussions on goals of care and in time advance care planning [57].
- Organizational barriers. Integrated PC promotes a holistic and patient-centered approach of care and requires the efficient collaboration of multiple disciplines. Its implementation is inherently complex and the work overload of the healthcare personnel, the limited funding and the generic but not practical guidelines pose additional obstacles that need to be resolved [53, 58].

This list of barriers provides an insight on why PC is insufficiently integrated and implemented in CHF/COPD. However, a closer examination reveals weaknesses both in terms of interpretation and applicability. Perceptions of healthcare professionals, patients and their families as well as organizational issues are not a priori the same across countries. Differences in healthcare systems, in culture and in education have a direct influence both in perceptions and organizational aspects. Consequently, a better understanding of the barriers requires locally focused studies and subsequent meta-analysis of the results to establish whether and to what extent a "one size fits all" strategy is appropriate or integrated PC strategies should be developed locally. Although some efforts have been undertaken to explore perceptions of professional caregivers on PC and integrated PC in Belgium [59-60], perceptions of CHF/COPD specialists on integrated PC remain largely unexplored.

An additional gap in the literature, concerns the study and evaluation of existing guidelines[2] and pathways that hospitals and other medical assocotiations (facilities) utilize for the implementation of PC services. In fact, a systematic identification of existing guidelines/pathways and their comparison to the ones of cancer, that act as a benchmark, has not been performed [19, 61]. This gap becomes more relevant given the claim that integration of PC in chronic disease is twenty years behind cancer [62]. Even if this claim has merit, in the absence of a comparative analysis between CHF/COPD and cancer guidelines/pathways, it is difficult to differentiate between theoretical and practical limitations.

[2] Guidelines are systematically developed statements used to assist practitioners and patient decisions about appropriate health care for specific clinical circumstances. Care pathways, complex interventions used to assist mutual decision making and organization of care processes for a well-defined group of patients during a specified period. Consequently, existing guidelines and pathways contain valuable information on current practices for PC in patients with non-malignant disease (see also chapter 4) [19].

Finally, even though many theoretical studies [49, 63] shout the need for early PC integration in CHF/COPD, a systematic documentation and assessment of its empirically demonstrated benefits has not been performed. On the other hand, integrated PC, and PC more generally, is practically implemented through models[3] whose efficacy is then empirically assessed. Therefore, by systematically reviewing the literature for empirically tested integrated PC models, for CHF/COPD, we can identify the benefits of integrated PC as well as existing challenges. By developing a better understanding of the pros and cons of current practices we can in turn provide recommendations for their improvement [64].

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[3] Models of care are standardized designs that provide frameworks for the organization of care for people with a progressive life-threatening illness and/or for their (in)formal caregivers. As such, models determine the norms of PC practice and offer values and principles that professionals can use as guides and can thus provide important information for understanding integrated PC practices and evaluating their associated strengths and weaknesses (see also Chapter 2) [57].

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CHAPTER 2

Objectives and Specific Aims

General aim

The overall purpose of this thesis is to advance the state of the art of integrated PC in CHF/COPD by investigating theoretically and empirically the gaps mentioned in the previous section in Europe and in Belgium in particular. In this respect, the thesis builds the picture of integrated PC in CHF/COPD in Belgium and thus paves the way for its further integration. The purpose of the thesis is sub-divided into six well-defined objectives:

Objective 1: A systematic literature review of empirically tested models in Europe.

Implementation of PC is not ad-hoc but is usually based on different models. When empirically tested, these models determine not only the benefits, strengths and weaknesses but also the norms of PC practices. Our objective is to systematically identify and examine published and empirically tested models in Europe for malignant and non-malignant disease. Blending malignant with non-malignant disease is advantageous for the second part of this study, which concerns the development of a generic framework for future integrated PC models by combining the strengths and by rectifying the weaknesses **(Chapter 3)**.

Objective 2: A systematic literature review of CHF/COPD guidelines and pathways of integrated PC in Europe.

Having identified the state-of-the-art in PC models for malignant and non-malignant disease, we shift our focus to the investigation of existing guidelines/pathways of integrated PC in CHF/COPD in Europe. We perform a systematic review of the literature and narratively synthesize the outcomes. The results of this systematic review provide information about the current level of integration of PC in CHF/COPD. Furthermore, they allow for the critical evaluation of current practices and recommendations **(Chapter 4)**.

Objective 3: Comparison of level of PC integration between cancer and CHF/COPD guidelines/pathways.

With the results of the systematic review of objective 2 at hand, it is natural to ask how the levels of PC integration in CHF/COPD guidelines/pathways compare with those of cancer, which acts a benchmark. To answer this question we perform a meta-analysis of two previously published systematic reviews, one for CHF/COPP and one for cancer. On the basis of this analysis we also investigate whether the content of the guidelines/pathways constitutes a barrier for further PC integration in CHF/COPD **(Chapter 5)**.

Objective 4: Perceptions of CHF and COPD healthcare professionals on integrated PC.

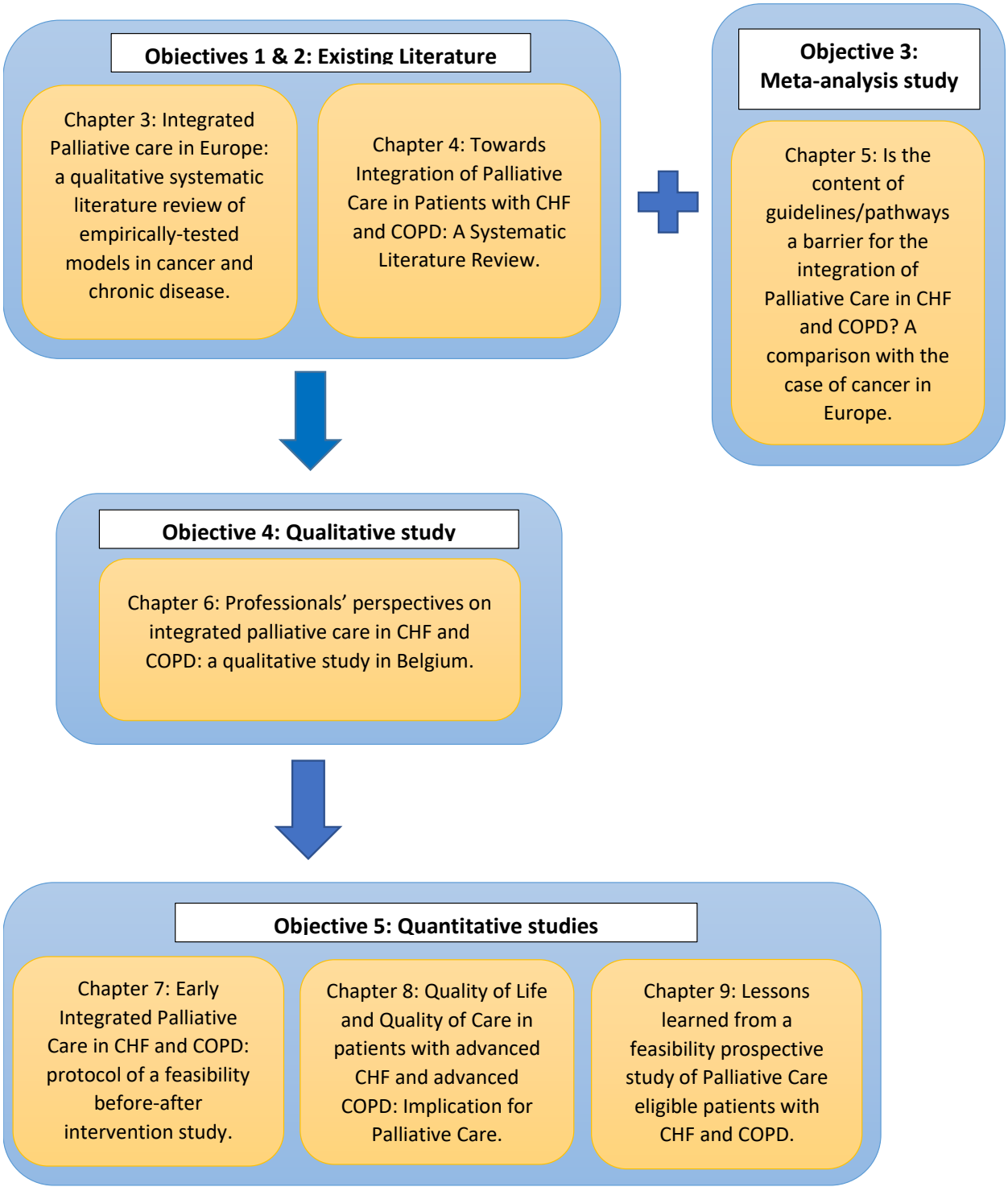
While objectives 1, 2 and 3 examine integration of PC in the theoretical level under the European umbrella, objective 4 focuses locally in Belgium. We perform a qualitative study with interviews of cardiologists and pulmonologists in Belgium in order to document their perceptions on integrated PC for CHF/COPD and current practices **(Chapter 6).**

Objective 5: A feasibility study of an early-integrated PC intervention for CHF/COPD patients in UZ Leuven.

The next objective of this thesis concerns the design and implementation of a feasibility prospective study of early-integrated PC in cardiology and pulmonology in UZ Leuven, Belgium. This study has three aims: i) to measure QoL and quality of care of eligible patients in acute cardiology and pulmonology wards, ii) to assess the efficacy of an "Early PC intervention" and iii) to identify the challenges that stem from the application of a PC study in the acute hospital setting **(Chapters 7, 8 and 9)**.

The structure of this thesis is illustrated in Figure 3. Chapters 3 to 6 address objectives 1 to 4 correspondingly. Chapters 7 to 9 concern objective 5. More specifically, chapter 7 includes the protocol of the feasibility study. Chapter 8 reports the results of the baseline phase of the feasibility intervention study. Finally, chapter 9 concerns the feasibility assessment, the difficulties faced and lessons learned during the baseline phase of the study.

Figure 3. Schematic structure of the PhD thesis.



PART I

Theoretical Part

CHAPTER 3

Integrated palliative care in Europe: a qualitative systematic literature review of empirically tested models in cancer and chronic disease.

This chapter has been published in BMC Palliative Care as:

Siouta N, Van Beek K, Preston N, Hasselaar JG, Hughes S, Garralda E, Centeno C, Csikos A, Groot M, Radbruch L, Payne S, Menten J. Integrated palliative care in Europe: a qualitative systematic literature review of empirically-tested models in cancer and chronic disease. BMC Palliative Care 2016; 15:56.

Integrated palliative care in Europe: a qualitative systematic literature review of empirically tested models in cancer and chronic disease.

Background: Integrated Palliative Care (PC) strategies are often implemented following models, namely standardized designs that provide frameworks for the organization of care for people with a progressive life-threatening illness and/or for their (in)formal caregivers. The aim of this qualitative systematic review is to identify empirically-evaluated models of PC in cancer and chronic disease in Europe. Further, develop a generic framework that will consist of the basis for the design of future models for integrated PC in Europe.

Methods: Cochrane, PubMed, EMBASE, CINAHL, AMED, BNI, Web of Science, NHS Evidence. Five journals and references from included studies were hand-searched. Two reviewers screened the search results. Studies with adult patients with advanced cancer/chronic disease from 1995 to 2013 in Europe, in English, French, German, Dutch, Hungarian or Spanish were included. A narrative synthesis was used.

Results: 14 studies were included, 7 models for chronic disease, 4 for integrated care in oncology, 2 for both cancer and chronic disease and 2 for end-of-life pathways. The results show a strong agreement on the benefits of the involvement of a PC multidisciplinary team: better symptom control, less caregiver burden, improvement in continuity and coordination of care, fewer admissions, cost effectiveness and patients dying in their preferred place.

Conclusion: Based on our findings, a generic framework for integrated PC in cancer and chronic disease is proposed. This framework fosters integration of PC in the disease trajectory concurrently with treatment and identifies the importance of employing a PC-trained multidisciplinary team with a threefold focus: treatment, consulting and training.

Background

According to the World Health Organization (WHO), Palliative Care (PC) aims to improve the quality of life of patients and families who face life-threatening illness, by providing pain and symptom relief, spiritual and psychosocial support from diagnosis to end of life care and bereavement. Further, the WHO recommends that PC becomes an integral part of health care and that all patients affected by a life threatening disease should have access to PC services [1]. This statement is further supported by the European Association of Palliative Care [2] and is also in agreement with the guidelines of the European Council towards the European Union (EU) Member States [3].

This consensus in favor of integrating PC within regular treatment offered to patients with life-threatening disease is supported by a growing amount of evidence that indicates the effectiveness of PC on the improvement of the quality of life of these patients [4-8].

The implementation of integrated PC strategies is often based on models. Models of care are standardized designs that provide frameworks for the organization of care for people with a progressive life-threatening illness and/or for their (in)formal caregivers. As such, models determine the norms of PC practice and offer values and principles that professionals can use as guides and can thus provide important information for understanding integrated PC practices and evaluating their associated strengths and weaknesses.

To date, a univocally accepted model for PC delivery and integration does not exist, even if we confine ourselves to cancer or a major chronic disease. However, there are calls for developing generic PC models that will incorporate recent findings concerning the early identification of patients with needs for PC services and foster the integration of PC early in the care plan and throughout the disease trajectory [9-15].

In the present study, we perform a qualitative systematic review of the available literature for evidence-based models of integrated PC in Europe. We confine ourselves to studies that empirically measure the effectiveness of the corresponding models and employ a high-quality methodological rigour. Further, we examine the conformance of the included studies with respect to how the characteristics and requirements of integrated PC and strengths and weaknesses are documented. By incorporating the strengths and by rectifying the weaknesses, we propose a generic framework that aspires to demonstrate how to integrate PC both in cancer and chronic disease. This study is part of the European project InSup-C that focuses on integration of PC in advanced cancer and chronic disease in Europe (http://www.insup-c.eu/).

Methods

A unanimously agreed definition of integrated PC does not exist as such. For the needs of the present study, a novel definition was developed in the course of the InSup-C meetings by the PC experts and the authors. This definition combines all the aspects of integrated PC, identified by both experts and literature. Our working definition is: “Integrated palliative care involves bringing together administrative, organisational, clinical and service aspects in order to realise continuity of care between all actors involved in the care network of patients receiving palliative care. It aims to achieve quality of life and a well-supported dying process for the patient and the family in collaboration with all the care givers (paid and unpaid)”.

It is important to note that this definition does not distinguish between timings that integration of PC can commence. Consequently, both early and end-of-life PC care can be part of this review. Finally, this qualitative systematic review was conducted in Belgium in September of 2013.

Selection criteria

Eligible studies included those focusing on models of integrated PC for adult patients with cancer or another chronic disease (COPD, renal failure, heart failure, HIV, dementia or other types of neurological diseases), that are, in turn, consistent with the above-mentioned definitions of models and of integrated PC. Since our primary objective concerns the identification of evidence based models, only those studies that empirically assessed the effectiveness of these models and provided relevant data were considered eligible. In particular, we considered randomized controlled trials (RCTs), quasi experimental studies, cohort studies, controlled before-and-after studies, observational studies and pilot evaluation studies whereas we excluded theoretical studies, audits, opinion-only studies in clinical case reports, editorials and letter.

We confided ourselves to studies published from 01-01-1995 (based on the publication year of the Calman-Hine report which constitutes the first national cancer plan in Europe [16]) to 31-12-2013 in one of the following languages: English, French, German, Dutch, Hungarian and Spanish which are the languages that the authors were knowledgeable of.

A final eligibility criterion concerned the quality of the included studies with respect to the methodological rigor. In the present systematic review, only studies that that scored at least 60 % (above 22/36) in the Hawker quality assessment scale were included in this systematic review; see Quality assessment section below.

Search strategy

The following databases were searched electronically: The Cochrane Central Register of Controlled Trials (CENTRAL), PubMed, EMBASE, CINAHL, AMED, BNI, Web of Science and NHS Evidence. The search in the databases was performed via the use of keywords, MESH

terms and search terms as well as their permutations and combinations. Validation of the search strategy was performed against five key papers [4-8].

Additionally, the following journals were hand-searched: BMJ Supportive & Palliative Care, European Journal of Palliative Care, Journal of Pain and Symptom Management, Palliative Medicine and Medicina Paliativa. Citation tracking was also performed for the included studies.

Two different grey literature searches were performed. First, we identified and contacted experts in national scientific medical organizations in order to acquire additional information on existing models. Second, we carried out an electronic search in Google by utilizing a language-tailored strategy; more specifically, each country used relevant key-words and search terms translated into its corresponding language.

Selection procedure

In the first phase, two reviewers (NS & KVB) screened all the search results on the basis of their title and their abstract. Non-English titles were screened and translated by two native speaker reviewers. The full texts of articles selected by both reviewers were sourced. Following standard practice, discrepancies were resolved by consensus.

Data extraction

Data were extracted from papers meeting the inclusion criteria using an extraction form built upon the one described in Hawker et.al. This extraction form was modified for the purposes of this study following consensus in the InSup-C project meetings [17]. For each included paper, data extraction was carried out by the first two authors independently for the cross-checked their results and reached consensus on discrepancies. Extracted variables were: first author's name, year of the study, country the study was conducted,

design, quality assessment, description of the study model, outcome measures, results, focus of the model, setting, time frame of the model, disciplines represented and collaboration strategy.

Quality assessment

The methodological rigour of each included study was formally assessed by the numerical scoring system designed by Hawker et al. [17]. This scoring system is based on nine criteria that are evaluated with a four-point Likert scale: good (4) to very poor (1), thus yielding a maximum score of 36. The nine criteria are: abstract/title, introduction/aims, methods/data, sampling, data analysis, ethics and bias, findings/results, transferability/generalizability, implications/usefulness. It is important to note that the criterion corresponding to methods takes into account the design of the study as well, e.g. RCT, observational study etc. It is on this premise that in the present systematic review we have included studies with different designs and not only RCTs. A detailed presentation of the Hawker tool is reported in Table 1. Our choice is also influenced by Oishi et al. and Rigby et al. who used the Hawker tool while conducting a PC-related systematic review [18, 19].

Table 1. Hawker tool description.

1. Abstract and title: Did they provide a clear description of the study?	
Good	Structured abstract with full information and clear title.
Fair	Abstract with most of the information.
Poor	Inadequate abstract.
Very poor	No abstract.
2. Introduction and aims: Was there a good background and clear statement of the aims of the research?	
Good	Full but concise background to discussion/study containing up-todate literature review and highlighting gaps in knowledge.
	Clear statement of aim AND objectives including research questions.
Fair	Some background and literature review.
	Research questions outlined.

Poor	Some background but no aim/objectives/questions, OR
	Aims/objectives but inadequate background.
Very poor	No mention of aims/objectives.
	No background or literature review.
3. Method and data: Is the method appropriate and clearly explained?	
Good	Method is appropriate and described clearly (e.g., questionnaires included). Clear details of the data collection and recording.
Fair	Method appropriate, description could be better.
	Data described.
Poor	Questionable whether method is appropriate.
	Method described inadequately.
	Little description of data.
Very poor	No mention of method, AND/OR
	Method inappropriate, AND/OR
	No details of data.
4. Sampling: Was the sampling strategy appropriate to address the aims?	
Good	Details (age/gender/race/context) of who was studied and how they were recruited.
	Why this group was targeted.
	The sample size was justified for the study.
	Response rates shown and explained.
Fair	Sample size justified.
	Most information given, but some missing.
Poor	Sampling mentioned but few descriptive details.
Very poor	No details of sample.
5. Data analysis: Was the description of the data analysis sufficiently rigorous?	
Good	Clear description of how analysis was done.
	Qualitative studies: Description of how themes derived/respondent validation or triangulation.
	Quantitative studies: Reasons for tests selected hypothesis driven/numbers add up/statistical significance discussed.
Fair	Qualitative: Descriptive discussion of analysis.
	Quantitative.
Poor	Minimal details about analysis.
Very poor	No discussion of analysis.
6. Ethics and bias: Have ethical issues been addressed, and what has necessary ethical approval gained? Has the relationship between researchers and participants been adequately considered?	
Good	Ethics: Where necessary issues of confidentiality, sensitivity, and consent were addressed.
	Bias: Researcher was reflexive and/or aware of own bias.

Fair	Lip service was paid to above (i.e., these issues were acknowledged).
Poor	Brief mention of issues.
Very poor	No mention of issues.
7. Results: Is there a clear statement of the findings?	
Good	Findings explicit, easy to understand, and in logical progression.
	Tables, if present, are explained in text.
	Results relate directly to aims.
	Sufficient data are presented to support findings.
Fair	Findings mentioned but more explanation could be given.
	Data presented relate directly to results.
Poor	Findings presented haphazardly, not explained, and do not progress logically from results.
Very poor	Findings not mentioned or do not relate to aims.
8. Transferability or generalizability: Are the findings of this study transferable (generalizable) to a wider population?	
Good	Context and setting of the study is described sufficiently to allow comparison with other contexts and settings, plus high score in Question 4 (sampling).
Fair	Some context and setting described, but more needed to replicate or compare the study with others, PLUS fair score or higher in Question 4.
Poor	Minimal description of context/setting.
Very poor	No description of context/setting.
9. Implications and usefulness: How important are these findings to policy and practice?	
Good	Contributes something new and/or different in terms of understanding/insight or perspective.
	Suggests ideas for further research.
	Suggests implications for policy and/or practice.
Fair	Two of the above (state what is missing in comments).
Poor	Only one of the above.
Very poor	None of the above.

Data synthesis

The included studies were characterized by a substantial heterogeneity as studies with both clinical and methodological diversities were included. For this reason, a narrative synthesis was favoured over a meta-analysis and data are reported in tables; hence the

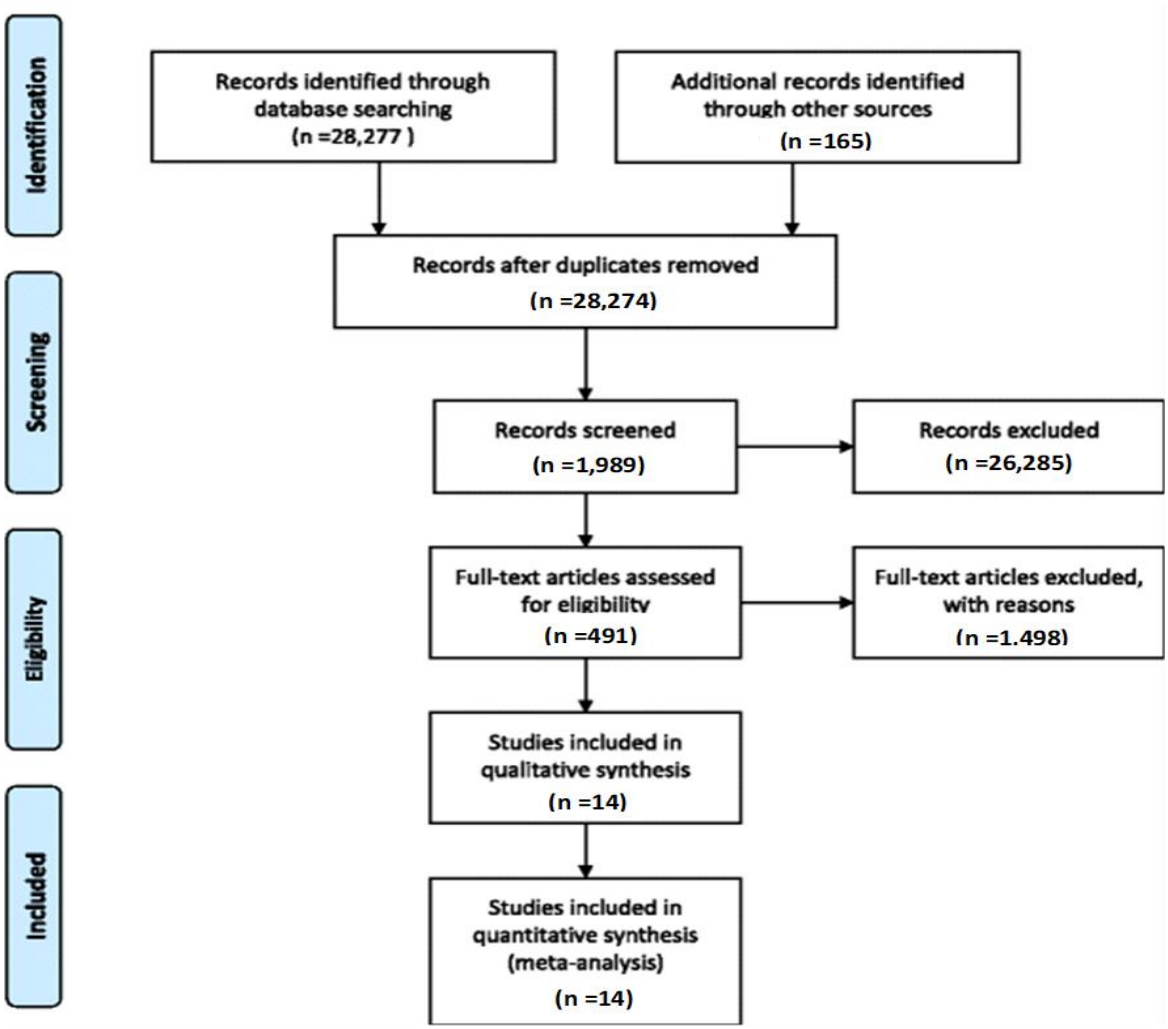
qualitative nature of the review mentioned above. This heterogeneity has also affected the presentation of the results. Comparative analysis was only possible by using a specific number of categories (design, study populations, assessments and outcomes) that will be presented in the following sections.

Results

The database search returned 28,274 hits, excluding duplicates. From the studies that were screened based on abstract/title, 1989 were found to be eligible for full-text screening. Upon full text screening, 491 studies qualified for further assessment of their eligibility. Finally, 14 studies were found to comply with all the selection criteria (see relevant section above). The grey literature search did not add any empirical studies. A flow diagram of the selection procedure and the results is shown in Fig. 1.

From the 14 studies, 7 evaluated models about chronic disease (dementia, multiple sclerosis, chronic heart failure, HIV/AIDS and advanced chronic disease in general), 4 about integrated care in oncology, 3 about cancer and chronic disease (end-of-life patients). The majority of the included studies were from the UK (6 out of 14), 2 were from Spain, 2 from The Netherlands, and one each from Italy, Germany, Norway and France. The preponderance of UK studies is clear in chronic disease where all 6 included studies were from this nation.

Figure 1. Flow diagram of study selection procedure.



The 14 included studies were built upon quite different designs (Table 2) [20-33]. More specifically, there were 6 RCTs, 2 observational studies, 2 cohort studies, 2 pilot evaluation studies, 1 uncontrolled before-and-after studies and 1 quasi-experimental study.

Table 2. Characteristics of the included studies according to different disease categories.

First Author, Year, Country	Design	Quality Assess.	Model	Outcome measurements	Results/ Effectiveness of the model
Cancer					
Jordhøy et al. 2001, (Norway) [20]	Cluster Randomised Trial	33	Collaboration between palliative medicine unit and community service	HRQL*: physical, emotional functioning, pain, psychological distress. Place of death, hospital utilisation.	There was no evidence of any impact on the patients' HRQL*. There was no tendency in favour of any treatment group on the main outcomes in assessments that were made within 3 months before death.
Smeenk et al. 1998, (The Netherlands) [21]	Quasi-experimental study	31	Transmural home care programme: collaboration primary care team and supporting hospital care team.	Re-hospitalization, QoL*, home death	Patients in the intervention group underwent significantly less re-hospitalization during the terminal phase of their illness; the intervention contributed significantly positive to the patients physical QoL; A higher, not significant percentage died at home.
Colombet et al. 2012, (France) [22]	Case series study nested in a cohort	30	Impact of oncologist's awareness of PC, clinical intervention of PCT* and timing, multidisciplinary decision-making.	Indicators: location of death, number of ER* visits in last month of life, chemotherapy administration in last 14 days of life.	58 patients died at home, 45 in an ICU or ER, and 253 in an acute care hospital; 185 patients visited the ER* in last month of life and 75 received chemotherapy in last 14 days of life. OPM* independently

					decreases the odds of receiving chemotherapy in last 14 days of life. Early PCT* intervention had no impact on indicators, whereas OPM* reduced the odds of persistent chemotherapy in the last 14 days of life. Decision-making with oncologists and the PC* team is the most critical parameter for improving EoLC*.
Schreml et al. 2000, (Germany) [23]	Observational study	25	Integration of PC into regular internal ward services in general hospital.	Release of pain, respiratory distress, dying in hospital, length of hospital stay.	It is possible to integrate PC into a regular internal medical ward, with positive impact on recorded outcome measures.
End-of-life (Liverpool Care Pathway)					
Constantini et al. 2013, (Italy) [24]	Cluster Randomised Trial	34	LCP* for cancer patients dying in hospital medical wards.	Quality of EoLC* from perspective of bereaved family member; communication between ward staff and GPs* (VOICES)*.	Aspects of quality of EoLC* improved (emotional, spiritual needs, self-efficacy); slight improvement in communication, no significant improvement in symptom control.
Veerbeek et al. 2008, (The Netherlands) [25]	Uncontrolled before and after study	27	Effect of the LCP* on 3 health care settings (hospital, nursing home, home).	Comparison of level of documentation, symptom burden (EORTC QLQ-C30* questionnaire) and aspects of communication (VOICES)* before and after introduction of LCP*.	Introduction of LCP* increased documentation, decreased symptom burden.

Malignant and Non-malignant Disease					
Grande et al. 2000, (UK) [26]	Randomised controlled trial	33	Cambridge Hospital at Home for palliative care (CHAH).	Symptom control, adequacy of care, likelihood of remaining at home in their final 2 weeks, GP visits.	CHAH appeared to be associated with better quality home care.
Vicente et al. 2010, (Spain) [27]	Retrospective and prospective cohort study	30	Influence of the Integrated Plan of PC* of the Autonomous Community of Madrid in the medical activity of a hospital based PC* unit.	Improvement in continuity of care, coordination amongst assistant bodies, increase in mean stay at the PCU*, increase in number of home deaths, etc.	PC home care improves continuity in care of patients. Transfers to intermediate stay care centers and deaths at home increased. Median stay at the PCU* decreased.
Dementia					
Sampson et al. 2011, (UK) [28]	Randomised controlled trial	28	Pilot implementation of the assessment of PC needs of patients with severe dementia and discussion with principal carers to improve EoLC*.	Kessler Distress Scale, EQ-5D*, Decision Conflicts Scale, Decision Satisfaction Inventory, State Anger Scale, Life Satisfaction Scale, Satisfaction with EoLC*, Advanced Dementia Scale (FAST Scale); Pain and distress (the Abbey pain scale, the PACSLAC and the Doloplus), delirium	General unwillingness to address EoL* issues. All carers were keen to receive more information about EoL* issues in dementia, found discussions very helpful. Participation of clinical MD* team facilitated integration of intervention with the clinical service.

				(Confussion Assessment Method),	
Multiple Scherosis					
Higginson et al. 2009, (UK) [29]	Randomised controlled trial	36	Evaluation of cost-effectiveness of a new PC service for people with MS*.	Use of services, patient symptoms (UNDS*, EDSS* and POS-8*), other outcomes, caregiver burden (ZBI*).	Short-term PCT* was found to be cost-effective, reducing inpatient and community costs, caregiver burden and possibly patient pain.
Edmonds et al. 2010, (UK) [30]	Randomised controlled trial	36	Evaluation of a novel PC service.	MS Impact Scale, POS-8*, ZBI*, Modified Lawton positivity questionnaire.	MS patients who received PC* service had improvements in 5 key symptoms (pain, nausea, vomiting, mouth problems and sleeping difficulties) on the POS and improved informal caregiver wellbeing.
HIV/AIDS					
Koffman et al. 1996, (UK) [31]	A descriptive pilot evaluation	23	Pilot evaluation of hospice at home service for patients with advanced HIV/AIDS; 24-h terminal care.	STAS*, evaluating pain control, other symptom control, patient/family anxiety, patient/family insight and communication between patient and family, between professionals, between professionals and patient and family.	80 % died at home; STAS* showed improvements in items 'other symptoms control' and family insight.
Chronic Heart Failure					

Pattenden et al. 2012, (UK) [32]	Non-randomised pilot evaluation	30	Collaborative PC* for advanced heart failure.	Death in preferred place of care; hospital admissions averted; costs of medical procedures, inpatient care and directs costs of intervention.	This pilot study provides tentative evidence that a collaborative home-based PC* service for patients with advanced CHF may increase the likelihood of death in place of choice and reduce inpatient admissions.
Advanced Chronic Disease					
Navarro et al., 2011, (Spain) [33]	Observational, retrospective and descriptive study	26	EoLC* of advanced chronic non-cancer patients identified by multidimensional evaluation and interdisciplinary teamwork in a medium and long term hospital.	General data, terminal criteria, diagnostic and prognostic information, development of advance directives, limiting levels of effort care, times from admission, risk of complicated bereavement.	Identification of advanced chronic non-cancer patients and their needs by interdisciplinary teamwork enabled indication for PC soon after admission and ensured appropriate care during their stay.

Table 2 describes studies by each disease category according to author, year, country, design, quality assessment score, model, outcome measures and results/findings.

**Abbreviations: PC* palliative care, *QoL* quality of life, *PCT* palliative care team, *OPM* onco-palliative meeting, *EoL* end of life, *VOICES* Views of Informal Carers – Evaluation of Services questionnaire, *ER* emergency room, *MDT* multidisciplinary team, *QoC* quality of care, *GSFCH* Gold Standards Framework in Care Homes, *LCP* Liverpool Care Pathway, *PCU* palliative care unit, *UNDS* United Kingdom Neurological Disability Scale, *EDSS* Expanded Disability Status Scale, *POS-8* Palliative Care Outcome Scale, *ZBI* Zarit Carer Burden Inventory, *ESH* Hospital Support Team, *EQ-5D* EuroQOL five dimensions questionnaire, *EoLC* end of life care, *MD* medical doctor, *MS* multiple sclerosis, *STAS* Support Team Assessment Schedule, *ICU* intensive care unit, *CKD* Chronic Kidney Disease.

Table 2 provides information concerning the quality of the included studies, as measured via the Hawker et al. tool. Two (2) studies [29-30] scored a perfect 36 while 3 other studies scored 33 or 34. The majority of the remaining studies scored in the range between 23 and 31. Table 2 includes detailed information concerning the models of the included studies, their outcome measures and the results/effectiveness of the corresponding models. From this table, we can infer that although RCTs tend to score higher and observational studies lower, other designs perform reasonably well. The latter indicates that such studies have a sound basis, despite the fact that they do not employ an RCT for their assessment.

Even though some of the models bear similarities, (see Table 3 Screening), differences associated with the care setting and the compositions of the team render further grouping and comparison difficult. Upon detailed examination, a common ground for comparison was found in the following categories: focus of intervention, the setting, the timing of the intervention in the disease trajectory, the collaboration strategy and the effectiveness of the models. In the following section, we confine the presentation of the results to these categories.

Table 3. Characteristics of the models.

First author	Focus of the model	Setting	Time frame	Disciplines represented	Collaboration strategy
Cancer					
Jordhoy et al. [20]	treating, training, consulting	Hospital, GP's, nursing homes, home care	end of life	GP, community nurse, consultant nurse, physician from PMU.	Model-responsible team meetings[a]
Smeenk et al. [21]	treating, training, consulting	Hospital, primary care team	concurrent, end of life	Specialist nurse coordinator, oncology ward nurses + medical specialist, transmural home team with nurses from hospital + day care.	Model-responsible team meetings, protocol
Colombet et al. [22]	treating, consulting	Hospital	concurrent, end of life	15 referral physicians: oncologists who prescribe chemotherapy, of whom 2 have been trained in PC fundamentals. MDT: PCT and oncology staff. PCT: PC specialists, nurses, secretary assistant, psychologist. Oncology staff: physicians, nurses, head nurses, social workers, psychologists, secretaries.	Model-responsible team + additional experts meeting[b]
Schreml, et al. [23]	treating, training, consulting	Hospital	concurrent, end of life	Physicians and nurses.	Model-responsible team meetings
End-of-life (Liverpool Care Pathway)					
	treating, training	Hospital	end of life	PCT: 2 physicians, 3 nurses, 2 psychologists.	protocol

Constantini et al. [24]				LCP training: nurses and physicians of the hospital wards.	
Veerbeek et al. [25]	treating	Hospital, nursing home and home	end of life	Physicians and nurses.	Model-responsible team meetings, protocol
Malignant and Non-malignant Disease					
Grande et al. [26]	treating	Home	end of life	Six qualified nurses, 2 nursing auxiliaries, CHAH coordinator, agency nursing care.	Model-responsible team meetings
Vicente et al.[27]	treating	Hospital, home	end of life	PC home team as an MDT comprised by physicians, nurses, nurse assistants, and administrative assistants, social workes, psychologists.	Model-responsible team meetings
Dementia					
Sampson et al. [28]	treating, training, consulting	Hospital, home	end of life	Senior nurse experienced in dementia and trained in PC; clinical MDT.	Model-responsible team meetings
Multiple Sclerosis					
Higginson et al. [29]	treating, consulting	Home, hospital outpatient clinic, care homes, hospital	concurrent	Part-time PC medicine consultant, 1 part-time clinical nurse specialist, 1 administrator, 1 psychosocial worker.	Model-responsible team meetings
Edmonds et al. [30]	treating, consulting	Home, hospital outpatient	concurrent	Part-time consultant in PC Medicine with specialist interest in neurological	Model-responsible team + additional experts meeting

		clinics, care homes, hospital		conditions, part-time clinical nurse specialist, full time administrator.	
HIV/AIDS					
Koffman et al. [31]	treating, consulting	Hospice, home	end of life	Nurses trained in PC; bank nurses for night-sitting; 2 PC medicine consultants.	Model-responsible team + additional experts meeting
Chronic Heart Failure					
Pattenden et al. [32]	treating, consulting	Homes, hospice, 'care of the elderly' wards	concurrent, end of life	Heart Failure nurse specialists, MCN nurses, MCN health care assistants, cardiology, 'care for the elderly' consultants, district nurses, GPs.	Model-responsible team + additional experts meeting, protocol
Advanced Chronic Disease					
Navarro et al. [33]	treating	Hospital	concurrent	The MDT consists of physicians, head nurse, ward nurses, auxiliary nurses, collaborating with a dietician, psychologist, social worker, rehabilitation physician, physiotherapist, occupational therapist and speech therapist.	Model-responsible team + additional experts meeting

Table 3 describes five characteristics of the included studies: the focus of the model, the setting, the time frame of the model, the functions represented, and collaboration strategy involved

PC palliative care, *GP* general practitioner, *PMU* palliative medicine unit, *PCT* palliative care team, *MDT* multidisciplinary team, *LCP* Liverpool Care Pathway, *MNC* Marie Curie Cancer Care, *CHAH* Cambridge hospital at home service, *ESAD* Home Care Support Team, *MDM* multidisciplinary meetings

[a]meetings of the team that is involved in the implementation of the model

[b]meetings between the team responsible for the implementation of the model and other disciplines involved in the treatment of the patient

Focus of intervention: All the included studies placed their focus on symptom treatment. In particular, the objective of these interventions was to improve physical symptoms (dyspnea, pain, constipation, nausea, vomiting, diarrhea), emotional symptoms (agitation, confusion, fear, delirium) and to a lesser extent cognitive and social functioning [20, 23, 28-31]. Nine studies focused on consulting about end-of-life care decisions, advance care planning, advice for coping with life-threatening disease and referrals to specific care-settings. Five studies focused on the training of the nurses and physicians involved in the interventions. The various training programs included training of the staff to support patients over the telephone [21], education on the symptoms of the disease [28] and more general educational programs for community professionals about palliative care services [20, 24, 28].

Setting: The implementation of the models has taken place in a variety of settings. In fact, most studies took place in more than one setting with the majority focusing on inpatient (11/14) and home care (9/11).

Timing of PC initiation: As regards the timing of the initiation of PC, three types of studies were identified; those focusing on end-of-life (11), on concurrent care setting (where PC care is provided alongside regular treatment)(3) and on both (4). For the end-of-life setting, included patients typically were expected to die within a range spanning from a few weeks (2 weeks [26]) to few months (e.g. 2–9 months [20]). For the concurrent care setting, eligible patients were referred by clinicians as potentially benefiting from PC assessments [29-30]. Finally, for the combined setting, various eligibility categories were identified. For example, in [23] all patients with malignant disease independent of the disease trajectory were eligible.

Composition of team: Three different team compositions were identified from the included studies. The first type refers to teams comprising medical and nursing staff; 2 studies [23, 25]. The second type concerns multidisciplinary teams comprising different

professions: general practitioners (GPs), medical specialists, nurses and specialist nurses, psychiatrist and psychologists, health coordinators, administrative assistants, social workers, ambulance services, dieticians and rarely occupational therapists and speech therapists; 4 studies [21, 26, 33]. The third type corresponds to multidisciplinary teams that additionally involve PC experts. Besides being multidisciplinary, these teams also have PC physicians, PC nurses and PC psychologists; 8 studies [22, 24, 31].

Collaboration strategy: The collaboration strategy refers to the ways that the represented disciplines cooperate and assess emerging issues. As shown in Table 3, the included studies employ three different collaboration strategies and their combinations: i) meetings of the team that is involved in the implementation of the model (model-responsible team) [20-28], ii) meetings between the model-responsible team together with experts from other disciplines involved in the treatment of the patient [22, 29-33], iii) utilization of predefined protocols [21, 24-25, 32]. It is important to note that the collaboration is not necessarily related to the composition of the team. For example, a model-responsible team may be multi-disciplinary but still base its decisions on meetings where additional disciplines are represented. In other words, the principal difference between (i) and (ii) is the participation of experts that are not directly related to the implementation of the model in question on a frequent basis.

Effectiveness of the model: As regards effectiveness, all but one study [20], showed positive outcomes in terms of better symptom control and better quality of life, better communication between personnel, patients and caregiver, more deaths at the patients' homes and more cost-effective care. However, this result should be interpreted with care given the variability in the design of the interventions, some of which were not RCTs and therefore of lower quality.

Importantly, even within RCTs, that constitute the most robust design, further comparisons between the results are cumbersome to perform. This is because

discrepancies are observed both in the outcome measures and in the tools employed for their assessment. For example, as regards the evaluation of symptom management, some of the studies used the European Organization for Research and Treatment of Cancer guidelines (EORTC QLQ-C30) questionnaire [24-25, 34], whereas others employed the United Kingdom Neurological Disability Scale (UNDS) [35], the Expanded Disability Status Scale (EDSS) [36], the Palliative Care Outcome Scale (POS-8) [37] and the Support Team Assessment Schedule (STAS) [29-31, 38] or the Abbey pain scale [39], the PACSLAC [40] and the Doloplus [28, 41]. Also, communication aspects were assessed via the Views of Informal Carers-Evaluation of Services (VOICES) [42] tool [24-25]. Further, caregivers' burden was measured with the help of the Zarit Carer Burden Inventory (ZBI) [43], [29-30]. Finally, stressful events were assessed via the Impact of Event Scale (IES) questionnaire [44].

Discussion

We reviewed existing literature on evidence-based models for integrated PC in patients with cancer or chronic disease in Europe. Since the focus of the present study was on the effectiveness of existing models, only specific designs were considered as eligible e.g. RCTs, cohort studies, etc. whereas others, such as theoretical studies, audits, etc., were explicitly excluded. In addition, in order to exclude empirical studies that were conducted with low-quality standards, the numerical tool of Hawker et al. [17] was employed for the assessment of the methodological rigour. In this respect, only those studies that scored at least 60 % in this tool were eligible.

The database search resulted in 14 empirical studies that fulfilled the inclusion criteria. According to our findings, there are only a few models of integrated PC in Europe whilst the geographic distribution of the origin of these interventions is imbalanced, with 6 out of 14 studies coming from the UK.

Only 6 out the 14 studies were RCTs whilst the remaining employed different designs, e.g. observational studies. However, as mentioned above, studies employing a different design for their assessment scored highly on Hawker's tool as well. Consequently, such non-RCT studies can provide valuable insight into the strengths and weaknesses of extant studies that has to be taken into consideration if a complete description of the current state-of-the-art is targeted, as is the case of the present study.

Even though the included studies employ different outcome measures and a direct comparison is not possible, the effectiveness of the models (as assessed by the outcome measures) was confirmed in 13 out of 14 studies. In particular, as mentioned above, the positive impact typically involves better symptom control, higher quality of life, less caregiver burden, improvement in continuity and coordination of care, fewer hospital admissions, patients dying more frequently at home, and improved cost-effectiveness. Even though only 6 out of 14 studies were RCTs, and thus the results of the assessments for the remaining studies should be treated with care, the positive outcomes still add to the growing bulk of evidence corroborating the effectiveness of both usual and integrated PC on the improvement of the quality of life of patients with life-threatening disease [4-8].

We now shift to the development of a framework of integrated PC that could serve as a first step towards the development of a generic model for both malignant and non-malignant disease. Although the included studies suggest practices that are in concordance with existing recommendations and empirical findings, no study presents an intervention that is optimal in all aspects. Consequently, the generic framework that we propose is based on a selective combination of the strengths of the included interventions alongside a critical evaluation of their weaknesses and shortcomings. First, we present the aspects of the generic framework and subsequently we rationalize our choice and motivations.

This generic framework consists of the following aspects.

- Focus of intervention: The focus of intervention will be placed on symptom treatment, consulting of patients/family and training of the personnel.
- Setting: The design of the framework is such that it can be applied to every care setting.
- Timing of intervention: The intervention can be initiated throughout the disease trajectory either concurrently or in the end-of-life.
- Composition of team: The framework requires a multidisciplinary team with members that are trained in the delivery of PC. This team can consist of GPs, physician specialists, nurses and specialist nurses, psychologists, social workers and administrative assistants.
- Collaboration strategy: The collaboration strategy, which refers to the ways that the represented disciplines cooperate and assess emerging issues, should be based on the involvement of the multidisciplinary team and its meetings and the utilization of protocols.

The proposed framework has a threefold focus: treatment, consulting and training. In our context of integrated PC, treatment corresponds to the alleviation of the physical (dyspnea, pain, constipation, nausea, vomiting, and diarrhea) and psychological symptoms (agitation, confusion, fear, delirium). On the other hand, consulting refers to discussions and communications over treatment options and at a later stage to end-of-life care decisions. Moreover wishes, desires and needs of the patients can be taken into account as part of this advance care planning. Training involves the education of nurses, physicians and other related health care providers involved in the interventions. Training programs can be very diverse, however, their principal focus should be on PC, its benefits and its provision.

The benefits of focusing on treatment are apparent, however, the benefits of the remaining two aspects are also well documented. As regards consulting, PC typically

involves difficult medical and ethical decision making [4-8] for patients and their (in)formal caregivers. Importantly, the same studies assert that the burden associated with this decision making can be ameliorated with the assistance of trained PC staff through systematic consulting and informative discussions.

By contrast, regarding training, we first note that the generic framework should be utilized with extreme caution because these suggestions may need to be tailored to the specific situation. In other words, this framework pertains to assist PC teams in their planning and implementation of PC strategies and not to provide black-box solutions. In this respect, it should be highlighted that the improper application of generic frameworks, and in fact of every integrated PC framework, can jeopardize the effectiveness of the employed PC practices. A notable example is the case of the Liverpool Care Pathway (LCP) [45], which has been sometimes erroneously employed, leading to poor outcomes and has in turn been used as an excuse for poor quality care [46, 47]. Public outcry from the poor implementation of the LCP led the UK government to stop the use of the LCP.

Recent studies explicitly state that there is a correlation between the successful implementation of the LCP and the training of the staff [48]. Importantly, this constitutes a characteristic of integrated PC in general [49-51]. For this reason, future efforts should explicitly foster the educational aspect of the professional members.

The choice of the timing of the intervention and thus the referral criteria is a contentious topic in the literature of PC. Historically, PC studies focusing on cancer opted for an end-of-life time frame based on the premise that once cancer reaches the terminal phase, the disease trajectory declines rapidly so that end-of-life prognoses can be fairly accurate [52-53]; still, prognosis in cancer is frequently over-optimistic [54]. However, early integrated PC is increasingly supported by various studies, because it has been documented to improve quality of life in the last days and increase survival [4].

Moreover, end-of-life prognosis for non-malignant disease is problematic. For example, the typical trajectory of Chronic Heart Failure (CHF) consists of acute crises or exacerbations followed by elongated periods of stability. At the same time, CHF patients are in high risk of sudden death [55]. Consequently, for non-malignant disease, an end-of-life frame is cumbersome to realise and a concurrent time frame of the initiation of PC is deemed more appropriate [56]. On the other hand, there is a growing number of studies supporting the decoupling of the initiation of PC from the traditional end-of-life time frame and the shift to the early integration of PC in the disease trajectory [57-61].

According to our definition of integrated PC, the timing of the initiation of PC care is not determined so that models that focused on either concurrent PC or end-of-life care were eligible. Despite the fact that, as mentioned above, end-of-life care in patients with non-malignant disease is difficult to realise in practice, this is not reflected in our results since representatives of both categories are included for patients with either malignant or non-malignant disease. As a consequence, our generic framework necessarily employs a diverse number of timings, ranging from concurrent to end-of-life. This is not without implications as offering a spectrum of options, over a uniquely defined one, implies that the final choice falls within the jurisdiction of the involved teams. In turn, this might lead to significantly diverse practices and, therefore, impede the benefits associated with PC. Future studies should thus focus on the convergence of opinions on the timing of PC so that ideally a standardized recommendation is crafted.

In the proposed generic framework, the involved team should be multidisciplinary in nature and involve experts from different fields. Functionality of multidisciplinary teams may be impeded by ambiguity of the distributed roles, conflicts between the team members, communication problems and issues related to leadership [62-63]. However, extant studies in PC for patients with both malignant and non-malignant disease support the results of this study showing that multidisciplinary teams (MDTs) lead to better results

when compared to uni-disciplinary ones because they enhance continuity of care, evidence-based decision making, ACP and high quality care delivery [4, 64-66].

As the integration of PC requires bringing together specialists from different backgrounds and their well-orchestrated coordination, the development of protocols that quantify their collaboration is imperative for the successful implementation of PC. As mentioned in the Results section, the included studies employ miscellaneous collaboration strategies consisting of distinct components: collaboration between the team members (intra-team collaboration), multidisciplinary team meetings and protocols. The intra-team collaboration, which constitutes the only common component of all studies, is important because it assures the efficient implementation of the PC strategy. Further, for the aforementioned reasons multidisciplinary team meetings are also important for enhancing the continuity of care. Lastly, protocols have compelling advantages because they provide a clear guide for the next steps to be undertaken [67]. Since none of these components are redundant and our results show that they are complementary to each other in our generic framework, we propose to employ a strategy based on a combination of these.

Having addressed all the components of this generic framework, a comment on the implications that this framework has on the recommendations of the WHO [1] is in order. Overall, the proposed framework accords very well with the definition of PC provided by the WHO, however, two important differences are identified. First, the proposed framework highlights the training of the healthcare providers, which is essential for the successful implementation of integrated PC; this is not the case of the WHO definition where training is absent. Second, although WHO recognizes the need for employing a team approach no explicit reference on multidisciplinarity is made. By contrast, the proposed framework emphasizes the importance of utilizing PC teams the members of which come from various backgrounds.

Finally, it is interesting to juxtapose the timings of PC. As mentioned above, due to the fact that the InSup-C definition of integrated PC does not comment on the timing, the proposed framework offers a multitude of timings; from concurrent to end-of-life. The definition of WHO states that PC "is applicable early in the course of illness, in conjunction with other therapies that are intended to prolong life…". However, as stated, this phrase does not explicitly promote early integration but rather on its range of applicability. In other words, the WHO definition does not narrow down the timing of PC to concurrent but rather expends to a spectrum of option in a manner similar to the proposed framework. Consequently, if attention has to be shifted to a concurrent timing, this should be explicitly reflected in the corresponding definitions.

Additional information may be drawn by comparing the five aspects of the generic framework against indicators for integrated PC. Such sets of indicators do exist in the literature, however, they correspond to PC in patients with cancer. Still, since cancer also pertains to the present such a comparison is fruitful. A recent systematic review provided a set of 38 indicators for integrated PC in oncology [68]. These indicators were grouped into five groups namely: structure of clinical programs, processes of clinical programs, education, research and administration. The same grouping was employed in the subsequent study [68], where a set of 43 indicators (13 major and 30 minor) was proposed based on a consensus of experts. Interestingly, with the exception of research, the generic framework, and the models that has been composed from, satisfies the majority of these indicators for both studies.

Study limitations

The first limitation of this study concerns the broadness of the topic under investigation. Integrated PC in cancer and non-cancer patients and without time specification is a very large area and requires a quite generic search strategy. Moreover, in view of this

broadness, we were confronted with a substantially heterogeneous set of results that could only be accessed through a qualitative description.

The search strategy employed was developed upon consensus between the PC experts involved in the project meetings. However, a unanimously agreed definition for integrated PC does not currently exist. Consequently, even though our strategy is broad, some evidence might have been missed due to the keywords used for the search strategy.

A third limitation concerns the choice of the languages of the included studies. The present study is confined to studies published in Dutch, English, French, German, Hungarian and Spanish, that were the languages that the project partners were knowledgeable of. It is, therefore, possible that studies published in other EU languages are available and not included [69].

Finally, we stress that the generic framework proposed herein has been based on models for patients with cancer and non-cancer disease. Its validity, therefore, is formally limited to these particular diseases. Although extrapolations to other types of life-threatening disease are tempting, further study in this direction is clearly needed. Also even though the proposed framework aims to be generic, one has to acknowledge limitations stemming from differences between healthcare systems, cultural and geographic factors and funding levels. Moreover, the preponderance of UK studies in this review should not go unnoticed. This is further supported by [70] who argue that generic models have to be flexible enough to be tailored to different settings; as a consequence, their recommendations should not be extremely stringent.

Conclusions

This is the first qualitative systematic literature review of models on integrated Palliative Care (PC) in patients with malignant and non-malignant disease in Europe. It represents

the combined effort of an international consortium of six partners in six different European countries (Belgium, Germany, Hungary, Spain, The Netherlands and United Kingdom).

Based on the results, we have proposed a generic framework for integrated PC in patients with cancer and chronic disease. The proposed generic identifies the importance of employing a PC-trained multidisciplinary team and of having a threefold focus: on treatment, consulting and training. Each component of our framework has been already empirically assessed, however, the overall framework has not. Although one could extrapolate the existing empirical evidence in favour of our framework's efficacy, we believe that an empirical study for the framework as a whole should carried. Such a study not only will provide empirical evidence on the framework's efficacy but will also shed light on possible weaknesses that can be only traced post-implementation. Additionally, it would be interesting to conduct the same systematic review in non-European countries and performed a comparative analysis in a worldwide scale.

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CHAPTER 4

Towards integration of palliative care in patients with chronic heart failure and chronic obstructive pulmonary disease: a systematic literature review of European guidelines and pathways.

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Towards integration of palliative care in patients with chronic heart failure and chronic obstructive pulmonary disease: a systematic literature review of European guidelines and pathways.

Background: Despite the positive impact of Palliative Care (PC) on the quality of life for patients and their relatives, the implementation of PC in non-cancer health-care delivery in the EU seems scarcely addressed. The aim of this study is to assess guidelines/pathways for integrated PC in patients with advanced Chronic Heart Failure (CHF) and Chronic Obstructive Pulmonary Disease (COPD) in Europe via a systematic literature review.

Methods: Search results were screened by two reviewers. Eligible studies of adult patients with CHF or COPD published between 01/01/1995 and 31/12/2013 in Europe in 6 languages were included. Nine electronic databases were searched, 6 journals were hand-searched and citation tracking was also performed. For the analysis, a narrative synthesis was employed.

Results: The search strategy revealed 26,256 studies without duplicates. From these, 19 studies were included in the review; 17 guidelines and 2 pathways. 18 out of 19 focused on suffering reduction interventions, 13/19 on a holistic approach and 15/19 on discussions of illness prognosis and limitations. The involvement of a PC team was mentioned in 13/19 studies, the assessment of the patients' goals of care in 12/19 and the advance care planning in 11/19. Only 4/19 studies elaborated on aspects such as grief and bereavement care, 7/19 on treatment in the last hours of life and 8/19 on the continuation of goal adjustment.

Conclusion: The results illustrate that there is a growing awareness for the importance of integrated PC in patients with advanced CHF or COPD. At the same time, however, they signal the need for the development of standardized strategies so that existing barriers are alleviated.

Background

The World Health Organization's (WHO) "Global Burden of Disease" study estimates that, since 2002, chronic or non-communicable conditions have accounted for 87 % of deaths in high-income countries. Moreover, the proportion of deaths worldwide due to such conditions is projected to reach 69 % by 2030 [1].

Chronic heart failure (CHF) and Chronic Obstructive Pulmonary Disease (COPD) are two prominent causes of chronic conditions. CHF in particular is the leading cause of death worldwide whereas COPD is projected to rise to the third highest cause by 2030 [2-3]. In Europe, more specifically, CHF and COPD are responsible for 1.9 and 2.9,000,000 annual deaths, respectively [4-5].

Palliative Care (PC) is a specialized medical care targeted in patients living with life-threatening conditions. The aim of PC is the promotion of physical and psychosocial health and thus the improvement of the quality of life of such patients and their families. In order for these objectives to be reached, the focus of PC is typically placed on three principal areas: 1) the alleviation or control of symptoms and side effects of either the disease and/or curative treatment, 2) the timely and continuously updated communication of treatment goals between physicians, patients and their families and 3) the efficient psychological, social and spiritual support for both patients and their families throughout the course of the illness trajectory [6].

Owing to its generic definition, PC can in principle be integrated with curative treatment for both malignant and non-malignant disease [6]. Consequently, even though PC mostly began in cancer care in Europe, it is not surprising that awareness for patients with non-malignant disease has increased [7-8]. Moreover, extant studies have empirically showed that PC practices can significantly improve the quality of life of patients with chronic conditions [9]. Importantly, there is a general acknowledgement that optimal care for

patients with advanced stages of CHF and COPD should rest upon an integrated and holistic approach while simultaneously taking into account patients and family needs throughout the course of the illness [8, 10].

Delivery of PC in patients with advanced CHF and COPD, however, is quite challenging because of the following three barriers i) both diseases are associated with complicated trajectories resulting in uncertain prognostication [11-12], ii) sudden deaths are common making planning difficult [13-14], iii) since there is usually a variety of treatment options, patients are not typically well informed about their disease and therefore do not participate actively in decision making. Further, this inhibits the discussion of end-of-life issues [15-16]. With current evidence showing that access to PC is dominated by patients with cancer [17-19], it is conceivable that these barriers have a prominent role on this aspect.

The implementation of PC in both malignant and non-malignant disease is often based on guidelines and/or pathways. Guidelines are defined as systematically developed statements to assist practitioners and patient decisions about appropriate health care for specific clinical circumstances. Care pathways, on the other hand, are defined as complex interventions for the mutual decision making and organisation of care processes for a well-defined group of patients during a specified period. Consequently, existing guidelines and pathways contain valuable information on current practices for PC in patients with non-malignant disease. Additionally, they provide concise answers to two questions that are critical in planning PC for patients with non-malignant disease: a) when should PC initiate and b) how to integrate PC with curative treatment.

The aim of this study is to systematically review guidelines and pathways of integrated PC for people with advanced CHF and COPD in Europe. By doing so, we obtain an overview of the current level of integration of PC in advanced CHF and COPD in Europe while we document and critically evaluate current practices and recommendations. This study is

part of the multi-country European project InSup-C that focuses on integration of PC in cancer and chronic disease in Europe (http://www.insup-c.eu/).

Methods

To date, a unanimously agreed definition of integrated PC does not exist. For the needs of this study the following definition based on consensus of the InSup-C experts has been employed:

"Integrated palliative care involves bringing together administrative, organisational, clinical and service aspects in order to realise continuity of care between all actors involved in the care network of patients receiving palliative care. It aims to achieve quality of life and a well-supported dying process for the patient and the family in collaboration with all the care givers (paid and unpaid)".

Search strategy

For the purpose of this study, guidelines and pathways are defined as follows. Guidelines are systematically developed statements used to assist practitioners and patient decisions about appropriate health care for specific clinical circumstances. Care pathways, complex interventions used to assist mutual decision making and organization of care processes for a well-defined group of patients during a specified period. Consequently, existing guidelines and pathways contain valuable information on current practices for PC in patients with non-malignant disease

The search strategy for this review included an electronic search of the following databases: PubMed, Web of Science, The Cochrane Central Register of Controlled Trials (CENTRAL), CINAHL, EMBASE, BNI, AMED, NHS Evidence, and National Guidelines Clearinghouse. The exact search terms and keywords used for the electronic search are available as an electronic supplement to this paper as well as in the InSup-C website

www.insup-c.eu. Besides the electronic database search, the search strategy included citation reference and the hand-searching of the following journals: European Journal of Palliative Care, BMJ Supportive & Palliative care, Palliative Medicine, Journal of Pain and Symptom Management, Medicina Paliativa.

Additionally, for the grey literature search we followed two strategies: i) we contacted named individuals within national scientific medical organizations in order to gather information on guidelines and pathways for CHF and COPD and ii) we performed an electronic search in Google (which was translated in the other six languages of the authors participating in this study). In the UK due to the size of the grey literature, we performed an electronic search in the NHS Evidence database.

Selection criteria

A systematic review of the literature was conducted of guidelines and pathways about integrating PC into standard care for patients with advanced CHF and COPD. In conformance with the objectives of the InSup-C, the present review is confined to the identification of existing guidelines and pathways in Europe. The other selection criteria of the study are presented in the Table 1 and the exclusion criteria in Table 2 below:

Table 1. Inclusion Criteria describes the inclusion criteria for the guidelines and pathways of this study.

1. Guidelines and pathways for adult patients
2. Guidelines and pathways for CHF and COPD (latest possible versions)
3. European guidelines and pathways.
4. Guidelines and pathways published from 01-01-1995 to 31-12-2013 (with the start date based on the publication of the Calman-Hine report [81])
5. Languages: English, French, German, Dutch, Hungarian and Spanish (the languages of the authors)

6. Guidelines and pathways that fulfilled at least 2 out of 11 IPC criteria (see explanation below and Table 3).

Table 2. Exclusion criteria describes the exclusion criteria for the guidelines and pathways of this study.

1. Papers on chronic disease in general.
2. End-of-life guidelines and pathways.
3. General palliative care guidelines/pathways.
4. Guidelines and pathways for children.
5. Guidelines/pathways in languages other than the included ones.

The sixth inclusion criterion concerned the completeness of the content of the included guidelines/ pathways with regard to integrated palliative care. In order to measure the level of the integration of the PC content of the studies we employed a widely used tool with 11 criteria based on the study by Emanuel et al. 2004 [20] (Table 3). A consensus in the InSup-C consortium was reached for the determination of the entry level filter (fulfilment of at least two out of 11 criteria) of this tool.

Table 3. Integrated Palliative Care (IPC) Criteria describes the eleven criteria of Integrated Palliative Care for the evaluation of the content of the included guidelines and pathways.

1. Discussion of illness limitations and prognosis.
2. Recommendations for conducting a whole patient assessment including the patient's physical, social, psychological, and spiritual issues, their family and community setting.
3. Recommendations for when to make these assessments
4. Recommendations on when PC should be integrated-referral criteria.
5. Assessment of the patient's goals for care.
6. Continuous goal adjustment as the illness and the person's disease progresses.
7. Palliative care interventions to reduce suffering as needed.
8. Advance care planning.

9. Recommendation of involving a PC team.
10. Recommendations on care during the last hours of living.
11. Recommendations on grief and bereavement care.

Selection procedure

Two authors (NS and KVB) screened all the English search results based on their title and their abstract. The guidelines and pathways that were in the other included languages were screened and translated by two native speaker researchers. Subsequently, NS and KVB sourced and reviewed the translated full texts based on the inclusion criteria and exclusion criteria. Disagreements were reconciled by either consensus or by open discussions in the InSup-C project meetings.

Data extraction

An extraction form based on the study by Hawker et. al (2002), and it was modified towards the project goals was used to examine included papers [21]. The first two authors extracted data from English guidelines/pathways independently and then cross-checked the results. The same procedure was followed by two native speaker researchers for the non-English ones. Discrepancies were resolved by consensus.

Data synthesis

Due to heterogeneity of the results, a narrative synthesis was deemed more appropriate and guidelines are presented in Table 4 and pathways in Table 5, while an overall synthesis is presented in Table 6.

Table 4. Quality assessment of the Evidence describes the four different categories of the quality assessment of the included guidelines and pathways of this study.

High Quality Evidence	Medium Quality Evidence	Low Quality Evidence	Very Low Quality Evidence
Guidelines/pathways based on both systematic reviews and consensus methods or those developed following the NICE protocol [82].	Guidelines/pathways based on systematic review only or based on other types of well referenced evidence.	Guidelines/pathways based on consensus methods only.	Guidelines/pathways that are unclear (e.g. apparently evidence based but failing to clarify how this was obtained).

Table 5. Characteristics of included guidelines.

Title/Country/Year	Disease	Setting	Integrated Palliative Care Criteria (IPC)	Quality of Evidence
Multidisciplinary guideline Heart Failure/The Netherlands/2010 [22].	Heart Failure	inpatient/outpatient	9 IPC: Discussion of illness limitations and prognosis, Holistic assessments, Timing of PC introduction, Patient's goals, Continuous goal adjustment, Suffering reduction, ACP*, Involvement of PC team, Last hours of living care.	High
Guideline Palliative care for people with COPD/The Netherlands/ 2011 [23].	COPD	inpatient/outpatient	8 IPC : Discussion of illness limitations and prognosis, Holistic assessments, Timing of holistic assessments, Timing of PC introduction, Patient's goals, Suffering reduction, ACP, Involvement of PC team.	Medium
Guideline COPD/ The Netherlands/ 2010 [24].	COPD	inpatient/outpatient	5 IPC: Discussion of illness limitations and prognosis, Timing of PC introduction,	Low

			Patient's goals, Continuous goal adjustment, Suffering reduction.	
Guideline Heart failure/The Netherlands/2010 [25].	Heart failure	inpatient/outpatient	7 IPC: Discussion of illness limitations and prognosis, Holistic assessments, Timing of PC introduction, Patient's goals, Suffering reduction, Involvement of PC team, Last hours of living care.	Low
Multidisciplinary guideline diagnostics and treatment of COPD/ The Netherlands/ 2010 [26].	COPD	inpatient/outpatient	5 IPC : Discussion of illness limitations and prognosis, Holistic assessments, Timing of PC introduction, Patient's goals, Suffering reduction.	High
95 Management of chronic heart failure. A national clinical guideline/UK-Scotland/2007 [27].	Heart failure	inpatient/outpatient	4 IPC: Discussion of illness limitations and prognosis, Timing of holistic assessments, Patient's goals, Suffering reduction.	High
Living and dying with advanced heart failure: a palliative	Heart Failure	inpatient/outpatient	10 IPC: Discussion of illness limitations and prognosis,	High

care approach/UK-Scotland/2008 [28].			Holistic assessments, Timing of holistic assessments, Timing of PC introduction, Patient's goals, Continuous goal adjustment, Suffering reduction, ACP, Involvement of PC team, Last hours of living care.	
NICE clinical guideline 101: Management of chronic obstructive pulmonary disease in adults in primary and secondary care/UK/2010 [29].	COPD	inpatient/outpatient	3 IPC: Holistic assessments, Suffering reduction, Involvement of PC team.	High
Chronic Obstructive Pulmonary Disease Services/UK-Scotland/ 2010 [30].	COPD	inpatient/outpatient	5 IPC: Discussion of illness limitations and prognosis, Holistic assessments, , Patient's goals, ACP, Involvement of PC team.	High
Global Strategy for Diagnosis, Management, and Prevention of COPD/UK/ 2013 [31].	COPD	inpatient/outpatient	7 IPC: Discussion of illness limitations and prognosis, Timing of holistic assessments, Timing of PC introduction, Continuous goal adjustment, Suffering reduction, ACP,	High

			Involvement of PC team.	
Heart Disease: quick reference guide/UK/ 2012 [32].	Heart Failure	inpatient/outpatient	3 IPC: Discussion of illness limitations and prognosis, Timing of PC introduction, Suffering reduction.	Low
IMPRESS guide for commissioners on supportive and end of life care for people with COPD/UK/ 2012 [33].	COPD	inpatient/outpatient	9 IPC : Discussion of illness limitations and prognosis, Holistic assessments, Timing of PC introduction, Patient's goals, Continuous goal adjustment, Suffering reduction, ACP, Involvement of PC team, Grief and bereavement care.	High
Services for people with chronic obstructive pulmonary disease CMG43/UK/ 2011 [34].	COPD	inpatient/outpatient	11 IPC: Discussion of illness limitations and prognosis, Holistic assessments, Timing of holistic assessments, Timing of PC introduction, Patient's goals, Continuous goal adjustment, Suffering reduction, ACP, Involvement of PC team, Last	High

			hours of living care, Grief and bereavement care.	
Services for people with chronic heart failure/UK/2011 [35].	Heart Failure	inpatient/outpatient	9 IPC : Discussion of illness limitations and prognosis, Holistic assessments, Timing of holistic assessments, Timing of PC introduction, Suffering reduction, ACP, Involvement of PC team, Last hours of living care, Grief and bereavement care.	High
Chronic obstructive pulmonary disease: Management of chronic obstructive pulmonary disease in adults in primary and secondary care/UK/ 2010 [36].	COPD	inpatient/outpatient	2 IPC: Suffering reduction, Involvement of PC team.	High
Best practice guidance on developing a respiratory service specification/UK/ 2008 [37].	COPD	inpatient/outpatient	2 IPC:, Suffering reduction, Last hours of living care.	Low
ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012/Europe/2012 [38].	Heart Failure	Acute setting	8 IPC: Discussion of illness limitations and prognosis, Holistic assessments, Timing of holistic assessments,	High

			Timing of PC introduction, Continuous goal adjustment, Suffering reduction, ACP, Involvement of PC team.	
The included guidelines are described in different categories: title, country and year, type of disease, setting. *Abbreviations: Integrated Palliative Care (ICP) criteria and quality of evidence. ACP= Advance Care Planning, COPD= Chronic Obstructive Pulmonary Disorder.				

Table 6. Characteristics of included pathways.

Title/Country/Year	Disease	Setting	Integrated Palliative Care Criteria (IPC)	Quality of Evidence
Consensus on Integrated Care for Disease Exacerbations of COPD. (ATINA-EPOC)/Spain/2012 [39].	COPD	-	8 IPC: Discussion of illness limitations and prognosis, Holistic assessments, Timing of holistic assessments, Timing of PC introduction, Patient's goals, Continuous goal adjustment, Suffering reduction, ACP*.	Low
End of life care in heart failure: A framework for implementation/ UK/ 2010 [40].	Heart Failure	inpatient/outpatient	7 IPC: Holistic assessments, Patient's goals, Suffering reduction, ACP, Involvement of PC team, Last hours of living care, Grief and	Low

			bereavement care.	
The included pathways are described in different categories: title, country and year, type of disease, setting, Integrated Palliative Care (ICP) criteria and quality of evidence. ACP= Advance Care Planning, EoL=End-of-Life, COPD= Chronic Obstructive Pulmonary Disorder.				

Quality assessment

For the evaluation of the quality of the evidence a four-point Likert scale tool (high quality (4) to very low quality (1)) was developed by the project consortium (Table 4). It is important to highlight that the assessment employed in the present systematic review does not assess the quality of the implementation of the included guidelines/pathways. Rather, it provides a means of evaluating the principles upon which they have been proposed.

Results

We identified a total of 31,298 potentially relevant articles, with 28,277 originating from the electronic database searching and 3021 from the grey literature and the citation tracking. The process of contacting professional experts did not return any further result. After the exclusion of the duplicate results we had 26,256 results of which 25,223 were excluded based on their titles or abstracts. From the 1033 remaining results, we identified 235 guidelines/pathways eligible for full-text screening. The final review included 17 guidelines and two pathways (in total 19) [22-40]. The properties of these studies are available in Tables 5 and 6. A flow diagram of the selection procedure and results (using the PRISMA tool [41]) is presented in Fig. 1 below.

Seventeen guidelines and two pathways were included in the study. Of the 17 guidelines included in the final review, eleven originated from UK, five from the Netherlands and one from more than one European country. Of the two pathways, one pathway originated from Spain and one from UK. From these results, eleven guidelines/pathways were concerned with COPD and eight with CHF. A synthesis of the key point recommendations for all the included CHF and COPD guidelines and pathways in relation to the 11 IPC Criteria is presented in Table 7. Moreover, throughout this section results correspond to the combined set of pathways and guidelines.

Table 7. Key point recommendations in relation to the IPC criteria provides the key recommendations of Integrated Palliative Care of the included guidelines and pathways.

IPC Criteria	**References of guidelines and pathways**	**Key point recommendations**
Discussion of illness limitations and prognosis	[22-28, 30-35, 38-39] (15/19)	"Open communication between patient and doctor."
Holistic assessment	[22-26, 28-30, 33, 34-35, 38-40] (13/19)	"Address physical, emotional, social and spiritual needs."
Timing for holistic assessments	[23, 27-28, 31, 33-35, 38-39] (9/19)	"Work closely with clinicians to agree on the indicators for the exact timing of the holistic assessments."
Timing for PC introduction	[22-26, 28, 31-35, 38-39] (13/19)	"Early integration of PC in the disease trajectory."
Patient's goals assessments	[22-28, 30, 33-34, 39, 40] (12/19)	"Disease specific management plans and care plans should be based around patient's personal goals."
Continuous goal adjustment	[22, 24, 28, 31, 33-34, 38-39] (8/19)	"Regular assessment of patients' PC needs and continuous communication and collaboration between care teams and organizations."
Suffering reduction	[22-29, 31-40] (18/19)	"Timely access to symptom control and administration of appropriate medication"

Advance care planning (ACP)	[22-23, 28, 30-31, 33-35, 38-40] (11/19)	"Early discussion of ACP, including patients' end-of-life needs and preferences."
Involvement of PC team	[22-23, 25-26, 28-31, 33-36, 38, 40] (14/19)	"Specialist PC is provided by multi-professional PC teams, including physicians, nurse specialists, psychologists, chaplains, social workers, pharmacists and other appropriate allied health professionals."
Recommendations on care during the last hours of living	[22, 25, 28, 34-35, 37, 40] (7/19)	"Care in the last days of life should be available 24 h a day, including rapid access services, symptom control and assessment of end-of-life preferences."
Grief and bereavement care recommendations	[33-35, 40] (4/19)	"Provide family bereavement support and ensure there is access to spiritual care and chaplaincy services."

There was almost unanimous agreement (18/19) that the focus of PC interventions should be placed on reduction of suffering through the provision of appropriate medication and psychological support. Recommendations for discussions about illness prognosis and limitations were found in 15 out of 19 of the included guidelines and pathways.

It was found that the holistic approach, i.e. the assessment of the patient's physical, psychological, social and spiritual issues, was recommended in 13 out of 19 guidelines/pathways, however, only 9/19 included instructions on when these assessments should take place.

Recommendations concerning the involvement of a PC team were reported in 14/19. All these 13 guidelines and pathways additionally promote the composition of a

multidisciplinary PC team that involves professionals from different disciplines e.g. physicians, disease specialists, nurses, psychologists, psychiatrists, chaplains, nutritionists, physiotherapists, etc. Seven guidelines/pathways recommend the involvement of personnel that are additionally trained in PC. On the other hand, the utilization of advance care planning and the assessment of the patients' goals of care were mentioned in 11/19 and 12/19 guidelines and pathways respectively.

From the included guidelines/pathways 13 out of 19 discussed explicitly the referral criteria, i.e. the point at which PC should be initiated. However, among those that made an explicit recommendation, the analysis yielded large variations. A minority (4/19) used the specific referral criteria mentioned in the Gold Standards Framework or stages III or IV in the New York Heart Association (NYHA) [42] or stages III and IV in the Global Initiative for Chronic Obstructive Lung Disease (GOLD) [22, 24, 28, 35, 43]. The timing as to when to initiate PC varied with 3/19 saying in the last six months but none of them invoked the surprise question [23, 25-26]. One guideline reported that PC should be applied in the last 12 months of life [39], whereas another one stated that the referral criteria should be for terminally ill people without however defining the exact timing [40]. One guideline encouraged considering integration of PC from the moment of diagnosis or as soon as possible [27]. Finally, one guideline recommended that the exact PC timing should depend on the frequency of hospital admissions or exacerbations [38]. The referral criteria distribution is presented in Fig. 2.

Fig 1. Flow diagram of study selection procedure.

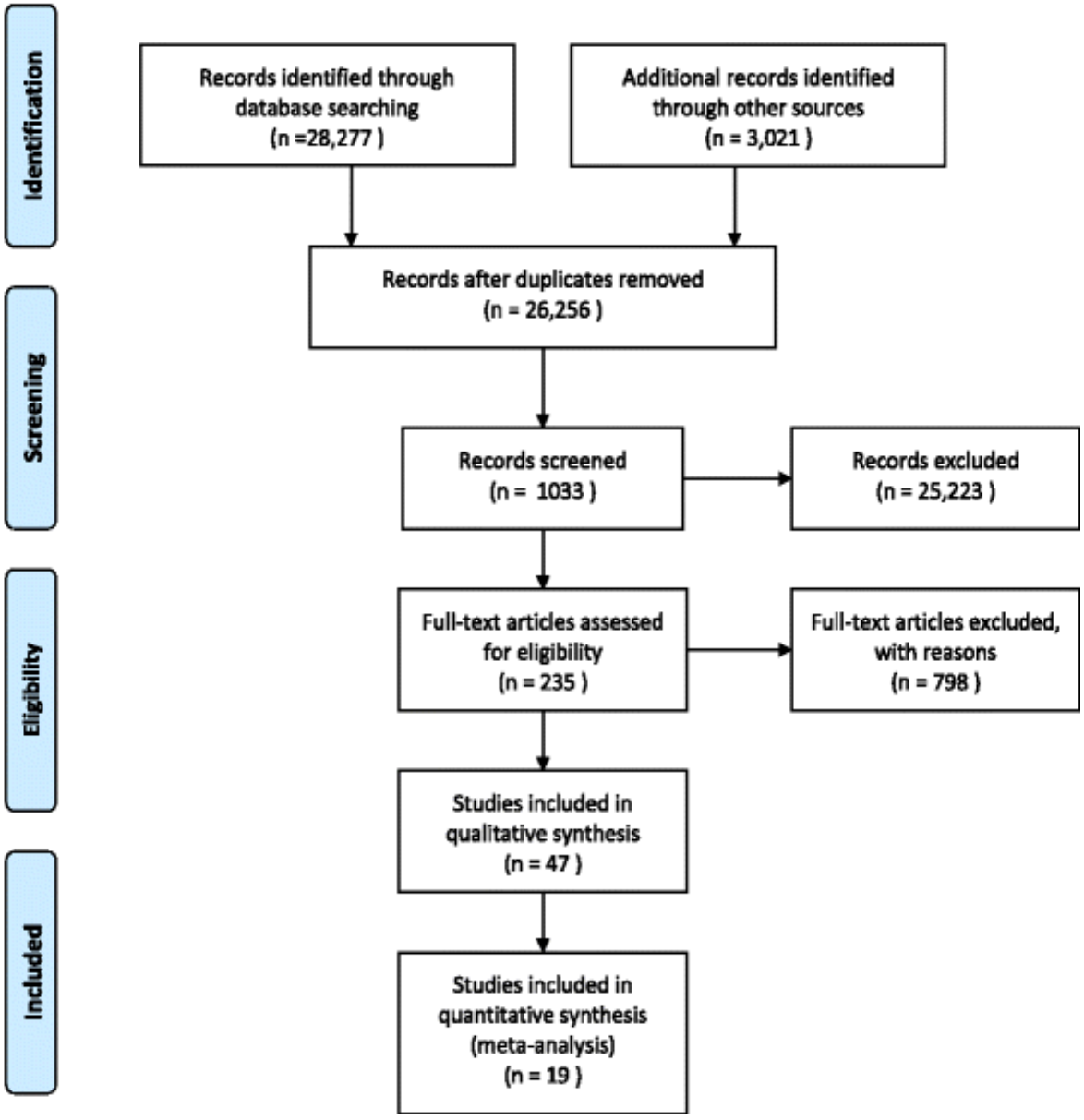
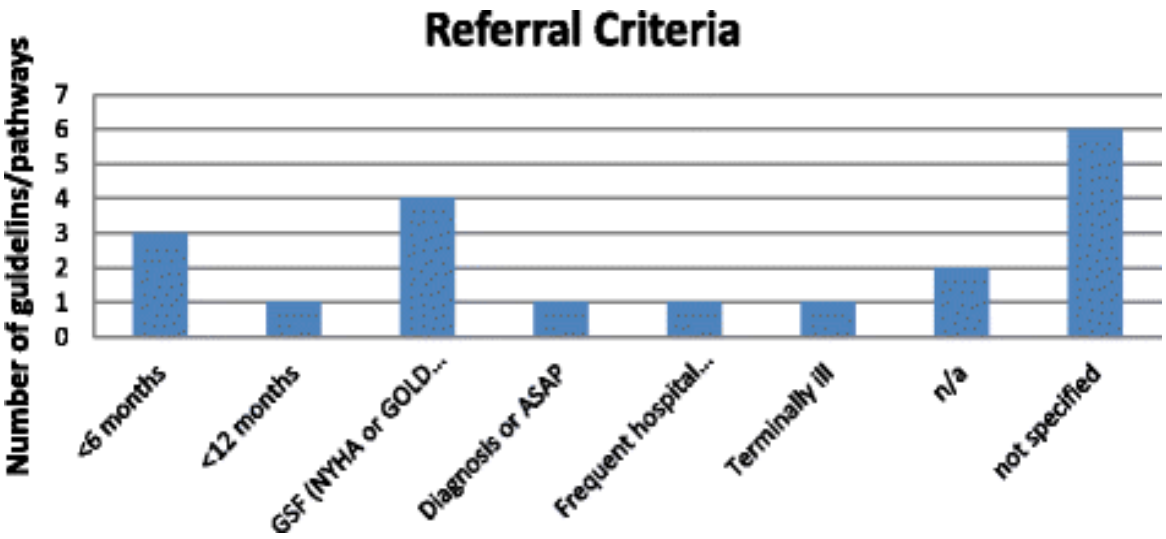


Fig 2. Absolute number of guidelines/pathways in relation to the referral criteria for PC.



Only four (4/19) of the included guidelines/pathways elaborate on aspects such as grief and bereavement care (post mortem), seven (7/19) gave recommendations on how to treat the patient in the last hours of life and with continued goal adjustment mentioned in 8/19 of the examined documents.

Using the quality assessment for the evaluation of the evidence (see Table 4), 6/17 guidelines/pathways scored low for quality as they were based on consensus methods only. One guideline was categorised as medium quality; based on systematic review only or based on other types of well referenced evidence. Finally, 12/19 of guidelines/pathways were classified as high quality evidence. According to our findings, the majority of the guidelines/pathways were not devised in collaboration with PC physicians. At this point it is important to highlight that the assessment employed in this review does not assess the quality of the implementation of the included guidelines/pathways. Rather, it provides a means of evaluating the principles upon which they have been proposed.

Discussion

The majority of the included studies originated from the UK (11 guidelines and one pathway). This is probably due to the fact that PC originated from the UK [44]. The results revealed considerable discrepancies in the integration of PC guidelines, not only in the level of implementation, but in the level of what is conceptually deemed important as well. However, despite such disparities, almost all guidelines/pathways emphasise that the priority of integrated PC should be the reduction of suffering, by effective symptom control. This convergence of opinion is noteworthy for two reasons. First, it accords with what organizations such as the WHO [45], the European Society of Cardiology [46], the European Respiratory Society [47] and others identify as the primary objectives of PC. Second, it conforms to perceptions of both physicians and patients [48-49].

The determination of the referral criteria in the application of PC to patients with advanced CHF or COPD has been a subject of debate [12, 50-54]. This is mainly due to the fact that, as opposed to cancer, illness trajectories of CHF and COPD are quite variable including sequences of deteriorations and (partial) relapses [55]. In fact, even though prognosis of both advanced CHF and COPD is poor [55-56], prognostication is inexact. Also, the predictive capacity of the various utilized tools is at best moderate and is further reduced by the frequent occurrence of sudden deaths, frequent relapses, comorbidity, and so on. Consequently, physicians are often reluctant to discuss PC options and, interestingly, when they do so, the reaction of patients involves negative surprise; this might also be attributed to the fact that public understanding of these diseases is not linked to dying, unlike for example cancer [57-58].

In the present study, nearly half of the included guidelines/pathways did clarify referral criteria. However, even among those that provide a recommendation, no appreciable convergence of opinions was observed, as our analysis demonstrated widely diverse referral criteria. Moreover, the appropriateness of many of these referral criteria is

questionable because they heavily rely on prognostication; in fact, even the three guidelines/pathways that opted for “last six months” did not based their recommendation on the surprise question but rather on prognostic models. Interestingly, at the same time, guidelines recognise the need for communication between clinicians and patients concerning the limitations of prognostication which appears to lead to a contradictory view. A possible way to resolve this issue was demonstrated by communicating to the patient the potential risks involved in future admissions so paving the way for an advance care planning discussion. Since only one guideline explicitly promoted the early inclusion of PC alongside standard treatment, it is evident that, despite recommendations of medical associations [47], the perception that PC should be primarily concerned with “end-of-life” still prevails [59].

Concerning decision making and advanced care planning, patients with advanced CHF or COPD are quite unlikely to get engaged in discussions concerning treatment options/preferences and end-of-life issues because i) patient-physician communication about end-of-life care might be less likely to occur, ii) it is more complicated to initiate this for patients with less certain prognosis [60, 61, 62] and iii) as mentioned above, public understanding of these diseases is not directly linked to dying which can inflict negative reactions from patients [57-58]. The scarcity of patient-physician discussions concerning treatment options/preferences and the frequent total absence of discussions on end-of-life issues result in less informed patients who are, nevertheless, willing to both familiarize themselves with aspects of their disease and express their preferences [63]; these adverse effects are more apparent nowadays because many patients search for relevant information on the web and can thus challenge or question medical decision making [64].

The majority of the included guidelines/pathways identified the need for enhanced communication for both treatment options/preferences and end-of-life issues and explicitly advocate for it. Nonetheless, the necessary further steps to achieve this, such as advance care planning and continuous goal adjustment are absent from a considerable

amount of the included studies. Consequently, since patient-physician communication, advanced care planning and continuous goal adjustment are interlinked, ignoring the latter two might result in suboptimal PC. It is interesting to note that similar findings were reported in a very recent systematic review of integrated PC in guidelines and pathways in cancer, which implies that poor communication is evident independently of the disease trajectory [19].

The holistic approach to care including comprehensive assessment of physical, psychological, spiritual and social needs is backed by robust evidence [65-69]. However, its practical implementation is quite challenging because it is based on the well-orchestrated coordination of and cooperation between different specialties while often requiring the assumption of additional, novel duties from the involved personnel. Current research has documented that these requirements are frequently unmet due to implemented i) the reluctance of physicians to advocate expansion of specialist PC services, ii) the obscurity of the roles of doctors and nurses in different specialties and iii) the limited funding and infrastructures [69-70]. As a consequence, the same studies hint that the holistic approach is often poorly implemented in practice. In view of these facts, we can infer that a stand-alone recommendation for the employment of the holistic approach is inadequate. Rather, such recommendations should be supplemented with detailed instructions that exemplify and quantify the roles of the involved personnel, their interaction and timing of the assessments. The prominence of the holistic approach is acknowledged by the majority of the included guidelines/pathways [22, 25, 28]. Moreover, they provide specific recommendations for controlling physical symptoms, relieving psychological issues and addressing spiritual needs of the patients.

As regards the composition of the PC team, most of the guidelines/pathways advocate a multidisciplinary approach that involves professionals from different disciplines who are additionally trained in PC [71]. The advantages of the multidisciplinary approach over the uni-disciplinary one have been documented and advocated for multiple times in the

literature both for CHF and COPD [17, 45, 72-75]. It is also important to note that combining a holistic approach with a multidisciplinary PC team has been posited to increase the benefits of PC [76]. The advantages of this combination have been recognized by most guidelines and pathways in this study.

Finally, our analysis revealed a lack of emphasis on recommendations on the last hours of life and bereavement care. It is striking that most of the guidelines/pathways identify PC as an end-of-life concept. Both aspects have consistently been identified as significant components of a complete and optimized integrated PC [12, 77]. However, and despite being explicitly promoted [50, 78, 79, 80], they are frequently overlooked as is the case with the present guidelines/pathways. Consequently, future guidelines and pathways should increase their focus on these aspects.

Study limitations

The search strategy employed herein is quite generic in order to cover as many guidelines/pathways related to CHF and COPD as possible which led to a large number of titles being screened. The main reason for employing this search strategy is because we conducted two studies, one focusing on cancer patients (reported elsewhere) and another focusing on CHF and COPD. It is conceivable that a different search strategy would reveal a somewhat different list of results. Still, the employed search strategy is deemed to be general enough to cover the vast majority of the existing CHF and COPD studies. This was supported through citation tracking and reference list checking.

The lack of a standardised and universally accepted definition of integrated PC constitutes a limitation of this study. As a consequence the search strategy uncovered a rather heterogeneous body of working touching on a variety of aspects of integrated PC. Still, the definition employed herein is deemed general enough to encapsulate the most relevant aspects of integrated PC.

A second limitation is linguistic and refers to the restriction to European guidelines/pathways published in Dutch, English, French, German, Hungarian and Spanish. It is quite possible that several guidelines/pathways exist in other European languages as well; our first electronic search returned potential candidates in Italian and Swedish that were excluded for the reasons described above. Further, additional information could have been obtained if we had included studies from other continents as well.

The third limitation of this study pertains to the tool employed for the evaluation of the completeness of the content of the guidelines/pathways. Following consensus between the authors and the experts participating in the InSup-C project, Emmanuel's criteria were adopted on the basis of their completeness. In fact, the range covered by Emmanuel's criteria is large enough to ensure an overlap with a potential alternative. Consequently, even though the employment of a different evaluation tool might have provided alternate results, modifications are expected to be minor. It doesn't however help us know which guidelines work the best in practice.

Conclusions

We have systematically reviewed the literature for guidelines/pathways of integrating PC in patients with advanced CHF or COPD in Europe. Existing guidelines/pathways thoroughly discuss the aspects like the reduction of suffering, the holistic approach, the enhanced communication and the involvement of multi-disciplinary PC team. However, other related aspects such as referral criteria, advanced care planning, recommendations on the last hours of life and bereavement care are only partially touched or addressed. Moreover, several suggested recommendations and solutions from the guidelines are either insufficiently clear or even at odds with existing directives and well-documented findings. For example, several guidelines/pathways recommended referral that rely on

prognostication while at the same time acknowledged the limitation for acquiring an accurate one.

Overall, the results of this systematic study illustrate that there is a growing awareness for the importance of PC in patients with advanced CHF and COPD. At the same time, however, they signal the need for the development of standardized and conceptually unambiguous strategies so that existing barriers are alleviated. In this respect, given that prognostication for both CHF and COPD is difficult, emphasis should be placed on the determination of referral criteria that are independent of it and thus straightforward to realise in practice. Moreover, particular attention should be paid to the communication of end-of-life issues that consistently appears as a bottleneck in PC for patients with advanced CHF and CODP. Further, it is critical that the nearly total absence of discussions concerning end-of-life issues is alleviated so that both the efficacy of PC services and the number of beneficiaries are enhanced. This is instrumental for the improvement of existing PC practices that have been consistently shown to be suboptimal.

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CHAPTER 5

Is the content of guidelines/pathways a barrier for the integration of palliative Care in Chronic Heart Failure (CHF) and chronic pulmonary obstructive disease (COPD)? A comparison with the case of cancer in Europe.

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Is the content of guidelines/pathways a barrier for the integration of palliative Care in Chronic Heart Failure (CHF) and chronic pulmonary obstructive disease (COPD)? A comparison with the case of cancer in Europe.

Background: There is a notable inequity in access to palliative care (PC) services between cancer and Chronic Heart Failure (CHF)/Chronic Obstructive Pulmonary Disease (COPD) patients which also translates into discrepancies in the level of integration of PC. By cross-examining the levels of PC integration in published guidelines/pathways for CHF/COPD and cancer in Europe, this study examines whether these discrepancies may be attributed to the content of the guidelines.

Design: A quantitative evaluation was made between integrated PC in published guidelines for cancer and CHF/COPD in Europe. The content of integrated PC in guidelines/pathways was measured using an 11 point integrated PC criteria tool (IPC criteria). A statistical analysis was carried out to detect similarities and differences in the level of integrated PC between the two groups.

Results: The levels of integration between CHF/COPD and cancer guidelines/pathways have been shown to be statistically similar. Moreover, the quality of evidence utilized and the date of development of the guidelines/pathways appear not to impact upon the PC integration in the guidelines.

Conclusion: In Europe, the empirically observed imbalance in integration of PC for patients with cancer and CHF/COPD may only partially be attributed to the content of the guidelines/pathways that are utilized for the PC implementation. Given the similarities detected between cancer and CHF/COPD, other barriers appear to play a more prominent role.

Background

In Europe, there is an aging population with an increased survival of patients with both malignant and non-malignant diseases and the number of patients in need for palliative care (PC) projected to significantly increase [1-2]. The substantial number of eligible patients and the complexity of their needs require a more integrated, systematic and sustained approach to the provision of high-quality care.

Integrated PC constitutes a potential unifying framework that enhances PC by integrating it alongside standard treatment that aims to prolong life. More specifically, integrated PC involves bringing together administrative, organisational, clinical and service aspects in order to achieve continuity of care between all those involved in the patient's care network. It aims to achieve quality of life and a well-supported dying process for the patient and the family in collaboration with all the care givers (paid and unpaid) [3, 4, 5, 6]. Importantly, there is evidence-based consensus that integrated PC results in the improvement of the quality of life of patients with both malignant and non-malignant diseases [7-21].

Nonetheless, empirical studies, carried out in a variety of countries, conclusively assert that there is no equity in the access and provision of PC services, [22-23]. In fact, when compared to patients with cancer, patients with Chronic Heart Failure (CHF) or Chronic Obstructive Pulmonary Disease (COPD) are much less likely to receive PC. Although the exact percentages vary between studies, typically cancer patients have access to PC services at a percentage close to or above 50% whereas the corresponding ones for CHF and COPD are usually much below 25%, sometimes even below 10%, [24-26]. Given that patients with CHF and COPD share the same prevalence of PC-related problems with cancer patients [26-29], this profound imbalance constitutes a critical point of concern. Furthermore, this inequity of access implies that the levels of PC integration for patients

with cancer and CHF/COPD are also disparate; this is true even in countries that have been designated as having reached an advanced stage of integration of PC [1, 30-31].

In practice, the implementation of PC is often based on guidelines or pathways [32]. Guidelines are systematically developed statements to assist practitioners and patient decisions about appropriate health care for specific clinical circumstances. They can be national, international or local. As such, they are often used as a means to reduce variations in treatments within health-care systems, to develop hospital-tailored protocols, to educate students and to assist insurers [32-34]. On the other hand, a care (or clinical) pathway is defined as a complex intervention for mutual decision making and organization of care processes for a well-defined group of patients during a well-defined period [35].

The frequent utilization of guidelines and pathways, combined with the foregoing discussion, suggest that the empirically observed discrepancies with respect to the levels of PC integration might be traced, among others, in the content of the corresponding guidelines/pathways. In this respect, the following hypothesis may be formulated:

The content of the available guidelines/pathways concerning integration of PC practices is different in cancer and in CHF/COPD and constitutes a barrier for the improvement of the level of PC integration.

Interestingly, even though the identification of barriers for the improvement of PC integration has attracted considerable attention, [36-38],the validity of the above hypothesis remains, to the best of our knowledge, an open question. A recent systematic review published by the authors, [39], identified existing integrated PC guidelines/pathways for patients with CHF and COPD in Europe. The study revealed, among others, that the level of integration of PC accommodated in existing guidelines/pathways is moderate. Although this finding does suggest that there is still

room for improvement, it does not allow for the acceptance or rejection of the aforementioned hypothesis. For a conclusive answer, one needs to juxtapose and analyse existing evidence for CHF and COPD with the corresponding ones for cancer.

The objective of this paper is to examine the validity of the abovementioned hypothesis in Europe. In order to do so, we carry out a comparison and quantitative analysis on the levels of integration of PC between the guidelines/pathways for cancer and CHF/COPD in Europe included in [39-40].

Before proceeding to the main body of this study, two comments are in order. First, as the notable case of the Liverpool Care Pathway [41] asserts, the completeness of the content of a guideline/pathway does not suffice for its successful implementation. In other words, even if a guideline/pathway has an excellent content on PC integration, its implementation might lead to totally undesirable outcomes. Nevertheless, the completeness of the content does constitute a necessary condition for a successful implementation which gives merit to our hypothesis. Second, in principle, one could directly compare the results from [39, 40] to conclude in favour or against our hypothesis. However, this approach is not well-founded due to the inequality in the number of guidelines/pathways, the differences in the quality of evidence that the guidelines/pathways have been built upon, the differences in the year of publication etc. In other words, a robust assessment of our hypothesis requires the performance of a suitable statistical analysis, like the one employed in the present study.

Methods

For the purpose of this study, guidelines and pathways are difined as follows. Guidelines are systematically developed statements used to assist practitioners and patient decisions about appropriate health care for specific clinical circumstances. Care pathways, complex interventions used to assist mutual decision-making and organization of care processes for a well-defined group of patients during a specified period.

Comparison and quantitative analysis

In the two systematic reviews [39-40], the measurement of the level of integration of the PC content of the guidelines was performed via an 11-criteria tool based on the study by [42]. This is a template designed by the American Hospice Foundation Guidelines Committee to provide a practical approach for guideline writers and others to integrate PC into disease management and care services whenever it is relevant. These criteria are described as follows and hereafter shall be referred to as “IPC criteria”.

Integrated Palliative Care (IPC) Criteria.

1. Discussion of illness limitations and prognosis.
2. Recommendations for conducting a whole patient assessment including the patient’s physical, social, psychological, and spiritual issues, their family and community setting.
3. Recommendations for when to make these assessments (referral criteria).
4. Recommendations on when palliative care should be integrated.
5. Assessment of the patient’s goals for care.
6. Continuous goal adjustment as the illness and the person’s disease progresses.
7. Palliative care interventions to reduce suffering as needed.
8. Advance care planning.
9. Recommendation of involving a palliative care team.
10. Recommendations on care during the last hours of living.
11. Recommendations on grief and bereavement care.

Each guideline has been assessed via these IPC criteria and has been assigned the value ‘1’ for each criterion that it fulfils and the value “0”otherwise. By summing up the assigned values we can associate each guideline with a sum score that ranges from “0” to “11”.

The range of scores is interpreted on a 12-level Likert scale with zero (0) standing for no integration and eleven [11] standing for utmost integration. It is important to note that these IPC criteria constitute quality indicators for the content of integrated PC in the guidelines and do not provide any information on the efficacy of the implementation into clinical practice of the guidelines which needs to be measured via additional, clinical studies. Moreover, we underline that this assessment tool is yet to be validated. However, and to the best of our knowledge no such validated tool currently exists, which in turn supports our choice.

Evidence quality assessment

In order to assess the quality of the evidence of the guidelines/pathways in both systematic reviews, the authors employed a 4-level Likert scale presented as follows: a) High Quality Evidence: guidelines/pathways based on both systematic reviews and consensus methods or those developed following the NICE protocol [29], b) Medium Quality Evidence: guidelines/pathways based on systematic review only or based on other types of well referenced evidence, c) Low Quality Evidence: guidelines/pathways based on consensus methods only, d) Very Low Quality Evidence: guidelines/pathways that are unclear (e.g. apparently evidence based but failing to clarify how this was obtained). This quality assessment guide was agreed upon by consensus between the authors and the PC experts of the InSup-C project in the framework of which this study has been performed (http://www.insup-c.eu/).

Statistical analysis

In order to compare the levels of integration of PC and the levels of the quality of evidence between the guidelines/pathways for cancer and for CHF/COPD statistical significance tests were carried out. Given the ordinal character of the variables, the Mann-Whitney test was utilized at a 95% level of significance ($a = 0.05$). Correlation analyses, based on

the calculation of the Spearman coefficient, were also conducted in order to detect possible correlations between the variables. Additionally, standard descriptive statistics were employed to provide an insight in the general properties of the two groups of guidelines/pathways.

Results

The number of cancer guidelines was over thrice as high as the one for CHF/COPD (74 vs 19). Table 1 portrays the publication dates of the number of guidelines. The relative frequencies (%) of the IPC scores of the two groups (cancer and CHF/COPD) are depicted in Fig. 1. The medians are M = 5 and M = 7 for cancer and CHF/COPD, respectively.

Table 1. Publication dates of the guidelines/pathways.

Guidelines/ pathways	**Publication Dates**
Cancer (*n* = 74)	Date: number of guidelines
	1999: 1
	2002: 1
	2004: 5
	2005: 2
	2006: 2
	2007: 4
	2008: 7
	2009: 4
	2010: 11
	2011: 11
	2012: 12
	2013: 12
	No date available: 2
CHF/COPD (*n* = 19)	2007: 1
	2008: 2
	2010: 8
	2011: 3
	2012: 4
	2013: 1

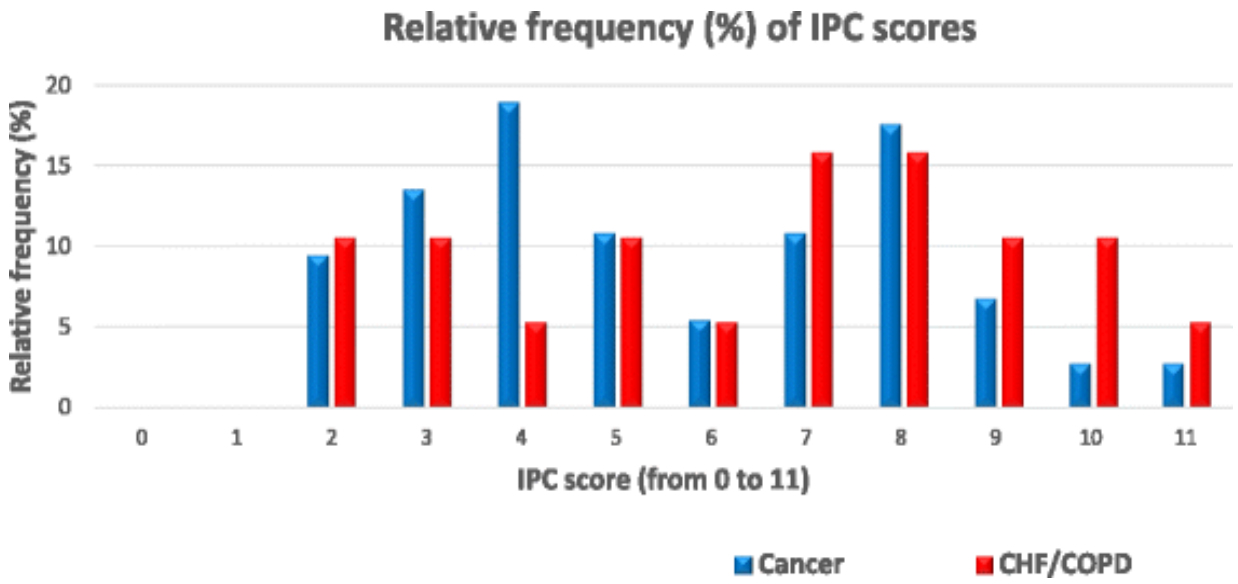


Figure 2. Distribution of Integrated Palliative Care (IPC) scores for cancer and Chronic heart failure/Chronic obstructive pulmonary disease guidelines/pathways. IPC Integrated palliative care; CHF Chronic heart failure; COPD Chronic obstructive pulmonary disease

The Mann-Whitney test revealed no statistically significant differences between the median IPC scores of the guidelines for cancer and CHF/COPD (U = 573, p = 0.19). In other words, the average level of integration of PC in the guidelines for cancer is statistically the same as that for CHF/COPD. The statistical power of the test, corresponding to a large Common Language Effect Size (CLES) = 0.7, was calculated to be approximately equal to 0.8 which is sufficiently large.

In Fig. 2 the relative frequencies of guidelines scoring on the respective IPC item is reported. In general, the levels of satisfaction are moderate, usually below 60% for both cancer and CHF/COPD. A remarkably low percentage is associated with the 11th criterion that concerns bereavement care.

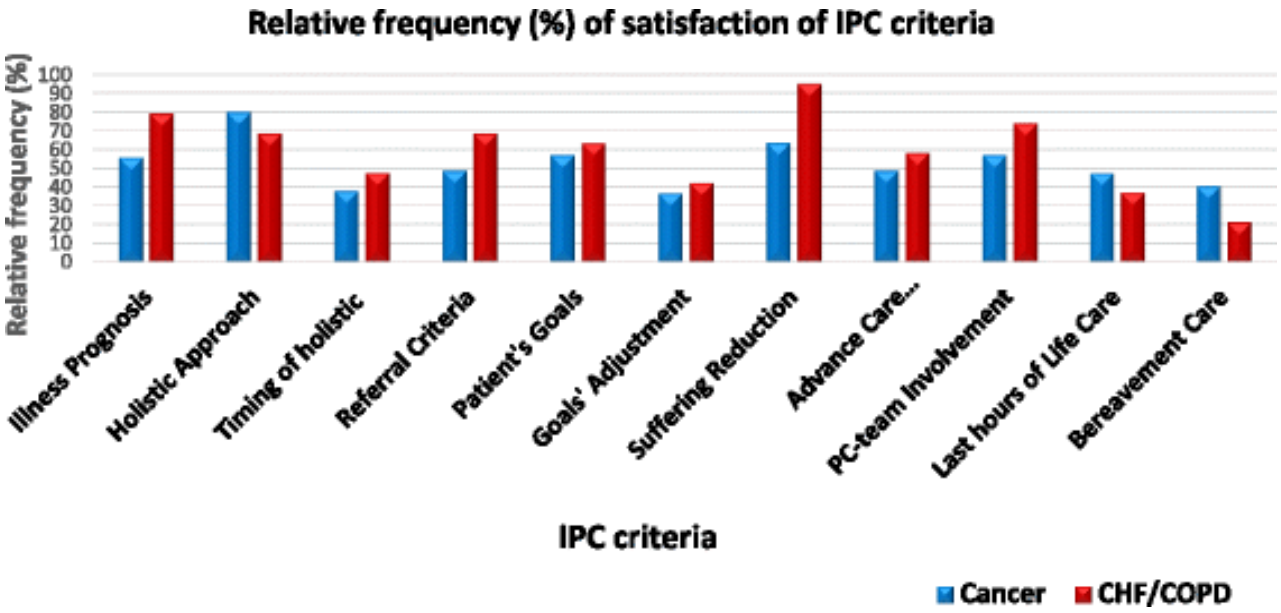


Figure 2. Percentages of cancer and Chronic heart failure/Chronic obstructive pulmonary disease guidelines/pathways satisfying each Integrated Palliative Care (IPC) criterion. IPC Integrated palliative care; CHF Chronic heart failure; COPD Chronic obstructive pulmonary disease

The different referral criteria recommended by the guidelines/pathways are summarized in Fig. 3. More specifically, Fig. 3 displays the frequencies (%) of the various referral criteria that the guidelines proposed. From this figure, we can infer that only a small number of guidelines/pathways recommended early initiation of PC for either cancer or CHF/COPD.

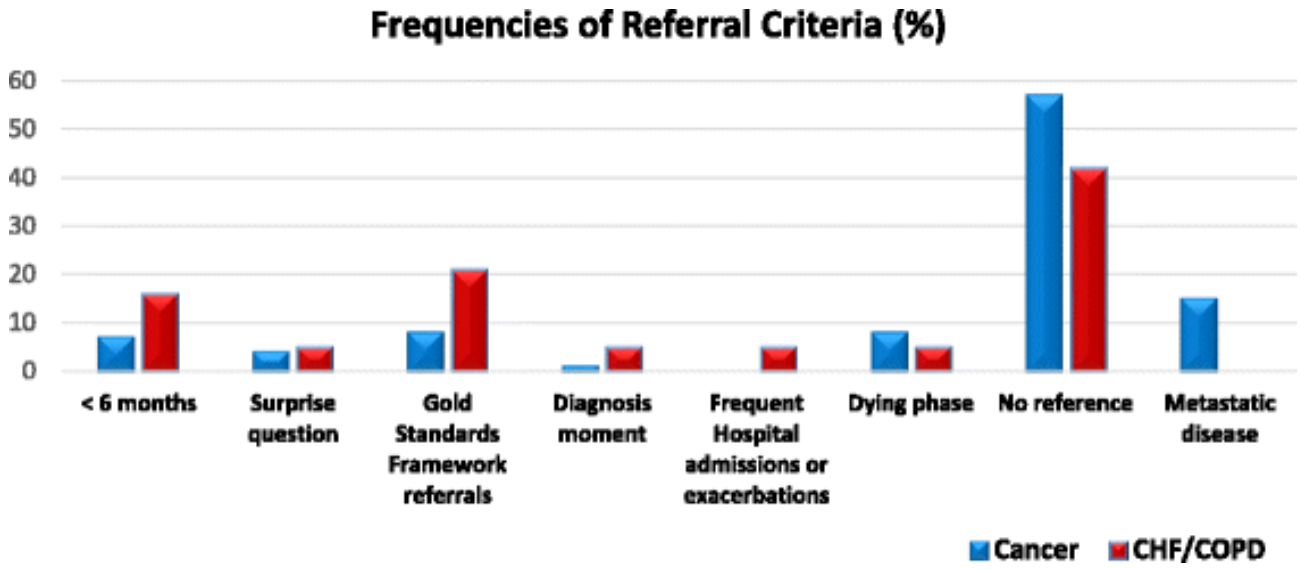


Figure 3.Frequencies of palliative care referral criteria recommended in cancer and Chronic heart failure/Chronic obstructive pulmonary disease guidelines/pathways. PC Palliative care; CHF Chronic heart failure; COPD Chronic obstructive pulmonary disease; Surprise Question = a screening question for physicians "'Would you be surprised if this patient died in the next year?" that aims to identify end-of-life patients, Gold Standards Framework referrals = see http://www.goldstandardsframework.org.uk/

The relative frequencies of levels of quality of evidence are portrayed in Fig. 4. The majority of the guidelines/pathways for both cancer and CHF/COPD were of high quality evidence. However, nearly a third of both were of low quality. The Mann-Whitney test showed no statistically significant differences between the medians of quality of evidence level categories between the guidelines/pathways for cancer and CHF/COPD ($U = 557.5$, $p = 0.13$).

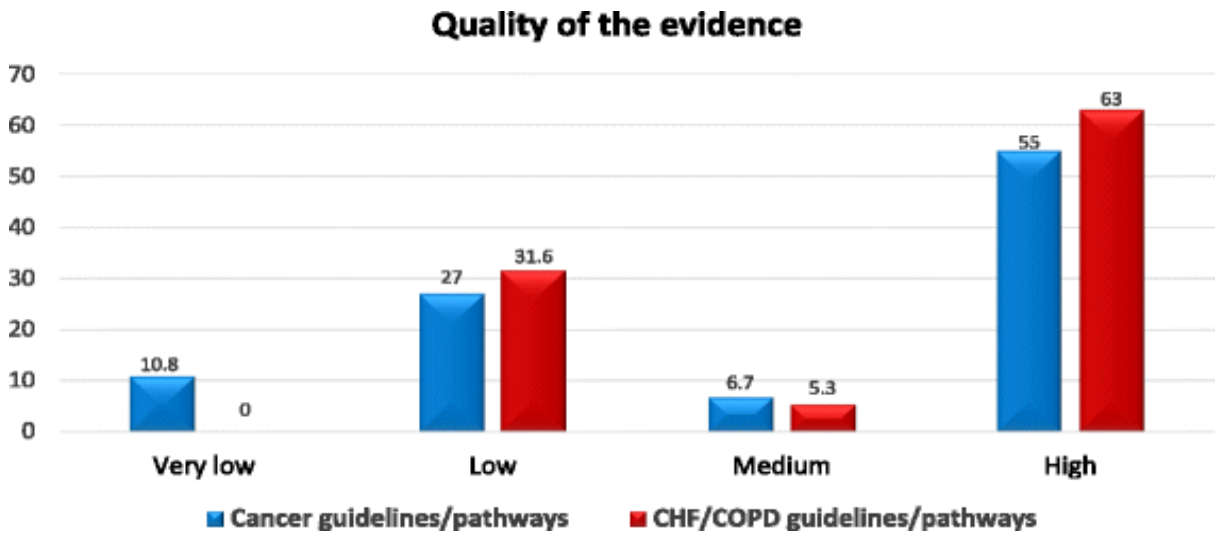


Figure 4. Percentages of cancer and Chronic heart failure/Chronic obstructive pulmonary disease guidelines/pathways meeting each level of quality of evidence. CHF Chronic heart failure; COPD Chronic obstructive pulmonary disease.

In order to examine whether the statistically observed similarity concerning the levels of integration is biased from the varying levels of quality of evidence, we have performed an additional Mann-Whitney test restricting to guidelines/pathways of high quality. Again, no statistical difference was observed between medians of the samples ($U = 328$, $p = 0.08$).

We also calculated correlations between the IPC score, the quality of evidence level and the year of publication. The results, based on the calculation of the Spearman coefficient, showed that no statistically significant correlation exists among these various pairs for either cancer or CHF/COPD; see Table 2.

Table 2. Correlation analysis between Integrated Palliative Care (IPC) score, quality of evidence and year of publication for cancer and Chronic Heart Failure/Chronic Obstructive Pulmonary Disease guidelines/pathways.

		Spearman Co-efficiency	***p*-value**
IPC score vs level of quality of evidence	CHF/COPD	0.272	0.259
	Cancer	−0.164	0.162
IPC score vs year of publication	CHF/COPD	0.258	0.206
	Cancer	0.136	0.341
Level of quality of evidence vs year of publication	CHF/COPD	−0.055	0.898
	Cancer	0.005	0.961

Discussion

Our analysis reveals that, at least statistically, there is no difference between the levels of integration of PC in the content of the guidelines/pathways for cancer and CHF/COPD. Moreover, the results remain unaltered even if we confine ourselves to guidelines/pathways that have been built on high quality evidence. This outcome suggests that the content of the guidelines/pathways is inasmuch a barrier for the integration of PC in CHF/COPD as it is for cancer.

Given this statistical equality and the overall moderate level of integration that is observed, it is interesting to examine the satisfaction of the IPC criteria separately. As evidenced in Fig. 2, the trends of the satisfaction of the IPC criteria are also similar. For instance, both groups pay insufficient attention to bereavement care notwithstanding that its importance is well documented [15, 43-45]. Further, one may observe that although the holistic approach is heavily advocated the timing of the holistic assessments is usually not clarified. Finally, it is striking that nearly half of the guidelines/pathways for both groups do not propose specific referral criteria whilst no appreciable consensus was detected among those that did made a recommendation.

The absence of referral criteria from such a high percentage of guidelines in both cancer and CHF/COPD is a perplexing result because it inhibits their efficient implementation by

enforcing local services to take initiatives at will. As regards CHF/COPD, it is known that these disease trajectories are quite complex and are typified by interchanging sequences of worsening and partial recovery, with sudden death being a frequent phenomenon [46]. As a consequence, referral criteria for patients with CHF/COPD based on prognostication are quite problematic. On the other hand, the typical trajectory of cancer comprises a gradual decline followed by a short dying phase [47]. Despite the fact that it has been empirically asserted that physicians tend to overestimate the life-expectancy of patients [48-50], referral criteria for cancer based on prognosis can be (and have been) developed based even on international consensus; see, for instance the very recent study of [51]. This, however, is not reflected in our results.

A more striking result concerns the absence of an appreciable correlation between the level of PC integration, the quality of evidence that the guidelines/pathways have been built upon and the year of publication (Table 2). Overall, it suggests that the fact that guidelines/pathways were developed at different times and in different ways (e.g. consensus approaches, systematic review, or expert opinion) is of low importance concerning the content level of PC integration. This is counter-intuitive as one would expect that more recent guidelines/pathways, based on high quality evidence, would perform better in terms of the content of PC integration. A possible explanation for this result is the presence of on-going barriers such as, for example, the determination of referral criteria mentioned above, that inhibit progress in this direction. Moreover, the lack of international consensus on even what is understood by the terminology integrated PC might adversely affect further improvements, as detailed in [12, 18].

Our analysis thus far suggests that the content of PC integration of guidelines/pathways is statistically the same between cancer and CHF/COPD. Furthermore, it does appear to constitute a barrier that is actually comparable in both cases, as evidenced by the individual examination of the criteria. In turn, these point towards the rejection of our research hypothesis. However, one needs to be careful when interpreting the quality of evidence that the guidelines/pathways have been built upon. Indeed, the number of

empirical studies (e.g. RCTs) that can provide the basis for guidelines/pathways for cancer are much more than those for CHF/COPD. Consequently, even though two guidelines/pathways may be assessed to be of high quality, in principle, a cancer guideline/pathway may utilize empirical evidence from a larger and more mature basin of studies. Another interesting point concerns the difference in scores above which two guidelines/pathways may be considered to describe appreciable differences in the level of PC integration; this is actually a kind of effect size. In our case setting such a lower limit is actually an ad-hoc procedure. A reasonable option is to partition the 11 IPC criteria as follows: 1,2,3 = low integration, 4,5,6 = medium integration, 7,8,9 = high integration, 10,11 = very high integration. Then a difference of three [3] always moves a guideline/pathway to the next or previous category and thus 3 constitutes a safe choice. Although such have not been observed in the medians of our population one might not exclude their appearance in future relevant studies that will include additional guidelines/pathways e.g. newer ones or outside Europe.

Limitations

The present study is subject to several limitations. First, the results of this study are limited to Europe and, as such, are not a priori extendable or generalizable to other geographical regions.

Second, a major limitation concerns the tool employed for the measurement of the content of integrated PC. Indeed, the 11-criteria tool employed herein has not been validated in the past. Moreover, some of the criteria are not completely independent; as, for example, reduction of suffering constitutes a necessary, albeit not sufficient, condition for holistic approach that needs to be accounted for separately. However, even though previous studies have documented indicators for the integration of PC [18], to the best of knowledge, no standardized tool for the assessment of PC integration exists in the

literature. Consequently, despite the shortcomings of the employed tool, one can still exercise to get, at least, an insight in the problem of interest.

Another limitation could stem from the relatively low number of CHF/COPD guidelines. Even though our sample corresponds to the actual number of the published guidelines/pathways, one might argue that the size of the sample is small. Nevertheless, the statistical power of our study is high enough to capture large effect sizes (CLES = 0.7). Finally, as expected, the present study inherits all the limitations of the systematic reviews [39-40] from which it has mined the data.

Conclusions

The present study has examined whether the content of the guidelines/pathways concerning integration of PC in CHF/COPD constitutes a barrier for the further advancement of PC integration in practice. In order to do so, a comparison and a quantitative evaluation between the corresponding contents in published guidelines/pathways for cancer and CHF/COPD in Europe has been performed. The analysis reveals that content of the levels of integration of PC in patients with cancer and CHF/COPD is statistically the same and it constitutes a barrier that is comparable in both cases.

Despite the limitations of our study, our results have interesting implications. They suggest that, although the content of published guidelines/pathways is a factor that impedes the further integration of PC, it cannot solely justify the remarkable inequity in access of PC between patients with cancer and CHF/COPD. Such imbalances require barriers of higher gravity; such as perceptions of the role of PC for patients with chronic disease or gaps in relevant PC education.

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PART II

EMPIRICAL PART

CHAPTER 6

Professionals' perceptions and current practices of integrated palliative care in chronic heart failure and chronic obstructive pulmonary disease: a qualitative study in Belgium.

This chapter has been published in BMC Palliative Care as

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Professionals' perceptions and current practices of integrated palliative care in chronic heart failure and chronic obstructive pulmonary disease: a qualitative study in Belgium.

Background: Patients with Chronic Heart Failure (CHF) and patients with Chronic Obstructive Pulmonary Disease (COPD) share similar symptom burden with cancer patients, however, they are unlikely to receive palliative care (PC) services. This article examines the perceptions of health care professionals and the current practices of integrated palliative care (IPC) in Belgium.

Methods: Cardiologists and pulmonologists, working in public hospitals in Belgium, participated in this study with semi-structured interviews based on IPC indicators. One researcher collected, transcribed verbatim the interviews and carried out their thematic analysis. To increase the reliability of the coding, a second researcher coded a random 30% of the interviews.

Results: A total of 22 CHF/COPD specialists participated in the study. The results show that IPC and its potential benefits are viewed positively. A number of IPC components like the holistic approach (physical, psychological, social, spiritual aspects) via multidisciplinary teams, prognosis discussion and illness limitations, patient goals assessment, continuous goal adjustment, reduction of suffering and advanced care planning are partially implemented in several health centers. However, PC specialists are absent from such implementations and PC is still an end-of-life care.

Conclusions: Misconceptions about PC and its association to death and end-of-life appear to be decisive factors for the exclusion of PC specialists and the late initiation of PC itself. The implementation of IPC components is not associated to PC, and as such, leads to suboptimal results. Improved education and enhanced communication is expected to alleviate existing challenges and thus improve the quality of life for the patients.

Background

Chronic Heart Failure (CHF) and Chronic Obstructive Pulmonary Disease (COPD) are two prominent life-threatening chronic diseases with a worldwide prevalence of 23 and 3 million respectively [1-2]. Patients with CHF/COPD face heavy physical and psychosocial burdens, comparable to cancer patients [3-6]. Although treatment for CHF/COPD is not curative but focuses on symptom management and life prolongation, survival rates have increased with time [7]. The Palliative Care (PC) needs of these patients are subtle and require a more integrated, systematic and sustained approach to the provision of high-quality care [7].

Integrated Palliative Care (IPC) involves bringing together administrative, organizational, clinical and service aspects in order to realize continuity of care between all actors involved in the care network of patients receiving palliative care.[1] It aims to achieve quality of life and a well-supported dying process for the patient and the family in collaboration with all the care givers [8]. IPC targets patients with both malignant and non-malignant disease [8-9] and empirical studies have demonstrated that it improves the quality of life of CHF/COPD patients and their families by reducing symptom burden and the frequency of hospitalizations and by addressing their goals and needs throughout the disease trajectory [10-11].

There is conclusive evidence that patients with CHF/COPD are much less likely to receive PC in general, than cancer patients [12-13]. In fact, only less than 20% of CHF/COPD patients ever have access to PC services whereas for cancer patients the corresponding percentage is usually higher than 50% [14-16]. Consequently, the percentage of CHF/COPD patients who will benefit from IPC either early or later in the disease trajectory is markedly less [8].

The inequity in the provision of PC between patients with CHF/COPD and cancer has attracted considerable attention. Several studies have tried to identify the roots of this inequity by examining the perceptions of the different medical specialists on PC. These studies have revealed the existence of several restricting factors. Among these factors, reported in the literature, are the limited PC knowledge of healthcare providers [17-20], misperception of PC as an end-of-life care [20], complexity of prognostication, especially of non-malignant diseases, and difficulties with the timing of referral [19-24], perception of CHF and COPD as "manageable" chronic diseases [22, 25-26] and inadequate communication and collaboration between the involved medical disciplines [8, 27-29].

On the other hand, much less is known about perceptions of medical specialists on IPC for patients with CHF/COPD. Moreover, current practices remain poorly understood. However, as IPC represents a change of mindset in the provision of PC and authorities are progressively advocating in favor of its incorporation, it is timely to examine both perceptions and current practices especially prior to the development/implementation of specific guidelines. As perceptions of specialists can be affected by a country's culture, and given that even within the European Union there is no uniformity on IPC current practices, it pertains to investigate these topics locally in the level of countries.

The present study aims to perform a step in this direction by examining perceptions of cardiologists and pulmonologists and current practices of IPC in patients with CHF/COPD in Belgium.

Methods

Design

In Belgium, acute wards of cardiology and pulmonology develop their own PC strategies. These strategies are shaped by and reflect the perceptions of specialists

(cardiologists/pulmonologists). Although its actor in these wards has his/her own perceptions on IPC, a natural first step would be to focus on the specialists and in particular on those cardiologists and pulmonologists who specialize in treating CHF and COPD patients respectively. In order to describe their perceptions on integration of PC in patients with CHF and COPD, a qualitative descriptive study was deemed more appropriate. The individuals that agreed to participate in the study provided their informed consent via e-mail and their interviews took place in person or via phone. The reason for studying CHF/COPD in a combined fashion is the fact that these two non-malignant and high prevalence diseases share heavy physical and psychosocial symptom burden, similarly complicated disease trajectories and they are not subject to curative treatment [3-6]. Consequently, one expects that CHF/COPD specialists will share similar views on the role of IPC for these diseases.

Inclusion criteria

Eligible participants were cardiologists, specializing in CHF and pulmonologists, specializing in COPD (treating CHF and COPD patients respectively in the wards). These participants had to be employed in public hospitals in Belgium (both outpatient and inpatient settings, including academic medical centers and different community based hospitals). Further, they had to be able to be interviewed in English.

Sampling and setting

For this study we initially aimed for a total population purposeful sampling [30]. For the identification of the eligible population we used a two-fold strategy. First, we contacted (via email and phone) the directories of every public hospital and we inquired their cardiologists and pulmonologists that were specializing in CHF and COPD. Second, when contacted these eligible specialists and besides asking for their participation to the study we also asked them for possible chain-referrals [31]. All eligible participants were

contacted via email and/or phone, followed up by a second reminder a month after the initial invitation. Our contact efforts stopped when we reached data saturation. The inclusion period of the study lasted for November 2016 until April 2017.

Data collection

The main researcher (NS) collected the interviews with an electronic audio recorder in person (in the hospital setting) or via phonecall, which was also recorded. Based on previous work a semi-structured interview containing 10 questions was developed [8, 32]. These questions are linked to the IPC indicators used in previous studies in order to measure the content of integrated PC in guidelines and pathways of cancer and CHF/COPD in Europe [8, 33]. The questions are shown in Table 1 in succinct form. In practice (NS) used these questions as starting point of discussion to encourage the participants to reflect and elaborate on the topics. The participants were not given the list of questions.

Table 1. Core questions for the semi-structured interviews.

1	Are patients usually informed about the prognosis of their disease? How easy/difficult is that?
2	Is it needed to have holistic assessment and who should do that? When should the holistic assessments be applied?
3	When should palliative care be initiated? For what is the patient referred?
4	Is it necessary that patients' goals are explored?
5	Do goals change during the disease trajectory?
6	What are the most frequently used interventions for suffering reduction?
7	Is advance care planning useful for cardiology/pulmonology? In what percentages of patients it is used?
8	When is the palliative care team involved?

9	Are there any specific recommendations on what to do in the patient's last hours of living?
10	Are there any specific recommendations for support of the family of the patient post-mortem? Is grief and bereavement care present?

Data analysis

The data collection and analysis was cumulatively iterative. The interviews were transcribed verbatim and were independently analyzed and coded with the NVivo 11 software program by the main researcher (NS). The interview data were analyzed based on thematic analysis [33]. One researcher (NS) read all the transcripts, coded sections of text and set up an initial list of codes that lead to a broader range of identified codes. To increase the reliability of the coding, a second researcher (KVB) coded a random 30% of the interviews. The two researchers met regularly in order to review the coding structure, to ensure codes were applied in a consistent manner and to resolve any possible discrepancy. Anonymity of the participants was preserved throughout the analyzing and coding process [34]. Additionally, three authors (NS, KVB, JM) discussed extensively the evolving themes of three randomly selected interviews to ensure further validity of the procedure. Data saturation was reached independently for both CHF and COPD specialists following the theory that data collection stops when additional interviews do not add more to the results of the prior findings [34]. Results are presented and discussed in a combined fashion when appropriate.

Results

We invited electronically via e-mail 312 cardiologists (CHF experts) and pulmonologists (COPD experts). The 22 individuals who participated in the study provided an informed consent via e-mail and the interviews took place in person (16/22) or by phone calls

(6/22). Three (3/22) were from the region of Brussels (French/Dutch speaking), eighteen (18/22) from Flanders (Dutch speaking) and one (1/22) from Wallonia (French speaking). The characteristics of the participants are presented in Table 2. The mean duration of the interviews was 32 min (range 20 to 50 min). Our analysis followed the scheme of the themes of the IPC indicators provided in Table 1.

Table 2. Characteristics of study participants.

Characteristics	**Full Sample**	**Cardiologists**	**Pulmonologists**
N	22	12	10
Age			
50–69 years	8	5	3
30–49 years	14	7	7
Gender			
Female	6	4	2
Male	16	8	8
Practice setting			
Academic	9	5	4
Non academic	10	4	6
Both	3	3	–

<u>Are patients informed about their prognosis? How easy/difficult is that?</u>

The majority of the participants agree that it is important to discuss the prognosis with the patients and they do this in practice. The core reason for doing so is the belief that it is honest and equally important to inform both patients and family on illness trajectories and treatment possibilities and limitations so that they can adjust their expectations.

The analysis revealed a large variation concerning the timing when prognosis discussions should take place. Some suggested that this discussion is a progressive process that

cannot take place in the first contact but should gradually start in the subsequent meetings when the physician is more aware of the psychological reaction of the patient. Few participants however declared that discussions on prognosis should take place while communicating the diagnosis of the disease or immediately after every re-hospitalization or after an exacerbation of the disease. Few participants suggested that these prognosis discussions should occur later in the disease trajectory e.g. when a patient has a GOLD stage D diagnosis, because it is perceived as very confronting and terrifying for the patient.

"You have to discuss it with the patient, but you cannot do it in one encounter. You have to feel how she/he is coping with that issue and try to go for a personalized choice together with the patient". Cardiologist 7

The majority of the participants found it difficult to discuss about prognosis because of the complicated and unpredictable nature of the disease (both CHF and COPD) while it is easier to predict the prognosis for oncologic patients.

"Now it's not easy to say….it's not easy to determine who's going to die in cardiology. It's not like in lung cancer where we have scientific evidence that survival is mostly between 4-6 months". Cardiologist 3

"For lung cancer patients when you see that the treatment doesn't work and that the patient gets more and more tumors then you know you call in the PC, but in COPD the interventions are not clear e.g. you one cannot check it on a CT scan or so…". Pulmonologist 3

Another factor to render such discussions as challenging is that PC is perceived as a "bad word". As it turns out, most patients and healthcare providers have connected this word with "death" and "dying" and also with the care that is mainly provided to cancer patients, but not to CHF/COPD patients.

"And to some certain extent I prefer the word "supportive" than "palliative". If I use the word palliative to a patient then they will think "oh, I'm immediately dying" and then it's a problem". Pulmonologist 6

Is it needed to have holistic assessment and who should do that?

All participants agreed that the provision of a holistic approach is crucial for the care of patients with CHF and COPD.

"Yes, of course. The medical treatment alone is not a holistic approach" Cardiologist 6

"Yes, I find a holistic approach very useful and that a patient can highly benefit from it". Pulmonologist 5

Almost all interviewed participants reported that the holistic approach for the hospitalized patients is provided by a multidisciplinary team (MDT). This team consists usually of medical specialists, nurses and specialist nurses, a social service expert, a psychologist, a physiotherapist/kinesiotherapist and a nutritionist. The MDT's meet on a weekly basis. Only few participants mentioned the presence of PC experts at the weekly meetings. In most meetings, the psychologist is not a standard member of the MDTs, but is available on demand.

When should palliative care be initiated?

Participants gave a variety of answers. Most mentioned that PC should start when the curative treatment is no longer realistic. Some reported that PC should be initiated if many repeated hospitalizations occur within a short period of time or when there is currently no longer an acceptable quality of life for the patient. Most participants are

aware that PC is implemented frequently at the end of life but that it should be ideally initiated earlier in the disease trajectory for the benefit of the patients.

"Normally, this happens pretty late, mostly at the end of life of the patient. I think that it should be initiated even earlier, let's say even from the moment that a patient is diagnosed with COPD so they can benefit as much as possible, because PC is not only for the end-of-life". Pulmonologist 5

One of the reported difficulties for defining the timing of PC initiation is the unpredictability of these diseases and the definition of PC itself. Some of the participants expressed that they had difficulties understanding what PC exactly is.

"I also don't know what do we understand as PC. Is it the life ending? Is it the active life ending? Is it a passive life ending?". Pulmonologist 8

<u>Is it necessary that patients' goals are explored?</u>

There is a unanimous agreement on the necessity to explore the goals, wishes and desires of the patients. All participants find it very important to explore and discuss patient's desires and wishes whenever possible, because the treatment goals should be adjusted accordingly and be adapted based on the stage of the disease. The lack of time is also mentioned as a potential barrier for not assessing the goals more regularly in reality; this is more apparent in the larger hospitals were physicians seem to be overloaded, work in teams with frequently need for replacements of each other and modus operandi does not allow for extensive interpersonal communications with the patients.

"Yes, that's important. A treatment of a patient is not a one-way communication, it's a two-way communication". Cardiologist 7

"In the local hospitals care is more personalized…". Pulmonologist 9

Do goals change during the disease trajectory?

All participants suggest that the goals and wishes of the patients do change during the disease trajectory. Most mention that both physicians and patients change and adapt their expectations according to the changes in the disease trajectory. The patients appear to have fewer expectations while the disease is progressing. Some participants commented that the duration of the patient's/specialist's relationship is important; the longer you know the patient the better you are informed for and keep up with their goals and wishes.

"Yes, we see it changing as the disease progresses. They have less expectations as the disease progresses". Cardiologist 9

What are the most frequently used interventions to alleviate suffering?

Almost all the participants suggest that morphine and sedatives are used to reduce physical suffering in advanced stages of CHF and COPD. Other frequently used interventions are the administration of diuretics (for CHF), or oxygen (for COPD). For the relief of psychological suffering, some participants mention the use of anxiolytics or benzodiazepines along the provision of psychological or spiritual support if this is asked by the patient. Some participants contact the PC team in case they feel that they comfort the patient insufficiently.

"We provide morphine and if we need to provide sedation we contact the geriatricians and the PC Support team to come and give some instructions to our team. But my opinion is that we always give sufficient diuretics". Cardiologist 11

"We supply oxygen for breathlessness and if oxygen doesn't help we give morphine, because that reduces the pain and the dyspnea. And sometimes also anxiolytics like Xanax to reduce stress". Pulmonologist 2

Is advance care planning useful for cardiology/pulmonology? In what percentage of patients is it used?

Almost all participants suggest that advance care planning (ACP) is central/mandatory to CHF/COPD patients. Further, the majority of the participants reports that ACP is realized in practice. However most of the participants could not provide the percentage of patients that receive ACP. There is no consensus on the timing of ACP; some participants mentioned that ACP is applied early in the disease trajectory while others initiate ACP close to the end-of-life.

When is the palliative care team involved?

Most of the participants report that in reality the PC team is not involved in the treatment of a patient with CHF/COPD or is involved much too late in the terminal phase of life. Some participants involve the PC team when the curative treatment is no longer effective or when the patient had multiple admissions in a short time. Few highlight the importance of involving PC earlier in the PC trajectory and not only when they are invited because the patients ask for it or because there is no longer a treatment option.

"I think PC is a bit underrated in CHF, because we tend to try to cure the patient till the last time. And also you need to have some guts to be able to talk about it with the patients, cause they are not always aware of it". Cardiologist 10

"We should ask the involvement of PC for these patients, but we obviously don't do it so much, but we call them in for the last months". Pulmonologist 7

Are there any specific recommendations on what to do in the patient's last hours of living?

The majority of the participants do not use any specific protocol or guideline in the last hours of a patient's life, but they do what they assess as necessary to be done. The emphasis on a personalized care is highlighted especially in smaller hospitals. Some participants use specific checklists and protocols that they follow at the end-of-life of a patient. Others call the PC team for assistance how to proceed further. Few participants think it is useful to consult colleagues for help in making decisions for the last hours. Many participants would welcome a protocol or a guideline on how to deal with the last hours of life of patient.

"I don't think we follow specific guidelines or a specific protocol. We do what it feels best to do. In the local hospitals care is more personalized and not so standardized".
Cardiologist 11

"We have a specific scheme that we try to follow, of course it may differ a bit from one doctor to the other". Pulmonologist 9

Are there any specific recommendations for the bereavement support of the patient's family?

The results revealed that most of the bereavement support is provided by the specialist physician and nurses who cared for the patient with listening, giving information and answers to questions. For this reason, some participants find it mandatory to discuss the expected dying process with the families before the patient dies. It is usually uncommon for the families to seek psychological support post-mortem. In case they do look for support, few participants mention the availability of a psychologist and in fewer cases the provision of spiritual care. Another aspect that inhibits the provision of grief and

bereavement support for the specialists is the variety of religious and cultural backgrounds.

"Yes, so we first we give them their time. Then the doctor that takes care of the patient will go there and then the nurse that takes care of the patient will talk to the family and ask what they need and what they want. If they need to talk to a psychologist, then we will contact the psychologist of the ward and the social service". Cardiologist 12

"As physicians, we need to be there at the end of life too, it's important to provide personalized care". Pulmonologist 7

Discussion

This is the first study that documents perceptions of cardiologists and pulmonologists and current practices of IPC in patients with CHF/COPD in Belgium. The results show a favorable view towards IPC and its potential benefits. Indeed, the holistic approach via MDT's, discussion of prognosis and limitations resulting from the illness, assessment of patient's goals, continuous goal adjustment, reduction of suffering and ACP constitute components of IPC have already been implemented (even partially) in many Belgian health centers. The occurrence of discussions on prognosis, in particular, is very interesting since previous studies have reported that patients with CHF/COPD are quite unlikely to get engaged in such conversations [35-37].

However, even though, some of the IPC's components have already been (partially) implemented, PC specialists are seldom involved and PC, in particular, is not initiated until the end-of-life. In other words, we have the conundrum that PC aspects are integrated alongside standard treatment without the involvement of a PC team. Second, even though participants explicitly stated their preference towards an earlier initiation of PC, they do not apply this in practice. In turn, this implies that PC practices are quite confined

and cannot grow easily to their full potential, not least because the specialized knowledge of PC specialists is utilized. Accordingly, this may impact the quality of life of patients and their families since the application of these IPC components might be suboptimal. For example, ACP in the end-of-life stage does not offer substantial benefits.

Based on the collected perceptions, we find two reasons for the explanation of these conundrums.

Misconceptions about PC and its role

When prompted to talk about PC, participants use cancer as a reference and comparison point. In other words, the fact that PC was initially applied in cancer continues to affect the mentality of specialists outside oncology. Further, even though the World Health Organization (WHO) promotes a more integrated approach to PC, the participants perceive PC as an end-of-life care. Consequently, the fact that PC is limited to the alleviation of suffering and symptom control during end-of-life and not concerned with other aspects of quality of life appears as a justifiable situation.

These findings are typically reported in studies focusing on PC for patients with non-malignant disease [20, 38]. Collectively, they suggest that there is i) a lack of communication concerning the overall role and benefits of PC in the quality of life of patients and ii) insufficient training and education of specialists in the fundamentals of PC.

PC has a "bad name" reputation (connotation)

The participants mentioned that the word "palliative" is a bad word that results in undesirable confrontation with both patients and their families. Given that prognosis discussions are already challenging in CHF/COPD and that the general public image of

CHF/COPD does not associate these diseases with death, participants are reluctant to mention the existence of such services, even more so early in the disease trajectory.

This finding is not surprising. Even in oncological wards, where PC is more standardized, the term “palliative” is associated with death and end-of-life and has been empirically demonstrated to adversely affect inclusion rates and early referrals [39]. In fact, empirical studies have found that renaming PC to “Supportive Care” can have a positive impact on both medical staff and the patients and leads to improved inclusion and referral rates. [40-42]. Berry et al. go far enough to suggest rebranding PC so that this “shadow” is removed [43]. It is not clear whether a change in the terminology will have a positive impact in CHF/COPD patients since Randomized Controlled Trials (RCTs) have thus far been restricted to oncology. Moreover, PC is inherently related to difficult concepts (e.g. prognosis discussions, ACP decisions) and this is independent of the name of such services. In other words, even if PC was renamed one would still need to address these difficult issues.

It is important to comment on bereavement care and support for the families post mortem. The analysis clearly shows that there is a lack of bereavement support. Conversations that aim to resolve questions with family members are not available and psychologists and spiritual caregivers are very rarely available. The low level of bereavement support is a recurrent finding that can even be traced in guidelines/pathways for PC in CHF/COPD. The systematic review by Siouta et al. shows that recommendations on bereavement support was among the weakest issues in the existing guidelines/pathways [8]. Consequently, bereavement support appears to be an important component that has not yet the necessary attention.

Limitations

The first limitation of this study concerns our sample. We have opted for a total population purposeful sampling, but only a fraction of the population agreed to participate. We are not aware of the reasons why eligible participants refused to participate since they ignored our invitation at the first place. Consequently, we can only speculate on the reasons of non-participation. It is possible that eligible medical specialists that did not/did participate in the study chose to do so because they were unfamiliar/familiar with IPC. If this is the case, then the generality and generalizability of our results is affected. In fact, even though we reached data saturation, sampling biases would be present if eligible specialists based their decision to participate on their knowledge of IPC.

A second limitation is that the interviews were conducted in English. As English is not among the official languages of Belgium (French, Dutch, German), but it had to be the language of the study since the interviewer was not fluent in these languages, it is possible that some specialists did not participate for linguistic reasons. In fact, two eligible specialists were excluded because they could not be interviewed in English. This might also be the reason for the under-representation of the French speaking community of Belgium (Wallonia). Consequently, whether or not the results apply to non-English speaking professionals is unknown. A third limitation might be a sample bias towards male participants with age 30–49 years. The age and gender demographics of the total population remains unknown, so their effect remains unassessed.

Another limitation concerns our interview methodology. Rather than allowing participants to freely elaborate on their general perceptions on IPC, we have evolved the conversations around 10 principal thematic questions. Therefore, it is possible that IPC perceptions not directly linked to our themes of interest have not been documented.

The last limitation concerns the generalizability of the results. This study has been confined to CHF/COPD specialists in inpatient setting. It is not clear whether the

documented perception would extend to other types of chronic disease, general practitioners, PC experts and nurses and to health-care personnel working in outpatient settings. Additionally, even within the European Union (EU), healthcare systems and practices vary considerably. Consequently, one should be careful before generalizing our hospital based findings to different countries, even within the EU or to other care settings.

Conclusions

Aspects of IPC appear to be embodied alongside curative treatment, however, PC experts are not usually involved and therefore current IPC practices are probably not optimal. Misconceptions about PC and its association to death/end-of-life seem to be significant reasons for the limited participation of PC specialists and the late initiation of PC itself.
Healthcare organizations in Europe and worldwide acknowledge the benefits that patients with CHF/COPD can receive from IPC. Targeted education and improved communication could increase the awareness of all involved parties on aspects of IPC and thus lead to improved practices and better quality of life for the patients.

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CHAPTER 7

Early Integrated Palliative Care in Chronic Heart Failure and Chronic Obstructive Pulmonary Disease: protocol of a feasibility before-after intervention study

This chapter has been submitted as:

Siouta N, Heylen A, Aertgeerts B, Clement P, Van Cleemput J, Janssens W, Menten J. Early Integrated Palliative Care in Chronic Heart Failure and Chronic Obstructive Pulmonary Disease: protocol of a feasibility before-after intervention study.

Early Integrated Palliative Care in Chronic Heart Failure and Chronic Obstructive Pulmonary Disease: protocol of a feasibility before-after intervention study.

Background: Palliative Care (PC) aims to optimize the quality of life for patients with Chronic Heart Failure (CHF) and patients with Chronic Obstructive Pulmonary Disease (COPD) and their families. The efficacy of early integration of PC services with standard care has been increasingly supported by research evidence, however, access to PC services for CHF/COPD patients remains substantially limited. We present the protocol of a feasibility prospective study that aims to explore if an "Early Integrated PC" intervention can be performed in an acute setting (cardiology and pulmonology wards) and whether it will have an effect on: i)the satisfaction of care and ii) the quality of life and the level of symptom control of CHF/COPD patients and their informal caregivers.

Methods: A before-after intervention study with three phases: i) baseline phase where the control group receives standard care, ii) training phase where the personnel is trained on the application of the intervention and iii) intervention phase where the intervention is applied, will be carried out in cardiology and pulmonology wards at University Hospital Leuven for patients with advanced CHF/COPD and their informal caregivers. Eligible patients (both control and intervention group) and their informal caregivers will be asked to complete the (Palliative Oucome Scale) POS, the CanHelp Lite and an ad-hoc questionnaire at the inclusion moment and three months after hospital discharge.

Discussion: The present study will assess the feasibility of carrying out PC focused studies in acute wards for CHF/COPD patients and draw lessons for the further integration of PC alongside standard treatment. Further, it will measure quality of life and quality of care of patients and thus shed light on the care needs of this population. Finally, it will evaluate the efficacy of the "Early Integrated Palliative Care" by comparing against existing practices.
Trial registration: Current Controlled Trials ISRCTN24796028 (date of registration August 30, 2018).

Background

Chronic Heart Failure (CHF) and Chronic Obstructive Pulmonary Disease (COPD) are the leading and third cause of death globally. Patients with CHF/COPD face heavy physical and psychosocial burdens, comparable to cancer patients [1-3] and whereas treatment for both diseases remains non curative, survival rates of these patients have increased with time [4]. These patients are amenable to and can benefit from PC services, however, the complexity of their needs requires a more integrated approach to the provision of high-quality care.

Integrated PC aspires to provide an holistic framework, tailored to the needs of such patients. It involves bringing together administrative, organizational, clinical and service aspects in order to achieve continuity of care between all those involved in the patient's care network. It aims to achieve quality of life and a well-supported dying process for the patient and the family in collaboration with all the care givers (paid and unpaid) [5-6]. Moreover, there is ample and ever-growing empirical evidence on the benefits of IPC on the quality of life of patients with both malignant and non-malignant diseases [4, 7-15].

However, when compared to patients with cancer, patients with CHF/COPD, are quite unlikely to receive PC services. It has been estimated then less than one out of five CHF/COPD patients has access to PC services while for cancer this number increases to one out of two. Consequently, CHF/COPD patients who will receive IPC either early or later in the disease trajectory constitute an even smaller fraction [10, 16]. The most commonly reported factors responsible for this inequity are limited PC knowledge of healthcare providers and predominant focus on standard treatment options [17-20], misperception of PC as an end-of-life care [15], complexity of prognostication [17-20], perception of CHF and COPD as "manageable" chronic diseases [21-23] and inadequate communication and collaboration between the involved medical disciplines [6, 24-26].

The nature of these inhibiting factors suggests that optimal practices will combine optimized strategies for the delivery of high-quality care vis-a-vis the efficient and effective organization of services within the local context and societal impact including optimal patient/professional experiences.

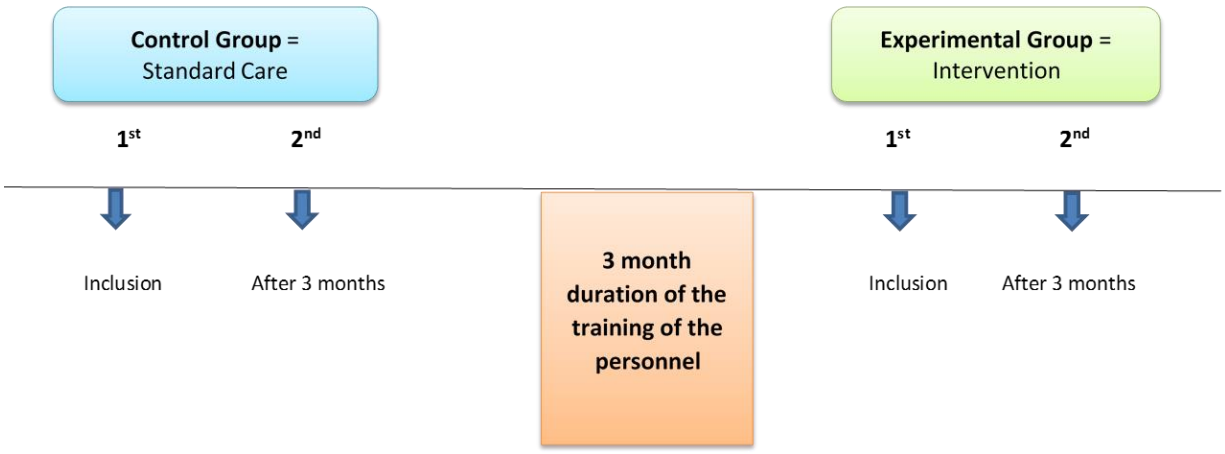
Aim

The aim of this study is to explore the feasibility of carrying an "Early Integrated Palliative Care" intervention in acute cardiology/pulmonology wards and evaluate the effect on: i)the satisfaction of care and ii) the quality of life and the level of symptom control of CHF/COPD patients and their informal caregivers.

Methodology and study design

We propose to conduct a before-after intervention study consisting of 3 sequential phases: baseline phase, training phase and intervention phase. During the baseline phase the control group will receive standard care. During the training period the personnel will be trained on how to use apply the "Early palliative care integration" intervention. Finally during the intervention phase, the intervention group will receive the updated care (Fig 1).

Figure 1. Sequence of the feasibility before-after intervention study.



In both groups (control and intervention), patients and their most important informal caregiver will be asked to complete the Canadian Health Care Evaluation Project Questionnaire (CANHELP Lite) Questionnaire [27] and the Palliative Outcome Scale (POS) Questionnaire [28] and an ad-hoc questionnaire developed by the Palliative Support Team (at the University Hospital Leuven) to measure the current level of integrated PC in the following 2 timings: i) inclusion moment after signing the informed consent and ii) 3 months after inclusion (for both baseline and intervention groups). The methodology of this study was developed based on the SPIRIT guidelines.

Inclusion Criteria

*Patients: Adult patients that have been readmitted at least once within a year with a New York Heart Association classification (NYHA) classification of III/IV for CHF (table 1) and with Global Initiative for Chronic Obstructive Lung Disease (GOLD) stages C/D for COPD (table 2). These patients should have an assessed life expectancy of at least 6 months.

Table 1. NYHA classification for CHF symptoms.

NYHA class	Symptoms
I	Cardiac disease, but no symptoms and no limitation in ordinary physical activity, e.g. no shortness of breath when walking, climbing stairs etc.
II	Mild symptoms (mild shortness of breath and/or angina) and slight limitation during ordinary activity.
III	Marked limitation in activity due to symptoms, even during less-than-ordinary activity, e.g. walking short distances (20–100 m). Comfortable only at rest.
IV	Severe limitations. Experiences symptoms even while *at rest*. Mostly bedbound patients.

Table 2. GOLD Criteria for COPD.

A = Low risk, low symptom burden

- Low symptom burden (mMRC of 0-1 OR CAT score < 10) AND
- FEV1 of 50% or greater (old GOLD 1-2) AND low exacerbation rate (0-1/year)

B = Low risk, higher symptom burden

- Higher symptom burden (mMRC of 2 or more OR CAT of 10 or more) AND
- FEV1 of 50% or greater (old GOLD 1-2) AND low exacerbation rate (0-1/year)

C = High risk, low symptom burden

- Low symptom burden (mMRCof 0-1 OR CAT score < 10) AND
- FEV1 < 50% (old GOLD 3-4) AND/OR high exacerbation rate (2 or more/year)

D = High risk, higher symptom burden

- Higher symptom burden (mMRC of 2 or more OR CAT of 10 or more) AND
- FEV1 < 50% (old GOLD 3-4) AND/OR high exacerbation rate (2 or more/year)

*Informal caregivers: informal caregiver is defined as that proxy person who takes care and supports the patient for most of the time. This caregiver may not necessarily be a family member. They should be aged 18 or above, should be able to communicate in Dutch and should be cognitively able to complete questionnaires.

Exclusion criteria

A potential participant (patient or informal caregiver) who meets any of the following criteria will be excluded from participation in the study:

i) under the age of 18,
ii) unable to communicate in Dutch,
iii) people who lack mental capacity to complete questionnaires,
iv) if the Surprise question “Would you be surprised if the patient died within 1 year?” is answered “Yes”.

Sample size

A convenience sample of 50 patients and 50 informal caregivers (25 patients and 25 informal caregivers for each disease) has been set as a target as follows. We aim to detect difference at 5% in the POS responses with a statistical power of 80%. Based on previous empirical results for the POS, the combined sample (CHF plus COPD) is 37. We have added a 30% attrition rate which result in the final sample 50 patients and 50 informal caregivers (25 patients and 25 informal caregivers for each disease).

Duration and Setting

The overall study is estimated to last 24 months and will be conducted in UZ Leuven in the Departments of Cardiology and Pulmonology (two nursing wards for CHF and one for COPD). We estimate 8 months duration for the baseline and the intervention phase and 3 months for the training period. An overall 25% of expected delays is also added.

Questionnaires

For this study, we surveyed the literature for appropriate questionnaires to evaluate the perceptions of patients and their informal caregivers on QoL and quality of care. Given the frailty of the targeted population, we specifically aimed at questionnaires that required a short completion time and were easy to comprehend. Based on these criteria we chose the following questionnaires.

The Canhelp Lite Questionnaire is a tool that is often used in clinical PC studies to evaluate the quality of care [27]. This is a validated questionnaire with two versions; one version for patients and one for the informal caregivers. It can be used in both in-patient and out-patient care settings and it has a completion time of approximately 10 minutes. The patient version has 21 questions that address, the satisfaction of the quality of care, the

relationship with the doctors, illness management, communication, decision making and a question concerning the patient's inner peace. For the caregivers the questionnaire includes 23 questions assessing the satisfaction of the overall care, the relationship with the doctors, the characteristics of doctors and nurses, illness management, communication, decision making and the involvement of the informal caregiver to patient's care.

The POS is validated tool that is frequently used in PC studies to measure i) the quality of life and ii) the symptoms of patients. This questionnaire has two versions; one for patients and one for informal caregivers and it has a completion time of approximately 7 minutes [28]. This questionnaire consists of the 12 questions, same for both patients and informal caregivers addressing their overall quality of life including physical and emotional symptom management and adequacy of information received.

The ad-hoc is a questionnaire that was developed by the Palliative Support Team of UZ Leuven and it is used to measure different elements of advance care planning. It has three versions; one for patients, one for the informal caregivers and one for healthcare providers (in this study the patient and informal caregiver versions will be used). It has a completion time of approximately 10 minutes. Due to the fact that currently there exist no questionnaires that measure existing advance care planning aspects, this questionnaire is considered the most suitable for the goal of our study, however it is yet to be validated. This questionnaire addresses questions over the perceptions of patients and caregivers concerning the current care, usefulness of discussions related to patient's health, desire for involvement in these discussions in the present and the future and evaluation of their emotional condition.

Recruitment

According to the design of the study, and following discussions with the health care providers of pulmonology and cardiology wards, the following model for the identification of eligible patients will be adopted. The researcher in charge after screening the patients' electronic hospital files and after consulting with the head-nurses of the cardiology wards and participating in their weekly multidisciplinary meetings of the wards, will identify the eligible CHF patients. For COPD, a pulmonology ward nurse is appointed to screen and report the eligible patients to the researcher upon examining the electronic files of the patients and cross-checking with assistant physicians of the corresponding ward during bilateral or multi-disciplinary meetings. The information of the eligible COPD patients will communicated via e-mail with the researcher. If any difficulties occur in the implementation of the recruitment process the research team will perform the necessary adjustments so as to enhance the recruitment process.

Data collection

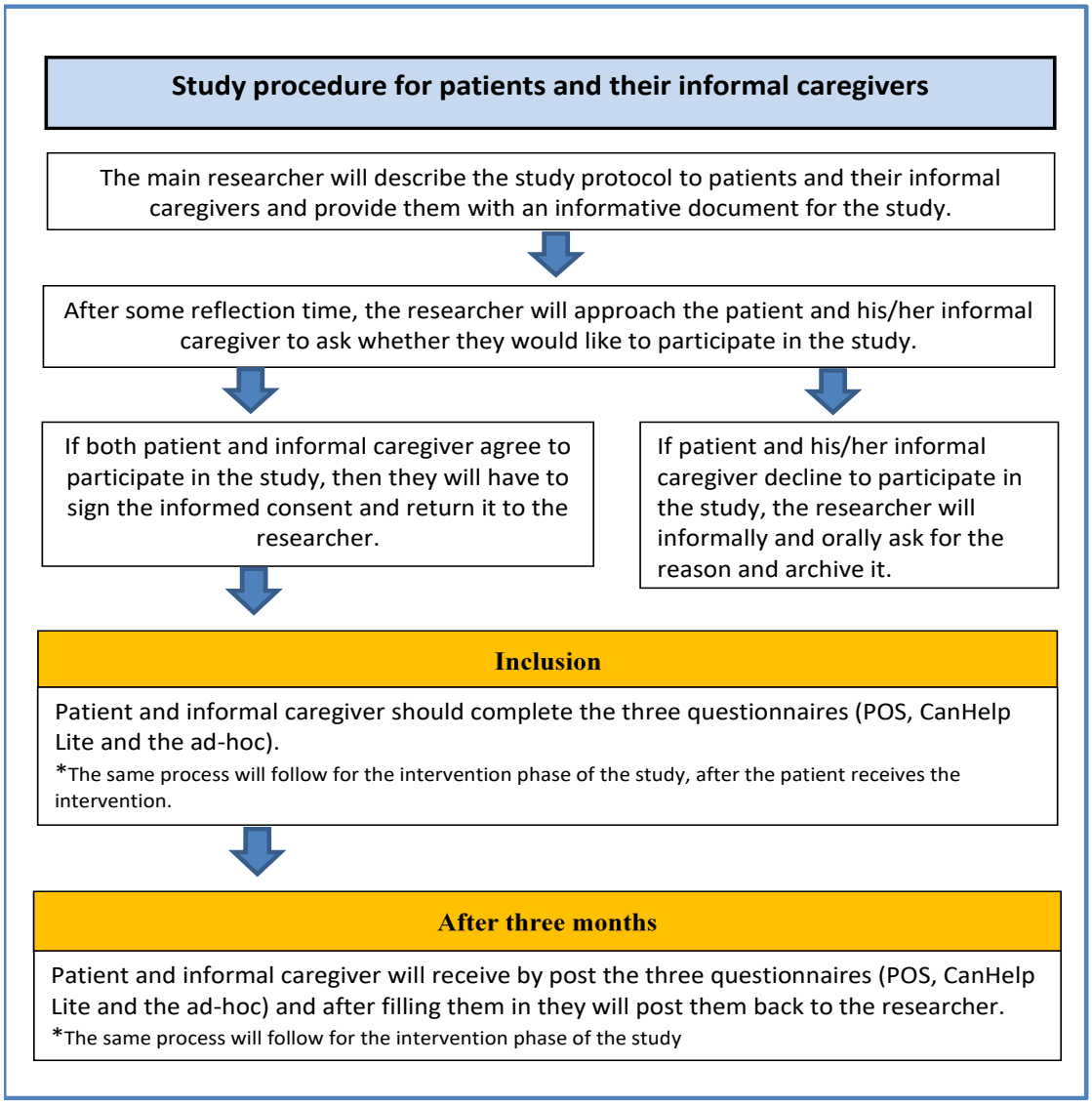
The main researcher (NS) will explain the study protocol to both patient that meets the inclusion criteria and his /her most important informal caregiver. The patient will receive the informed consent. After one or two days reflection time, the main researcher will contact them again personally to ask if they like to join the study. If the patient and informal caregiver decide to participate in the study, they will provide their signed consent.

After the completion of the informed consent, the participants (patients and their informal caregiver) will be requested to fill in the three questionnaires in two timings: i) at inclusion moment after signing the informed consent during the hospitalization of the patient and ii) at a follow up of three months after inclusion (for both control and intervention groups). If a patient or an informal caregiver has difficulty understanding the questionnaires, the researcher in charge can provide additional information and help the participants fill in the questionnaires. When the eligible patients or their informal caregivers decline to participate, the researcher will ask for the reason and archive it. No special document will

be provided to patients who will decline. Communication of the reason for not participating will be oral and informal.

For the second measurement after three months, the same questionnaires will be sent by post to each patient and their caregiver and will be sent back to the researcher after they are completed. In some cases, the follow-up questionnaires will be administered to the patients when they visit the hospital for a check-up examination. When the follow–up questionnaires that will have been posted are not returned back on time, then the researchers will contact the participants by telephone to remind them to complete them and post them back. The same process will be repeated for each patient and their caregiver for the intervention phase, after the implementation of the intervention. The study procedure for patients and their informal caregivers is described in Figure 2.

Figure 2. Study procedure for patients and their informal caregivers.



The intervention

After the completion of the baseline phase of the study (patients receiving standard care), the appointed intervention team for each ward will receive a training on how to apply the intervention in a 3-months period. The psychologist of UZ Leuven's Palliative Support Care Team, will be the one to train the personnel on how to apply the intervention to the experimental group. In cardiology, the assistant physicians will provide an introductory

flyer for the intervention to the patient and after the completion of this flyer, two psychologists and one psychology trainee will proceed with the implementation of the intervention. The same process will follow for pulmonology, where after the introductory flyer by the assistants physicians, a specialist nurse, two ward nurses and the spiritual counselor will proceed with the intervention.

The intervention will be based on the implementation of the Early Integrated Palliative Care Planning Intervention ("MIJN WENSEN voor mijn Gezondheidszorg"), a content validated communication tool (booklet) for advance care planning in life-thretening disease developed by the Palliative Support Team in UZ Leuven. This tool has already been implemented in various cancer departments in Gasthuisberg University Hospital e.g. at the lung cancer unit.

The booklet of MIJN WENSEN initiates discussions about prognosis and illness limitations and develops a patient-centered holistic approach by asking the patient to specify the areas in which they require more support (physical symptoms, emotional symptoms, social, financial and spiritual issues). As regards ACP discussions, it addresses the wishes and needs of the patients concerning the delivery and adjustment of present and future care. As such, it touches upon subjects like DNR codes, desirable/undesirable care treatments, appointing proxies for decision making at later stages of the disease. In general, MIJN WENSEN provides the means to identify each patient's values for their QoL and quality of care and therefore tailor treatment accordingly.

MIJN WENSEN can be perceived as an invitation to communication; as a guide for conversations with the caregivers and for matching the current and future care with the treatment specialists. Moreover, it can be used as either an informal or formal declaration of intent, to register the patient's indicated representative who will advocate the wishes of the patient in case she/he ever becomes unable of taking any decisions on their medical care.

Data Analysis

The statistical analysis will be carried out by the main researcher and will be performed using SPSS and Excel software. We will employ standard descriptive statistics for the basic characteristics of the population and the distributions of the scores of the tests (means, standard deviations etc.). We will use t-tests to explore equality of means for total scores of POS and CanHelp Lite between different pairs (e.g. COPD patients vs COPD caregivers). To compare continuous variables between the different study groups we will use Fisher's exact tests and Mann-Whitney U-test. Finally, we will use Mann-Whitney U-tests and Wilcoxon signed rank tests in order to analyze individual questions that will be treated as ordinal variables. Missing data will be included in the analysis and their implications will be clarified.

Expected Results

The present study will first evaluate the feasibility of carrying out PC focused studies in acute wards where PC is not considered as part of the treatment teams. This will allow us to detect possible weaknesses and strengths by observing the real time interaction of the medical staff with the patients. The learned lessons can then be juxtaposed with existing evidence and thus lead to recommendations and suggestions for the improvement of guidelines for the implementation of PC services outside PC wards.

Second, by evaluating current practices the study will document the state of the art from the view point of CHF/COPD patients. Since the needs of this population are not well understood, these results can help towards the development of PC practices tailored to the needs of these patients.

Third, the study will measure the efficacy of the intervention against existing practices. By doing so, we will be able to quantify the possible benefits of integrated PC in CHF/COPD. In particular, CHF/COPD patients who participate in the intervention are expected to be more aware of their condition, their treatment options and their personal role in decision making. We, therefore, expect that this awareness translates into higher scores in the CanHelp Lite, the ad-hock questionnaire and the components of the POS that are related to quality of care. Concerning physical symptomatology, even in the absence of PC, standard treatment focuses mainly on alleviation of pain and other physical symptoms. Consequently, awareness of the actual patient's condition is not expected to substantially affect the corresponding scores in the POS questionnaire.

As regards the psychological symptomatology of the patients and owing to the heterogeneity of the CHF/COPD population, the correlation between awareness and QoL is not one-way. We expect that the intervention will confirm the complexity of this correlation i.e. for some patients awareness of their condition will result and in a worsening of their psychology and thereby lead to lower scores in the corresponding questions. For some other patients awareness might resove psychological tention and uncertainty, offer peace of mind and thereby result to higher scores in the aministered questionnaires.

Finally, through the application of the intervention, medical stuff will be able to promptly identify the PC needs of CHF/COPD patients and their caregivers while being able to address them in a more efficient manner thereby improving existing quality of care and quality of life of these patients.

Discussion

Ethical considerations

The process of filling in the questionnaires could be potentially stressful for the patients and their informal caregivers. In order to the minimize the risk of emotional distress, we have chosen for this study questionnaires that a short completion time (based on previous empirical studies completion time for POS is approximately 7 minutes and for CanHelp Lite is 10 minutes). The overall risk of the study including societal risks or risks related to the design and the performance, is imperceptible.

The advantage of this study is that both patients and their informal caregivers will be given the chance to share their opinion for their chronic illness and to express their preferences for their care. Even though the patients and their informal caregivers might not be directly affected from the study, providing their feedback can have a significant impact for the improvement of the quality of care of such patients in the future.

Informed consent

The main researcher will explain the study protocol to both the patient who meets the inclusion criteria and his /her most important informal caregiver. The patient and the informal caregiver will receive the informed consent and a letter with the description of the study. After one or two days reflection time, the researcher (NS) will contact them again personally to ask if they like to join the study, which means that they will: a) have the patient's electronic records searched, b) both patients and informal caregivers will be asked to fill in two questionnaires at inclusion and three months after inclusion. If the patient and informal caregiver decide to participate in the study, they will provide signed consent. If there is no informal caregiver or the informal caregiver doesn't want to participate, then we will still include the patient in the study.

Data processing

All the data retrieved from the electronic files of the patients and all the questionnaires filled in by patients and their informal caregivers will be treated with strict confidentiality and will not be made public. The findings of the study will be processed following the regulations of the “Belgische wet op gegevensbescherming”.

After the collection of the data and the analysis, the main researcher will write the manuscripts and submit them to international PC related peer reviewed journals. Publications will be coordinated by the principal investigator of the project. The authorship of the publications will be regulated according to the requirements of the International Committee of Medical Journal Editors and according to the requirements of the respective targeted journals.

Ethics approval and consent to participate

This study (S58652) has received the Ethical Approval of the Medical Ethics Committee of UZ KU Leuven/ Research (Belg Regnr: B322201627749).

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CHAPTER 8

Quality of Life and Quality of Care in patients with advanced Chronic Heart Failure (CHF) and advanced Chronic Obstructive Pulmonary Disease (COPD): Implication for Palliative Care.

This chapter has been submitted as:

Siouta N, Heylen A, Aertgeerts B, Clement P, Janssens W, Van Cleemput J, Menten J. Quality of Life and Quality of Care in patients with advanced Chronic Heart Failure (CHF) and advanced Chronic Obstructive Pulmonary Disease (COPD): Implications for Palliative Care.

Quality of Life and Quality of Care in patients with advanced Chronic Heart Failure (CHF) and advanced Chronic Obstructive Pulmonary Disease (COPD): Implication for Palliative Care.

Background: There are many misconceptions among patients with CHF/COPD and their caregivers, on the life-limiting nature of their disease. Palliative care is less commonly implemented in current practice, compared to other chronic and life threatening diseases such as cancer. This observational prospective study explores i) the quality of life (QoL) and symptom control, ii) and the quality of care in CHF/COPD patients in an acute hospital setting.

Methods: Eligible patients and their informal caregivers filled in i) the POS questionnaire that assesses the QoL and the symptom control, ii) the CanHelp Lite that assesses quality of care and iii) a self-developed ad-hoc questionnaire that assesses quality of care and elements of ACP. These questionnaires were completed at inclusion and after a three-month-follow-up.

Results: The majority of the participants were 60 to 79 years old with mild to moderate symptomatology. Both patients and their informal caregivers share common and overall positive beliefs concerning patient's QoL and quality of care. Beliefs of both groups remain unchanged at both evaluation moments in the study.

Conclusions: The severity of the healthcare condition of the included patients appears to at odds with their positive evaluation of QoL and quality of care. Possible factors contributing to this finding might be the reluctance of physicians to engage to uncomfortable conversations, the patients' denial of "bad-news" and the overall taboo of communication about death. Resolving these issues requires being proactive and informing patients and family that they have the choice and the right to know more about their disease.

Background

Chronic Heart Failure (CHF) and Chronic Obstructive Pulmonary Disease (COPD) are two highly prevalent chronic diseases with high mortality rates and heavy symptom burden, comparable to that of patients with cancer [1]. The symptomatology of CHF and COPD includes physical symptoms such as pain, dyspnea, decreased physical activity and fatigue, and a number of psychological symptoms such as anxiety and depression [2-3]. Additionally, patients with CHF and COPD often have comorbidities that increase their symptom burden and render their condition more challenging to cope with [4-5]. The disease progression of CHF and COPD and recurrent episodes of exacerbation lead to several re-hospitalizations and a progressively declining quality of life (QoL) [6-7].

Early integration of Palliative Care (PC) alongside standard care and the provision of a holistic approach can significantly improve the QoL in patients with chronic non-curable diseases [8-9]. However, patients with CHF and COPD seldom receive this early integrated PC prior to reaching end-of-life stage. Only less than 25% of CHF/COPD patients have access to PC services, while this percentage is more than 50% for cancer patients [10-11].

Challenges in the implementation and integration of PC in CHF and COPD have been the subject of several studies. Three main barriers were identified i) the uncertainty/unpredictability of the disease trajectory, ii) perceptions of patients/families and health care providers that death is not near and iii) lack of PC education in medical specialists treating patients with CHF/COPD [12-14]. As regards (i), it is well-known that disease trajectories of CHF/COPD are complicated, comprising a series of relapses followed by short recoveries. Thus, although prognosis of the advanced stages of these diseases is poor, accurate prognostication[4] is cumbersome and uncertain, undoubtedly impeding discussions on goals of care and advance care planning [15-16]. As regards (ii),

[4] Prognosis refers to the likely course of the medical condition. Prognostication refers to the short to medium forecast of the disease trajectory.

patients and their families typically do not consider CHF/COPD as terminal diseases and tend to underestimate the severity of these illnesses [17-21]. Physicians, on the other hand, associate PC mostly with terminal and end-of-life care and not as a service that aims to support physical and emotional symptom management during the whole incurable disease trajectory, to maintain a reasonable quality of life and to enhance communication between patient, their family and healthcare providers [22]. Finally, as regards (iii) it is recurrently being demonstrated that lack of PC education inhibits further integration of PC, despite the availability of guidelines [23-24].

Given the misconceptions of the patients and their informal caregivers on the life-limiting nature of their disease, acquiring an evaluation of current practices within standard care in acute hospital wards, can be informative and helpful for the implementation of interventions that aim to foster the further early integration of PC.

The present study empirically examines the quality of life, quality of care and integration of PC of patients with CHF and COPD and their informal caregivers in an acute hospital based setting.

Materials and Methods

1. Design

This prospective observational study is part of an ongoing intervention study that took place in the University Hospital of Leuven (Belgium) in the departments of Cardiology and Pulmonology (two nursing wards for CHF and one nursing ward for COPD).

This prospective observational study was designed to evaluate in CHF/COPD patients in an acute hospital setting: i) the QoL and symptom control and ii) the quality of care. The patient duration of recruitment and data collection for the standard care was estimated to be 8 months based on regular admittance numbers in these wards.

2. Participants

Eligible patients had to fit the following inclusion criteria:

- Adult patients (>18 y.).
- Dutch speaking and capable of completing the 3 questionnaires.
- Classification of CHF (NYHA class III/IV) or COPD (GOLD stages C/D).
- At least one readmission for an exacerbation of the disease within the last year.
- Predicted/presumed life expectancy of at least 6 months.
- One informal caregiver for every patient had to participate in the study and had to be a Dutch speaking adult, capable of completing the 3 questionnaires.

3. Questionnaires

Each patient and the corresponding caregiver were asked to complete three questionnaires:

1. The Canadian Healthcare Evaluation Program (CANHELP) Lite Questionnaire, which is a validated tool for measuring the quality of care [14]. CANHELP Lite has two parts, one for the patient and one for the informal caregiver and requires approximately 10 minutes to be completed. The patient version has 21 questions that address the satisfaction of the quality of care, the relationship with the doctors, illness management, communication, decision making and a question concerning the patient's inner peace. The caregiver version includes 23 questions assessing the satisfaction of the overall care, the relationship with the doctors, the characteristics of doctors and nurses, illness management, communication, decision making and the involvement of the informal caregiver to patient's care.
2. The Palliative Outcome Scale (POS) Questionnaire, which is a validated tool used to measure quality of life and the symptoms of the patients in PC studies [15]. POS has two versions, one for patients and one for their informal caregivers and has a completion time of approximately 7 minutes. Both versions consist of the same 12

questions that are addressing the overall quality of patient's life including physical and emotional symptom management and adequacy of information received.

3. An ad-hoc questionnaire developed by the Palliative Support Team of UH Leuven to measure quality of care and elements of advance care planning (ACP). This questionnaire has a completion time of approximately 10 minutes for both the patient and informal caregiver versions. This questionnaire is yet to be validated, however, given the lack of questionnaires that measure different elements of ACP, this questionnaire was considered appropriate for our study. This questionnaire addresses questions over the perceptions of patients and caregivers concerning the current care, usefulness of discussions related to patient's health, desire for involvement in these discussions in the present and the future and overall evaluation of their emotional state.

4. Sample size

The sample size was calculated based on existing empirical studies that used the POS questionnaire. QoL is in POS measured with a 49 scale score, with 0 being the best score and 48 being the worst. Our study was designed with the objective to detect differences at the order of 5%, corresponding to plus/minus 3 points in the total score and to have a statistical power of 80%. The existing empirical studies were used to calculate the standard deviation and based on these values, the sample size (for a combined sample of CHF and COPD patients) was computed to be 37 patients and 37 informal caregivers. We considered a 30% attrition rate which resulted in a final sample of 50 patients and 50 informal caregivers (25 patients and 25 informal caregivers for each COPD and CHF).

5. Recruitment

For cardiology, the researcher (NS), in collaboration with the head nurses of the two wards, screened and identified eligible patients on a weekly base. For the pulmonology

ward, a dedicated research nurse was responsible for identifying and reporting eligible patients to the researcher. A cross-checking of eligibility criteria was performed via examination of the patients' electronic files in the presence of specialist physicians of the corresponding wards. Additionally, the researcher participated in the weekly multi-disciplinary meetings of the wards. The recruitment phase was marked with several difficulties, stemming from the topic of the study, the misconceptions of the involved personnel for it, the workload of the personnel and the external character of the researcher to the wards. The difficulties, led to adjustments of the adopted strategies. The challenges associated with recruitment have been documented in [25] and suggestions for their alleviation are presented.

The study received Ethical Approval of the Medical Ethics Committee of UZ KU Leuven/ Research (Belg Regnr: B322201627749).

6. Data collection

This study was administered by a principal, full-time researcher (NS). The patients and their informal caregivers were asked, after signing informed consent files, to complete the three questionnaires: i) at the moment of inclusion (during their hospitalization) and ii) three months after inclusion.

The following steps were performed after the identification of an eligible patient.

1) The researcher explains the study in detail.
2) If the patient (and one of his/her informal caregivers) agrees to participate, they both provide their informed consent.
3) The researcher administers the three questionnaires at the moment of inclusion and collects the completed versions from both patients and informal caregivers on the spot. In case of questions (not associated with cognitive impairment), the researcher provides additional information.

4) If patients or their informal caregivers decline to participate, they are asked to informally communicate/explain the reason for doing so.
5) Three months after inclusion, the researcher sends the same three questionnaires by post to each patient and his/her informal caregiver for the follow up phase. In case of delayed return of the questionnaires, the researcher contacts the participants by phone as a reminder.

7. Data analysis

Data analysis was carried out by the main researcher (NS). Statistical analysis was performed with Microsoft Excel software. Standard descriptive statistics were used for the analysis of the basic characteristics of the sample and the distributions of the scores of the tests (mean values, medians, standard deviations). T-tests were employed to examine equality of means for total scores of POS and CanHelp Lite between different pairs (e.g. CHF patients vs CHF informal caregivers). Responses to individual questions were treated as ordinal data and were analyzed with Mann-Whitney U tests and Wilcoxon signed rank tests.

Results

The total sample of our participants is N=48 with 23 CHF and 25 COPD patients. The gender distribution of the sample is dominated by males (almost 2 to 1). The CHF participants had a mean age of 64,8 years (SD= 14,33) and the COPD participants had a mean age of 67,1 years (SD=8,54).

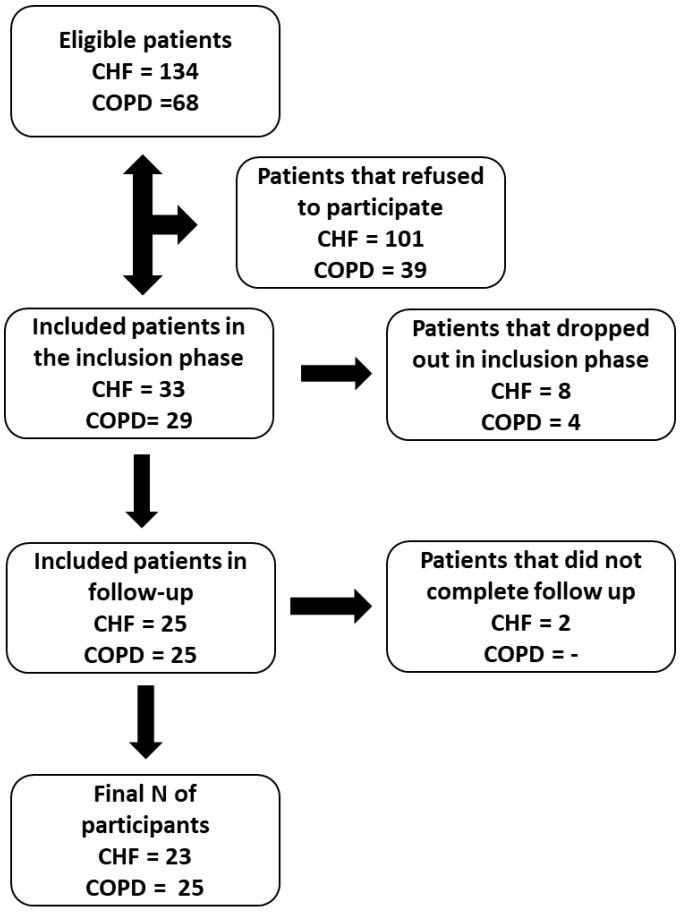
Table 1. Basic demographics of participating patients.

Characteristics	**Total sample**	**CHF patients**	**COPD patients**
N	48	23	25
Gender			
Male	32	15	17
Female	16	8	8
Age			

<45 46-59 60-79 >80 Died (after completing inclusion questionnaires) Died (after completing the study)	1 8 31 3 2 3	1 5 12 2 2 1	0 3 19 1 0 2
CHF patients: mean age = 64,8 (SD= 14,33) *COPD patients: mean age = 67,1 (SD=8,54)*			

Figure 1 demonstrates the flowchart of recruitment. The actual inclusion rate of eligible patients is only 18% and 36% respectively or CHF and COPD. For the 101 CHF patients and the 39 COPD patients that declined to participate in the study, the top four reported reasons were that: i) they were emotionally or physically exhausted (41% in CHF and 49% in COPD), ii) the study and filling in 3 questionnaires was too demanding (22% in CHF and 18% in COPD), iii) reasons were not specified (22% in CHF and 23% in COPD) and iv) the relatives refused to participate in the study (15% in CHF and 10% in COPD). The low to moderate participation is not without consequences and is further exploited in the discussion of this paper.

Figure 1. Flow chart: Inclusion process of eligible CHF and COPD patients in the study.



We observed that, as regards POS, where scoring system goes from 0 (excellent QoL) to 40 (low QoL), the overall score of both groups and their informal caregivers reflects a relatively high QoL and with narrow distributions (Table 2). As regards CanHelp Lite, where scoring system ranges from 0 (low quality of care) to 105 (excellent care) for patients and 115 for their informal caregivers. Again we observe relatively high satisfaction about the given care with small variations. Results for the Ad-Hoc questionnaire are presented in terms of separate questions because of the quantitative and qualitative nature of the questionnaire.

Table 1 Descriptive statistics of POS and CanHelp Lite scores

	POS inclusion	POS follow-up	CanHelp Lite inclusion	CanHelp Lite follow-up
COPD patients	M*=9.28 SD*=5.10	M=9 SD= 5.18	M=80.36 SD=12.80	M=78 SD=12.59
COPD family caregivers	M=8.16 SD=4.90	M= 7.56 SD=4.45	M=84.84 SD=13.05	M=86.72 SD=13.77
CHF patients	M=10.73 SD=5.76	M=10.39 SD=6.19	M=81.52 SD=13.59	M=79.17 SD=14.00
CHF family caregivers	M=11.52 SD=7.15	M=10.56 SD=6.27	M=80.82 SD=12.45	M=79.60 SD=11.48
*****M=mean score. *SD=standard deviation For POS: 0=highest score to 40=lowest score. For CanHelp Lite: 105= highest score to 0=lowest score				

In Table 3, we have tabulated the results of t-tests for various pairs for POS. We infer that that there is no evidence to reject the null hypothesis (the means equal) in any of the combinations. In other words, for both CHF and COPD, patients and their informal caregivers share on average the same opinion on the patient's quality of life, symptom management and quality of care at both inclusion and follow up.

Table 2 Results of t-tests for different combinations of pairs for the POS

POS Pairs of comparison	Outcome of t-test*
COPD patients inclusion vs COPD patients follow-up	t=0.29 p=0.766>0.05
COPD family caregivers inclusion vs COPD family caregivers follow-up	t=0.60 p=0.555>0.05
COPD patients inclusion vs COPD family caregivers inclusion	t=0.79 p=0.432>0.05
COPD patients follow-up vs COPD family caregivers follow-up	t=1.05 p=0.297>0.05
CHF patients inclusion vs CHF patients follow-up	t=0.35 p=0.723>0.05
CHF family caregivers inclusion vs CHF family caregivers follow-up	t=1.17 p=0.272>0.05
CHF patients inclusion vs CHF family caregivers inclusion	t=0.40 p=0.684>0.05
CHF patients follow-up vs CHF family caregivers follow-up	t=0.09 p=0.925>0.05
COPD patients inclusion vs CHF patients inclusion	t=0.92 p=0.357>0.05
COPD patients follow-up vs CHF patients follow-up	t=0.84 p=0.402>0.05
COPD family caregivers inclusion vs CHF family caregivers inclusion	t=1.91 p=0.062>0.05
COPD family caregivers follow-up vs CHF family caregivers follow-up	t=1.92 p=0.060>0.05
**t-tests are two-tailed at a 95% confidence level (p=0.05) appropriately using the paired sample or independent sample option. For independent samples only results with assumed equal variances are reported; results with unequal variance are available, however, no difference has been observed.*	

Comparisons for CanHelp Lite are more limited by the fact that patients and caregivers complete different questionnaires. Consequently, we cannot directly assess differences in the overall scores for patients versus their informal caregivers. The results for all pairs that are amenable to such analysis are shown in Table 4. Similarly to the POS case, no statistical difference is observed in the pairs that have been checked.

Table 3 Results of t-tests for different combinations of pairs for the CanHelp Lite

CanHelp Lite Pairs of comparison	**Outcome of t-test***	
COPD patients inclusion vs COPD patients follow-up	t=1.14	p=0.262>0.05
COPD family caregivers inclusion vs COPD family caregivers follow-up	t=-0.85	p=0.400>0.05
CHF patients inclusion vs CHF patients follow-up	t=0.89	p=0.380>0.05
CHF family caregivers inclusion vs CHF family caregivers follow-up	t=0.52	p=0.603>0.05
COPD patients inclusion vs CHF patients inclusion	t=0.30	p=0.761>0.05
COPD patients follow-up vs CHF patients follow-up	t=0.30	p=0.761>0.05
COPD family caregivers inclusion vs CHF family caregivers inclusion	t=1.08	p=0.282>0.05
COPD family caregivers follow-up vs CHF family caregivers follow-up	t=1.93	p=0.059>0.05
**t-tests are two-tailed at a 95% confidence level (p=0.05) appropriately using the paired sample or independent sample option. For independent samples only results with assumed equal variances are reported; results with unequal variance are available, however, no difference has been observed.*		

Besides examining the overall scores, we are also interested in responses to individual questions. In order to keep this paper within reasonable length, we only present and discuss a selection of questions that may help us to further interpret our findings and compare with existing literature. For POS we focus on questions (1)and (2) that concern physical symptoms, questions (3) and (8) that concern psychological aspects and question (5) that concerns the information that the patient received.

For CanHelp Lite we analyze question (6) that addresses the satisfaction of care of physical symptoms, question (7) which is related to the satisfaction of the psychological support received, question (12) which assesses the satisfaction of the care according the patient's wishes and questions (16, 17 and 19) that concern the satisfaction of discussions over future decisions.

Finally, for the Ad-Hoc questionnaire we report the results for questions/statements (4, 6 and 7) on the timing, clarity and helpfulness of ACP talks, for question (9) on the existence of a holistic approach, for questions (10, 11 and 12) on the accommodation of patient's current and future wishes and finally for questions (14,15 and 16) that deal with the psychological state of patients and their caregivers.

Table 4. Median scores of selected questions for POS, CanHelp Lite and Ad-Hoc

	INCLUSION				**FOLLOW-UP**			
	COPD pat.*	**COPD care.***	**CHF pat.**	**CHF care.**	**COPD pat.**	**COPD care.**	**CHF pat.**	**CHF care.**
POS								
Did you have pain in the past 3 days?	1	1	2	2	1	1	2	2
Did you have other physical symptoms in the past 3 days?	1	1	0	1	1	1	1	1
Did you have stress for your illness in the past 3 days?	1	1	2	2	1	1	1	2
Was anyone from your family stressed for your illness in the past 3 days?	2	2	2	2	1	1	2	1
CanHelp Lite								
How satisfied are you with the physical symptom management?	4	4	4	3	4	3	3	3
How satisfied are you with the emotional symptom management?	4	3	4	3	3	3	3	3
How satisfied are you with the care taking your wishes into consideration?	4	4	4	4	3	4	4	4
How satisfied are you with the doctor's explanation of the illness?	4	4	4	4	4	4	4	3
How satisfied are you with the discussions for the place of care when you will be unable to take decisions?	4	4	4	4	4	4	4	3
How satisfied are you with the discussion for life-prolonging techniques?	4	3	4	3	4	3	4	3
How satisfied are you with the discussions for relatives decisions of the care when	4	3	4	3	4	3	4	3

you will be unable to take decision?								
Ad-Hoc Questionnaire								
Talks over care are helpful	4	4	4	4	4	4	4	4
Talks over care should take place earlier	4	4	4	4	4	4	4	4
There is caring communication over the patient's health	4	4	4	3	4	4	4	4
There is care for patient's holistic needs	3	4	4	3	3	3	4	4
Patient's wishes for current needs are taken into account	4	3	4	4	3	3	4	4
Patient wishes for later stage care are asked	3	3	3	3	3	2	3	3
Talks for unwanted treatments are discussed	3	4	3	3	3	3	3	3
Talks make patient feel less stressed	3	3	3	3	3	3	3	3
Talks make patient feel less depressed	3	3	3	3	3	3	3	3
Talks family caregiver feels less stressed	3	3	3	3	3	2	3	3

* pat=patients
* care=informal caregivers

→For POS the scoring is: 0=not at all, 1=somewhat/rarely, 2= moderate/ occasionally, 3=seriously affected/often, 4= completely overpowered/constantly
→For CahHelp Lite the scoring is: 1=completely not satisfied, 2=not very satisfied, 3=slightly satisfied, 4=very satisfied, 5=completely satisfied.
→For Ad-Hoc the scoring is: 1=completely disagree, 2=disagree, 3=nor agree neither disagree, 4=agree, 5=completely agree.

The median scores of the questions of interest for all questionnaires are reported in Table 5. In addition to descriptive statistics, we have also performed appropriate tests for equality of distributions (Mann-Whitney U tests and Wilcoxon signed rank tests) for all possible combinations. In the vast majority of cases, no significant difference was observed. Overall a statistically significant difference was found in six (6) cases:

1. Question 4 POS: Was anyone from your family stressed for your illness in the past 3 days? Comparison pair: COPD patients at inclusion (median score = 2) vs COPD patients at follow up (median score = 1), (z score=1.936, p=0.026, effect-r=0.273)
2. Question 12 CanHelp Lite: Are your current care wishes taken into account? Comparison pair : CHF patients at inclusion (median score = 4) vs CHF informal caregivers at inclusion (median score = 4), (p=0.016, effect r=0.301, z score=2.132)
3. Question 10 Ad-Hoc: Are you current treatment wishes taken into account? Comparison pair: COPD patients at inclusion (median score = 4) vs COPD patients at follow-up (median score = 3), (p=0.029, effect r=0.266, z score=1,887)
4. Question 11 Ad-Hoc: The patient's later-phase care treatment wishes have been inquired. Comparison pair: COPD informal caregivers at inclusion (median score = 3) vs COPD informal caregivers at follow-up ((median score = 2), (p=0.017, effect r=0.297, z score=2.103)
5. Question 12 Ad-Hoc: The patient's unwanted care treatments have been discussed. Comparison pair: COPD informal caregivers at inclusion (median score =4) vs COPD informal caregivers at follow-up (median score = 3), (p=0.011, effect r=0.321, z score=2.271)
6. Question 16 Ad-Hoc: I feel less stressed as a family caregiver. Comparison pair: COPD informal caregiver at inclusion (median score = 3) vs COPD informal caregiver at follow-up (median score = 2), (p=0.009, effect size=0.331, z score=2.341)

Despite reaching statistical significance, the effect size in all cases is low to moderate. In other words, even in cases where significant differences are detected, the magnitude of these differences is not substantial.

In general, the results of both POS and CanHelp Lite show that patients, and informal caregivers alike, have a moderate to high level of satisfaction for quality of life and quality

of care. As regards the Ad-Hoc, it appears that patients and informal caregivers view the concept of early health care discussions as helpful. However, a more neutral response is observed for current and future wishes and for the emotional advantages of such discussions.

Discussion

The findings of this study can be summarized as follows:

i) Patients and their informal caregivers share common beliefs concerning QoL and quality of care.

ii) Both CHF and COPD patients and their caregivers evaluate positively both the patient's QoL and quality of care.

The agreement between the beliefs of patients and their informal caregivers in this study confirms previously reported data in both cancer and chronic diseases [26-28]. Our empirical evidence adds further to the generalizability and the aggregate robustness of this result. Having informal caregivers well aligned with patient's desires and perceptions is of particular relevance, especially at later stages of the disease trajectory, given that informal caregivers are often responsible for making decisions for the patients [29]. However, communication alignment between patient's and informal caregivers is not sufficient for the latter to make informed decisions. Doing so, requires a sufficient knowledge of prognosis and prognostication, even if the patient is, correctly or not, unaware of this information. Although our study has not directly assessed the awareness of patients and their informal caregivers concerning the terminal stage of the disease, previous studies report that the level of this awareness is low and related conversation are scarce [30-31]. Consequently, when death-related issues and decision making have to be raised, reactions are likely to be negative and lead to deterioration of trust [32].

At first, the positive evaluation of patients and their informal caregivers for QoL and quality of care might seem at odds with the severity of symptoms of CHF/COPD and the

classification (NYHA for CHF or GOLD for COPD) of the disease level. Even more so, given that some of these patients died shortly after the completion of the study. However, similar results have been reported for both CHF and COPD [33-34]. One explanation can be that our participants were recruited from acute wards and they were not referred to PC services and as a consequence it is unlikely that they were fully aware of their prognostication. In addition, the majority of the included patients, cognitively capable of filling in the questionnaires, were of a younger age ranging from 60-79 years old, as is often the case with studies similar to ours. These patients are more likely to suffer from or report mild to moderate symptoms [31, 35]. This does contrast with the characteristics of the eligible patients who declined to participate; these patients were on average older. Additionally, these patients frequently reported verbally their inability to participate due to severe (self-reported) emotional and physical symptomatology; although this does not provide a quantitative measurement but rather a qualitative one. Interpretations should, therefore, be conditioned on the characteristics of our sample, which constitutes a fraction of the overall population with advanced CHF and COPD.

Putting the positive evaluation of QoL and quality of care into perspective requires examining the public perceptions of CHF and COPD. In the absence of PC interventions, and in contrast to cancer, the public views CHF/COPD as a life-long disease that occasionally leads to hospitalizations but that is not necessarily linked to death [36]. Even when faced with advanced care planning (ACP) decisions on resuscitation, it is not uncommon that these patients choose in favor of cardiopulmonary resuscitation (CPR) and/or mechanical ventilation [31]. For these patients and their relatives, adjustment to exacerbations and development of new coping mechanisms is part of life [27, 37]. A hospitalization is not something unexpected, but it is rather perceived as a “fix” that helps them to overcome heavy symptoms and return home to their routine. For this population, a positive evaluation of QoL and quality of care reflects the acceptance of the status quo and their hope to return home after being “cured” [22, 36]. Interestingly, this mentality

is often fed by the improvement of patient-reported quality of life after hospitalization of CHF/COPD patients [38], prior to the next relapse.

On the other hand, CHF and COPD patients that have been referred to PC services are likely to develop different perceptions on and expectations for QoL and quality of care. For example, patients unaware of the existence of PC services can perceive their symptom control as adequate since they are not aware of additional symptom management options [39]. Further, since QoL depends partly on the emotional wellbeing of the patient, stress triggered or exacerbated by the possibility of an imminent death can lead to deteriorations of QoL [28,39]. Moreover, despite recommendations to the contrary, PC in CHF/COPD is still initiated very late in the disease trajectory (near the end of life) and often in an abrupt manner. Therefore, there is not enough time for the patients to receive the (empirically) demonstrated benefits of integrated PC [40-41].

The included patients have reported a relatively good physical and emotional QoL. In particular, levels of stress and anxiety were low during their hospitalization and three months afterwards (follow-up moment). This is in line with the aforementioned finding that hospitalization of CHF/COPD patients can act as a boosting mechanism up until the next relapse. The correlation between emotional status and QoL in general has also been observed in the past for both CHF and COPD patients. Indeed, there is empirical evidence indicating that patients with less emotional symptoms and with a better perception towards their disease are more likely to experience a higher QoL [42-44].

The explanatory framework presented above puts our results into a larger narrative. However, the implications of our study require careful consideration on two fronts.

First, we reiterate that we have employed a convenience sample consisting of patients with low or moderate symptomatology and on average of a younger age. The underrepresentation of older patients with presumably heavier symptomatology and

more comorbidities may hamper the generalizability of the results. Indeed, there is empirical evidence that the relative uniformity of opinions reported by our participants does not extend to elder populations with high symptom burden [30]. Given that PC needs of this population might be higher, it is pertinent that we take their opinions into account before building policy recommendations. This is a challenge on its own, especially given the frailty and burden of these patients.

Second, due to the public perception on CHF/COPD, the associated development of coping mechanisms by the patients and their own limited PC education, health care providers are uncomfortable to raise spontaneously issues on prognosis and prognostication which, in turn, perpetuates the limited awareness of CHF/COPD patients on these aspects [37]. However, despite often prolonged periods of stability, the trajectory of both diseases is characterized with steady declines in organ function and increasing numbers of exacerbations. Consequently, when patients reach a stage signified by multiple hospitalizations, coping mechanisms developed at this stage hint that patients and their informal caregivers might be in denial, which can be viewed as a defense mechanism against exposure to negative news. In response, PC studies recommend changing this mentality in favor of earlier and more transparent communications [45]. What complicates matters further is the fact that CHF/COPD patients share diverse opinions on prognosis/prognostication communications. There are studies showing that patients would desire a full disclosure of their illness and their options [27]. At the same time other studies have revealed that such patients are only a fraction of the overall population [30, 46]. For example, some patients are not willing to receive prognostic information whereas others would like to do so only if this would not decrease their hope [30]. What is important to underline is that these results do not contradict each other but rather reveal the complexity and heterogeneity of the CHF/COPD population as a whole.

Taking into account the heterogeinity of the CHF/COPD population, it becomes clear that the negative correlation between knowledge of prognosis and psychological wellbeing

and QoL concerns only a fraction of this population. Consequently, the common practice of physicians towards non-disclosure might be considered beneficial to only this fraction of this population, while ignoring the needs of those who want to know more about their condition. Accordingly, the recommendations of early integrated PC should be interpreted with this heterogeneity in mind as well. In other words, integrated PC should focus on the fraction of the CHF/COPD population for which awareness is beneficial. Therefore, the heterogeneity of this population states that presently both awareness and non-awareness have their own target groups.

The ”silent agreement” between all involved actors to keep death out of the picture, as much as possible, reveals that for CHF/COPD patients death and dying remain taboo topics, also for their informal caregivers and the healthcare providers[47]. As regards patients, even at an older age, their perceptions on death and dying are mixed. It is not clear whether openness to death and dying stems from awareness of the nature of the disease or from recognizing mortality due to aging [48]. As regards, CHF/COPD healthcare providers their inclination towards non-disclosure of death-related info is not without precedence. For example, in malignant disease in the sixties nearly 90% of doctors in the US opted for non-disclosure [49], but there was a dramatic shift in favor of disclosure towards the end of previous century [50]. The resolution of the death taboo in cancer has facilitated the accommodation of PC practices and thus allowed patients and their families to receive its benefits. For CHF/COPD the taboo of death and dying and the fact that PC is synonymous to death partially explain postponing the initiation of PC until the last hours of life for these patients [47, 51].

The main question to be answered is whether we can reconcile the benefits of PC with the heterogeneity that characterizes the population of CHF/COPD, the public image of these two diseases, the denial of patients, the taboo of death and the non-maleficence of health care providers. All the above show that a “one-size-fits-all” mentality for PC is not viable. A practical way to circumvent those issues is to adopt a more patient-oriented

approach: patients should be given the opportunity to choose whether they would like to know more about their disease, about their prognosis, about the possibility to be engaged in further ACP discussions and have access in PC services. Although our recommendation does not require the resolution of all the above mentioned issues, we encourage the healthcare specialists to communicate these possibilities to their patients.

Conclusion

This study has found that CHF/COPD patients and their informal caregivers share common and overall positive beliefs concerning patient's QoL and quality of the received care. The reluctance of physicians to engage to uncomfortable conversations, the patients' avoidance to deal with "bad-news" and the overall taboo of death vis-à-vis the public image of CHF and COPD, all contribute to the surprisingly positive evaluation of their QoL and quality of care. Resolving all these issues is a long term process and the first step towards this is to be proactive and inform patients that they have the choice to know more about their diagnosis and prognosis so as to optimize their care planning based on their own views and perceptions.

Limitations

This study has several limitations. As the study was administered by an external investigator who was not linked to the wards, eligibility of patients was determined in collaboration with the corresponding healthcare personnel. This has rendered recruitment more challenging and it is not clear whether all eligible patients have been contacted.

Although power calculations were made, we were not able to recruit many patients outside the range 60-79 years old. Given the frailty of the target population, it is possible that this study recruited patients with milder symptom burden. Moreover, the majority of eligible patients declined to participate for various reasons reported in another study

[25] raising questions on representativeness, as selection may be an important confounding factor.

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CHAPTER 9

Lessons learned from a feasibility prospective study of Palliative Care eligible patients with Chronic Heart Failure (CHF) and Chronic Obstructive Pulmonary Disease (COPD).

This chapter has been submitted as:

Siouta N, Heylen A, Aertgeerts B, Clement P, Vermandere M, Janssens W, Van Cleemput J, Menten J. Lessons learned from a feasibility prospective study of Palliative Care eligible patients with Chronic Heart Failure (CHF) and Chronic Obstructive Pulmonary Disease (COPD).

Lessons learned from a feasibility prospective study of Palliative Care eligible patients with Chronic Heart Failure (CHF) and Chronic Obstructive Pulmonary Disease (COPD).

Background: Initiation of PC practices in cardiology and pulmonology wards for patients with Chronic Heart Failure (CHF) and Chronic obstructive pulmonary disease (COPD) remains a challenging topic.

Objective: A feasibility prospective study was designed and implemented in the cardiology and pulmonology wards of the University Hospital of Leuven (Belgium) to measure the quality of life (QoL) and the quality of care in both chronic CHF and COPD patients and their informal caregiver.

Methods: Eligible patients and their informal caregivers were asked to complete the Palliative Care Outcome Scale (POS), the CanHelp Lite questionnaire and a self-developed ad-hoc questionnaire. These questionnaires were completed at inclusion and after a three-months follow-up. Informed consent was required.

Results: The feasibility assessment has overall been positive. The sample size (23 CHF and 25 COPD patients) was collected but older patients were underrepresented. The majority of the participants were younger and with milder symptomatology. Despite the well-designed eligibility criteria, it became necessary to readjust the recruitment process and directly involve the main researcher in the identification of eligible patients.

Conclusion: The positive feasibility assessment and the lessons learned from this study can assist similar future efforts in this area. However, the implementation of integrated PC interventions is expected to raise further challenges that will need to be investigated in seperate studies.

Background

Palliative Care (PC) was initially confined to cancer patients, however, there is a growing awareness for patients with advanced non-malignant chronic disease. Owing to their high prevalence and severe symptomatology, Chronic Heart Failure (CHF) and Chronic Obstructive Pulmonary Disease (COPD) have been at the core of relevant studies and it has been shown that such patients can significantly benefit from PC practices [1-3]. Since similar empirical findings for patients with cancer are well-established [4-8], there is a general consensus that PC has a positive impact on the quality of life for patients with both malignant and non-malignant diseases.

Studies for PC in cancer, dating already back to the 90's, have reported that relevant empirical studies are challenging to perform in clinical practice as a direct consequence of the patient population and its characteristics. Difficulties in recruitment, high attrition rates, compliance of the patients, methodological challenges, cooperation between the personnel and ethical issues have been explicitly reported as bottlenecks that can severely impact the duration, quality and outcome of empirical studies in palliative patients [9-10]. There are even examples where RCTs were forced to stop due to failure in reaching the inclusion of enough patients or in collecting enough data to reach the desired sample sizes for analysis [9-11]. The evolution of the number of high-quality empirical studies on PC in cancer asserts that these challenges have been mitigated or circumvented successfully. Consequently, PC in cancer has experienced substantial progress and, although current practices are not optimal, nearly 50% of cancer patients can benefit from PC services [12].

For patients with chronic disease, and in particular with CHF and COPD, the situation has been markedly different. With less than 25% of these patients receiving PC and for those who do only at the end of life, it is clear that PC practices are seldom included in the treatment that CHF/COPD patients receive in acute hospital wards [13]. This inequity of

PC provision has been attributed to the fact that CHF and COPD patients constitute of a population with unique characteristics. In contrast to cancer, the public does not perceive CHF and COPD as life-threatening disease, but rather as a chronic condition associated with frequent hospitalizations that requires adjustment to exacerbations and development of new coping mechanisms is part of life [14,15]. In response to these perceptions, healthcare providers feel uncomfortable to raise issues on prognosis and prognostication thereby delaying PC until the very end [16-17]

In view of the above, it is evident that the initiation of PC interventions in cardiology and pulmonology wards should not be done abruptly, by simply extrapolating the accumulated know-how from cancer. A feasibility study that will involve all actors: health-care personnel, patients and their informal caregivers, appears as a promising starting point that can shed light on the challenges and the transferability of cancer experience in this setting.

In the University Hospital (UZ) of Leuven (Belgium), a feasibility prospective study was designed and implemented with objectives the measurement of the quality of life (QoL) and the quality of care in both chronic CHF and COPD patients and their informal caregiver. We provide the feasibility assessment of our effort and we describe the challenges that emerged during the study and the lessons that we learned from conducting it.

Materials and Methods

8. Design

A feasibility prospective and observational study was designed. This study was expected to last about 8 months and was initiated in the UH Leuven in Belgium in the departments of cardiology and pulmonology (one nursing ward for CHF and one ward for COPD). The

8-month duration of the study was estimated based on the regular admittance numbers of eligible patients in these wards. This study received Ethical Approval of the Medical Ethics Committee of UZ KU Leuven/ Research (Belg Regnr: B322201627749).

9. Participants

Eligible patients for the study were adult patients with CHF (NYHA class III/IV) and COPD (GOLD stages C/D) that were readmitted with an acute exacerbation of the disease at least once within the last year. The patients needed to have an assessed life expectancy of 6 months or more. Additionally, for each patient, an informal caregiver also had to participate in the study. This informal caregiver was defined as that proxy person who mainly takes care of and supports the patient for most of the time. This caregiver may not necessarily be a family member, but had to be an adult able to communicate in Dutch and to complete the three questionnaires.

10. Questionnaires

Patients and their most important family caregiver (determined by the patient) were asked to complete the Canadian Healthcare Evaluation Program (CANHELP) Lite Questionnaire [18], the Palliative Outcome Scale (POS) Questionnaire [19] and an ad-hoc questionnaire developed by the Palliative Support Team of UZ Leuven to measure different elements of advance care planning (ACP). To reduce attrition risk and minimize potential burden, we chose questionnaires with a relatively short completion duration.

The Canhelp Lite Questionnaire is a validated tool frequently used in clinical PC studies to measure the quality of care [18]. It comprises two parts; one for patients and one for family caregivers. It can be used in both hospital and in out-patient settings and has a completion time of approximately 10 minutes. Validation of the CANHELP Lite has been performed in English but not yet in Dutch; at this stage it has gone through a two—way

translation in Dutch. Nevertheless, this tool is considered the most suitable for our study, because there is no similar questionnaire in Dutch or English that addresses the issues that this study is focusing on.

The POS is widely used questionnaire used in patients and family caregivers to measure quality of life and the symptoms of the patients in PC studies [19]. It has a completion time of approximately 7 minutes and it has two parts; one for the patients and one for the caregivers. This tool is validated in both English and in Dutch.

The ad-hoc questionnaire that was developed by the Palliative Support Team of UZ Leuven in Dutch is used to measure the quality of care and different elements of advance care planning (ACP) in the care provided to patients and to their informal caregivers in the hospital setting. It has a completion time of approximately 10 minutes for both the patient and caregiver versions. Since there currently exist no questionnaires that measure the different elements of ACP (e.g. discussions for patients' wishes and undesirable care treatments), this questionnaire was considered appropriate for addressing the issues we were concerned with in our study. This questionnaire is yet to be validated.

11. Sample size

We used a convenience sample of 50 patients and 50 informal caregivers (25 patients and 25 informal caregivers for each disease). The sample size was calculated based on existing empirical studies that used the POS questionnaire. Our study was designed with the objective to detect differences at the order of 5% and to have a statistical power of 80%. The existing empirical studies were used to calculate the standard deviation and based on these values, the sample size (for a combined sample of CHF and COPD patients) was computed to be 37 patients and 37 informal caregivers. We considered a 30% attrition rate which resulted in a final sample of 50 patients and 50 informal caregivers.

12. Recruitment

According to the design of the study, and following discussions with the health care providers of pulmonology and cardiology wards, the following model for the identification of eligible patients was adopted. For CHF, the head-nurse was appointed as the person responsible for the identification of eligible patients. The researcher was visiting the ward twice weekly and the head-nurse was pointing out the eligible patients. For COPD, a pulmonology ward nurse was appointed to screen and report the eligible patients to the researcher upon examining the electronic files of the patients and cross-checking with assistant physicians of the corresponding ward during bilateral or multi-disciplinary meetings. The results for COPD were communicated via e-mail with the researcher.

13. Data collection

This study was administered by a principal, full-time researcher who screened, identified and referred the eligible patients. The researcher was fluent in Dutch, but not a native speaker. Completion of questionnaires was requested in two timings: i) inclusion moment after signing the informed consent during the hospitalization of the patient and ii) a follow up of three months after inclusion.

When the researcher was explaining the study to the patients, she did not mention that this is a PC study. Rather, she informed them that the study aimed to analyze whether the quality of care and communication for patients and their relatives could be optimized. This was chosen based on the fact that i) the patients were not in a PC ward, and ii) bringing up suddenly advance care planning could disturb the patients emotionally. It was assumed that all patients were not aware of their disease prognosis[5].

[5] It is possible that some of the patients were aware of their prognosis. However, given the character of this study, we opted to avoid possible confrontation in case patients were unaware of the severity of their condition.

After the researcher had explained in detail the study and the patients agreed to participate, they were asked to fill in the informed consent (and their informal caregiver as well) and then the researcher administered to them the three questionnaires in the inclusion moment. If a patient or the informal caregiver had difficulty understanding the questionnaires, the researcher in charge could provide additional information and help the participants fulfill the questionnaires. When the eligible patients or their family members declined to participate, the researcher asked for the reason and archived it. No special document was provided to patients who declined and communication for the reason was oral and informal.

For the second measurement after three months, the same questionnaires were sent by post to each patient, and sent back to the researcher after completion of the questionnaires. In some cases, the follow-up questionnaires were administered to the patients when they visited the hospital for a check-up examination. When the follow –up questionnaires posted were not returned back on time, then the researchers contacted the participants by telephone to remind them to complete them and post them back.

14. Data analysis

For the analysis of the baseline characteristics of the population, standard descriptive statistics were employed. For the comparison of the different groups an analysis of variance was carried out based on t-tests and chi-square tests. The statistical analysis of this study was performed with Microsoft Excel software.

Results

Recruitment and data collection lasted in total 16 months. This reflects a 100% deviation from the original planning of eight months. As regards COPD, the responsible nurse was steadily reporting a small number of eligible patients to the researcher during the first 10

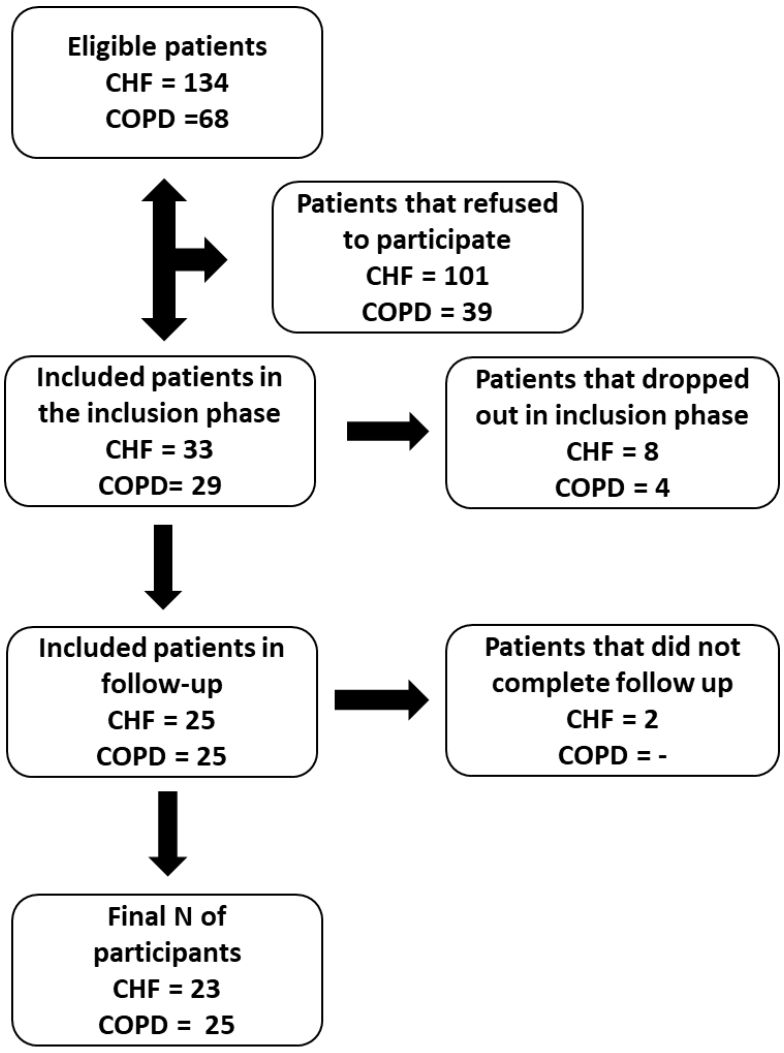
months; conversations with the COPD personnel revealed that, often, even though the nurse could identify a potential patient, she could not cross-check this with physicians prior to the release of the patient. A disruption was observed after the 10 months that led to a readjustment of the strategy. Following a two-month period of nearly no flow of patients, it was agreed that the researcher would also search for eligible patients by accessing the electronic flies and then directly consulting the assistants. In retrospect, it is certain that the overall number of eligible patients during the 18 months of the study is larger than the one reported although the exact number is quite difficult to compute.

As regards CHF, in the first two months, the researcher received alarmingly few reports of eligible patients by the responsible head-nurse. As a result, the recruitment strategy for CHF was also modified. Based on the revised recruitment strategy, the researcher was responsible for the identification of the eligible patients. In order to do this, she participated in weekly ward meetings in cardiology where the multidisciplinary team consisting of nurses, specialist physicians, social worker and spiritual counselor discussed every patient, and she also examined the electronic hospital files of each patient. Five months later and in order increase extra the flow of eligible patients the participation of an additional cardiology ward was to the study and the researcher followed there the same process for identification and inclusion of eligible patients.

Figure 1 shows the recruitment process for both CHF and COPD. Table 1 reports the characteristics of all the participants. From the 134 eligible CHF patients, 23 patients (17% inclusion rate) completed the two rounds of the questionnaires. Initially, 33 patients gave their informed consent, however, eight patients dropped out before completing the first round of the questionnaires (24% first dropout rate). From the remaining 25 patients one died before completing the follow up, whereas another one was lost to follow up (6% second dropout rate). Total dropout rate for CHF is 30%. The population of CHF had a mean age of 76.3 (SD=12.7).

In COPD, from 67 eligible patients, 25 patients completed the inclusion and the follow up questionnaires (37% inclusion rate). Initially 29 patients gave their informed consent, however, four of them dropped out before completing the first round of the questionnaires (14% first dropout rate). We did not have any dropouts during the second round of questionnaires (0% second dropout rate). Total dropout rate for COPD is 14%. The population of COPD had a mean age of 70.5 (SD=10.6).

Figure 1. Flow chart: Inclusion process of eligible patients in the study.



Following the recommendations of Steinhauser et al. we have examined whether replacing the non-native researcher with a native speaker one, would influence our recruitment rates. The native speaker approached 15 randomly selected eligible patients, but 13 of them declined to participate in the study. No appreciable difference was observed between the corresponding inclusion rates [20].

For both CHF and COPD we examined whether the age of patients and the gender were a factor that played a role for recruitment. As regards age, we performed t-tests for equality of means between the ages of those who participated against those who declined. In both cases, the t-tests revealed a significant statistical difference (CHF: t-stat=6.668>t-crit=1.980, df=118, p=8.77e-10| COPD: t-stat=2.653>t-crit=2.0, df=60, p=0.01). On average, those who participated tended to be younger than those who did not. The CHF participants had a mean age of 64,8 years (SD= 14,33) and the COPD participants had a mean age of 67,1 years (SD=8,54).

Gender was not found to play a role as the results of a Chi-square independence test were showed not appreciable correlation (CHF: Chi-stat=0.183 < Chi-crit=3.841, p=0.668 | COPD: Chi-stat=0.058 < Chi-crit=3.841, p=0.808).

For the 101 CHF patients and the 39 COPD patients that declined to participate in the study, the four reported reasons were:

i) they were emotionally or physically exhausted (41% in CHF and 49% in COPD)
ii) the study and filling in 3 questionnaires was too demanding (22% in CHF and 18% in COPD)
iii) reasons were not specifies (22% in CHF and 23% in COPD)
iv) The relatives refused to participate in the study (15% in CHF and 10% in COPD)

Table 1. Characteristics of eligible patients of the study.

	Total N of eligible patients	**Patients that refused to participate**	**Patients that dropped out during the inclusion phase (first dropout)**	**Included patients**	**Patients that did not complete the follow-up Phase (second dropout)**
CHF* patients	134	101	8	23	2
<u>Gender</u>					
Male	81	61	4	15	1
Female	53	40	4	8	1
<u>Age</u>	(M=76.3, SD=12.7)				
<45	4	1	1	2	-
46-59	9	3	0	5	1
60-79	55	39	4	13	-
>80	57	53	1	2	-
Died	9	5	2	1	1
Patient did not wish to participate in the study <u>Reasons</u> • Physically/emotionally exhausted • Study is demanding/ many questionnaires • Did not specify	n/a*	86 42 22 22	n/a	n/a	n/a
Relative did not want to participate – reasons not	n/a	15	n/a	n/a	n/a

specified (patient wanted to participate)					
COPD* patients	68	39	4	25	-
<u>Gender</u> Male Female	 46 23	 26 13	 2 2	 17 8	 - -
<u>Age</u> <45 46-59 60-79 >80 Died	(M=70.5, SD=10.6) - 9 42 11 5	 - 6 21 9 3	 - - 2 1 1	 - 3 19 1 2	 - - - - -
Patient did not wish to participate in the study <u>Reasons</u> • Physically/emotionally exhausted • Study is demanding/ many questionnaires • Did not specify	n/a	39 19 7 9	n/a	n/a	n/a
Relative did not want to participate (patient wanted to participate)	n/a	4	n/a	n/a	n/a
This table describes the characteristics of the total number (N) of eligible patients, the patients that dropped out before completing the first round of questionnaires, the included patients and the patients that did not complete the follow-up round. CHF=Chronic Heart Disease, COPD= Chronic Obstructive Pulmonary Disease, n/a=not appropriate					

The interaction between the researcher and the cardiology/pulmonology personnel allowed for an informal identification of their mentality towards PC. In both CHF and COPD the leading specialists were favoring and supporting the accommodation of PC in chronic disease in their wards. The researcher did not observe any adverse reactions from the nurses in the COPD ward, however, the CHF nurses expressed concerns on the compatibility of such a study with the objectives of an acute ward. More specifically, they communicated that in their opinion an acute ward aims for the treatment of the patients and as such is not aligned with the objectives of a PC ward.

For the feasibility assessment of our study we have employed the analytical framework of Bugge et al., adapted directly from Kane et al [21-22]. As this study is not a prelude to an RCT, some components are labeled as " Not Appropriate". The assessment is reported in Table 2.

Table 2. Summary of the findings against the 14 categories of methodological issues for feasibility research.

Methodological issues	Findings	Evidence
1. Did the feasibility study allow a sample size calculation for the main trial?	Not appropriate for this study. Sample size was calculated based on previous studies employing the POS questionnaire.	23 CHF and 25 COPD patients were recruited (the required sample size was achieved).
2. What factors influenced eligibility and what proportion of those approached were eligible?	The only subjective factor was the cognitive level of the eligible patients.	We approached only eligible patients.
3. Was recruitment successful?	Recruitment was successful but required readjustment of the employed strategies.	Assigning the identification of eligible patients to the involved healthcare personnel was problematic. Direct involvement of the main researcher alleviated the problems.
4. Did eligible participants consent?	Only a fraction with well-defined characteristics consented to participate in the study.	We eventually collected a convenience-based sample. Many of the eligible patients that decline participation in the study

		reported physical and emotional exhaustion or that the study/ completion of the questionnaires was very demanding.
5. Were participants successfully randomized and did randomization yield equality in groups?	Not Appropriate	Not Appropriate
6. Were blinding procedures adequate?	Not Appropriate	Not Appropriate
7. Did participants adhere to the intervention?	Good adherence to completion of the study questionnaires.	23 CHF and 25 COPD patients completed POS, CanHelp Lite and the ad-hoc in both inclusion and follow-up phase.
8. Was the intervention acceptable to the participants?	Not explored but we did not have any missing data.	Participants did not report any acceptability issues. Some eligible patients that declined participation commented that the topic is heavy.
9. Was it possible to calculate intervention costs and duration?	No focus on cost, but the initial calculation of the duration was underestimated.	Instead of the estimated time of 8 months, the study lasted for 16 months.
10. Were outcome assessments completed?	Yes.	Outcome assessments were completed in both inclusion and follow-up phase.
11. Were outcomes measured those that were the most appropriate outcomes?	Not Appropriate	Not Appropriate
12. Was retention to the study good?	Attrition rates were lower than estimated.	For CHF attrition was 30% and for COPD 14%.
13. Were the logistics of running a multicenter trial assessed?	This is not a multicenter study, but a multi-ward one (see also data collection	Two head nurses from cardiology wards and one dedicated COPD nurse from pulmonology ward.
14. Did all components of the protocol work together?	Components of the protocol worked together.	Despite difficulties duet o workload of the involved ward personnel, the process of patient identification and communication did not raise any concerns.
The methodological issues were based on Kane et al. and Bugge et al. [21-22].		

Discussion

The feasibility assessment of this study presented in table 2 is in general positive. However, the initial design has proven to be non-optimal. The lessons that we learned while conducting this study stemming from the challenges that we encountered can provide useful guidance for future studies.

Our experience with recruitment of eligible patients showed that patients <80 years are much more likely to accept to participate in the study. Looking at the profiles of those who declined to participate, we find older patients reporting heavier physical/psychological symptomatology or complaining that completing questionnaires is burdensome and demanding [23-24]. Therefore, our convenience sample exhibits a selection bias in favor of a group of younger patients with relatively milder symptomatology. Our analysis juxtaposed to existing empirical evidence hints that quantitative studies might not be well adapted to older and frailer populations and that this patients are more amenable to a qualitative approach [25-26].

The difference in the inclusion rates between younger and older patients also explains why our study had a much longer duration than the calculated one. Indeed, for our estimated duration of 8 months we considered hospital admission records of all the eligible CHF/COPD patients without differentiating between the ages. However, as our results corroborate, patients <80 constitute a considerable amount of the population, but are nevertheless very difficult to include. If we have opted for a representative sample and not a convenience sample this study would probably be still on-going.

Dropout rates in our study vary between CHF and COPD. CHF had a total dropout rate of 30% which is comparable to dropout rates reported in cancer studies [27] whereas COPD had less than half of that. In any case, a 30% attrition rate seems to provide a sufficient bound for the estimation of the sample.

More information may be recovered by looking at the distribution of dropouts. As mentioned in the results section, dropouts in our study are the sum of first dropouts (dropouts after giving informed consent but before completing the first round of questionnaires) and second dropouts (dropouts after completing the first round of questionnaires). Moreover, first dropouts are substantially higher than second ones; in fact both CHF and COPD patients who completed the first round of the questionnaires almost surely completed the second round as well. The negligible second dropout rates suggest a certain commitment from the patients; whether this is due to understanding of the merits of the study or due to a sense of duty stemming from their informed consent is unclear. The high first dropout rates might reflect that these patients were not convinced on the merits of the study or underestimated the effort required to complete the study and thus changed their mind.

The informal caregivers that refused to participate, even though the patients agreed, mentioned that their emotional state was not allowing them to focus their attention on the completion of the questionnaires. Further, some relatives chose to decline after having a screening of the questionnaires, mentioning that this is emotionally too heavy to handle. Opting for an informal caregiver's participation, alongside a patient makes the study ever more challenging, because it automatically requires the informed consent of two people. However, family caregivers, being third parties, can provide another perspective on the provision of care on this sensitive population.

Despite the well designed eligibility criteria, assigning the identification of eligible patients to the ward personnel involved in the study proved to be dysfunctional. The direct involvement of the researcher in the identification process resulted in substantial improvements. The necessity of the readjustment in the recruitment strategy can be attributed two possible factors: i) workload of the personnel and ii) external character of the study.

As regards the workload of the personnel, throughout the duration of this study, both nurses and physicians stated that they were overloaded with other duties that practically limited their participation in the recruitment phase because it naturally leads in prioritization of duties. Previous experience with similar cancer studies has shown that the full schedule of the practitioners can affect the access to eligible patients thus resulting not only in less participation but also in an ambiguity concerning the real number of eligible patients [28-30]. A heavy workload has additional implications. It prohibits healthcare providers from having extended conversations. Moreover, their function and education are oriented towards offering clinical information about the planned treatment and not towards listening to patients concerns. Studies similar to ours require professional caregivers to go out of their comfort zone, a difficult task on its own, which is even more challenging if the workload is high.

As regards, the external character of study, we note that our study was neither a pulmonology nor a cardiology study and focused on patients outside the PC ward. Furthermore, the main researcher as well as the rest of the PC team are not members of the cardiology and pulmonology wards of this study, nor are they part of their multidisciplinary teams. The study was viewed as an external research effort that added up to their regular workload. Further, due to the adopted methodology, uncontrollable internal ward complications e.g. shortage of specialist assistants, emergence of critical patient cases, were affecting the continuity of the study.

Given the nature of this feasibility study, the mentality of the personnel did not affect the flow of the study. However, subsequent studies will include PC interventions and, in the long run, the integration of PC alongside standard treatment. Although the picture is likely more complex, the partition of duties into treatment and PC indicates that the corresponding personnel understands PC to be an end-of-life concept. Consequently, sensitive topics like a poor prognosis, advance care planning, etc. are not likely to appear

early in the disease trajectory; this is a recurring finding in the literature and is usually associated with i) inadequate education and/or insufficient experience of the professional caregivers to start a dialogue about such topics [31] and ii) worries regarding the physical/emotional frailty of the patients [32].

The challenges and the lessons learned from this feasibility study can be summarized in the following recommendations:

i) Quantitatively oriented studies have a higher chance of success if they focus on relatively younger CHF/COPD patients (<80 years) with milder symptomatology. Inclusion of older patients can probably be improved with qualitative interviews.

ii) Attrition rates of 30% appear to be adequate for a priori sample calculations. When estimating the duration of a study, one should take into account previous admission records, but also consider that age groups have different inclusion rates.

iii) The active and direct involvement of the researcher in the identification of eligible patients is strongly recommended. The participation of the PC researcher in the multi-disciplinary team meetings of the wards increases awareness of PC and builds trust with the health care specialists as well.

iv) CHF/COPD patients in acute wards are quite likely unaware of their prognostication. Focusing on QoL and Quality of care, instead of explicitly referring to PC, provides a minimally invasive way for understanding the needs of this population; a prerequisite for successful PC implementation.

v) Successful integration of PC in CHF/COPD requires the training and education of the healthcare personnel on the basics of PC so misconceptions for PC are corrected and their mentality is gradually shifted.

Limitations

The first limitation of this study concerns the actual number of eligible patients. The only way to know the exact number of eligible patients is to retrospectively examine the patient online records for the exact duration of the study. Given that i) our initial recruitment methodology needed readjustment and ii) the flow of COPD eligible patients was much slower than initially expected (based on previous archives), it is certain that the actual number of eligible patients was higher.

A second limitation is the selection bias due to convenience sampling. Given the characteristics of the participants and those who declined to participate it is unclear how representative this sample is of the entire advanced CHF/COPD population.

The last limitation stems from the fact that the main researcher of this study is a non-native Dutch speaker. As mentioned above, we have assessed the effect of administering the study via a native Dutch speaker, which showed no appreciable difference. However, one might not exclude that some patients would feel more comfortable in the presence of native speaker.

Conclusions

The implementation of PC intervention and the overall integration of PC practices for CHF and COPD patients remains challenging. The present study has demonstrated the feasibility of a prospective observational PC study focusing on the QoL and quality of care of CHF and COPD patients in cardiology and pulmonology wards. The lessons learned from this study can assist similar future efforts in this area. However, the implementation of integrated PC interventions is expected to raise further challenges that will need to be investigated in future studies.

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CHAPTER 10

General Discussion

General Discussion

CHF and COPD are projected to become respectively the first and the third leading causes of death worldwide by 2030 [1-2]. Owing to their chronic character, diagnosis of CHF and COPD is followed by a prolonged period of gradual health declining and occasional exacerbations [3]. During this long-term process, patients and their families develop a variety of coping mechanisms and readjust their lifestyle so as to accommodate frequent hospital admissions due to relapses [4]. Living with CHF/COPD implies dealing with heavy symptomatology (physical, psychological, social and existential), comparable to the one of cancer patients, and often facing additional complications due to comorbidities [5-6].

Health care organizations have recognized that CHF/COPD patients are amenable to PC services and specifically recommend an early integrated approach for the provision of PC [7-8]. Despite these recommendations, access to PC for these patients remains limited and confined only in the end-of-life stage [9]. Improving patients' accessibility to PC services requires the systematic investigation of all the factors impeding the integration of PC in CHF/COPD. Therefore, the focus of this thesis has been the theoretical and empirical investigation of early integrated PC in CHF/COPD in Europe and in Belgium.

Part I. Theoretical part

Chapters 1, 2 and 3 were developed in the framework of the European InSup-C project (http://www.insup-c.eu/) that had as an aim the investigation and promotion of early integrated PC in both malignant and non-malignant disease in Europe.

Only few models of integrated PC exist in Europe and even fewer are RCTs, with the majority being observational and cohort studies. This also underlines the difficulty in carrying out RCTs with PC patients. In fact, for CHF and COPD the situation is worse than

in cancer since our systematic search returned only one CHF focus model (not RCT) and no COPD. More recently, RCTs focusing on CHF and COPD in Europe have appeared in the literature, but the overall number remains very small [10-11].

Despite the differences in their design, all the studies but one reported the positive effectiveness of the integrated PC models[6]. In practice, the effectiveness is realized through one or more of the following aspects: better symptom control, higher quality of life, less caregiver burden, improvement in continuity and coordination of care, fewer hospital admissions, patients dying more frequently at home, and improved cost-effectiveness. More recent models continue to report on the effectiveness of integrated PC in both cancer and chronic disease [12-13].

Besides systematically reviewing the literature, we went a step further and synthesized our results to develop a generic and disease independent framework that can serve as a basis for future integrated PC models. This framework specifies the focus, the setting, the timing, the composition of the involved team and the collaboration strategy of future integrated PC interventions. It has a threefold focus: treatment (referring to the alleviation of physical and psychological symptoms), consulting (referring to ACP discussions and physician-patient communication) and training (referring to the PC education of all the involved health care providers).

Having assessed the effectiveness of integrated PC interventions in both malignant and non-malignant disease, we then turned our focus specifically on integrated PC of CHF/COPD patients, which constitute the core focus of this thesis. In practice, the provision of PC services is based on guidelines and pathways. Understanding the current level of PC integration requires the documentation of existing guidelines/pathways and the evaluation of their content on integrated PC.

[6] The study that constitutes an exception (chapter 1 [20]) did not report any adverse effects of integrated PC, but rather found no appreciable impact on the QoL.

The way that guidelines/pathways deal with the PC referral criteria is alarming. With half of them ignoring the referral criteria completely and the other half offering a multitude of opinions of questionable applicability, it becomes clear that PC referral criteria in CHF and COPD remain a contentious and unresolved issue with severe consequences [14-18]. In fact, it inhibits the practical implementation of PC practices because it enforces local services to take initiatives at will. What complicates matters further, is the fact that early integration of PC, which renders the timing of the initiation of PC more tractable, is almost completely out of the picture. This reflects the still everywhere present perpetuation of the misconception that PC is synonymous to "end-of-life" care [19]. Paradoxically, even though the mentality behind these guidelines/pathways is that PC is an "end-of-life" concept, there is a systematic absence of recommendations on end-of-life communication.

Future guidelines/pathways have to be free from conceptual ambiguities and provide standardized and practically implementable strategies that facilitate the integration of PC for all palliative patients early in the disease trajectory. The resolution of the referral criteria debate is paramount for any further improvements.

As we mentioned already above, there is substantial inequity in the access to PC services between CHF/COPD and cancer patients, in favor of the latter. This inequity implies that the levels of early PC integration for patients with cancer and CHF/COPD also differ. Additionally, it suggests that the empirically observed discrepancies with respect to the levels of PC integration might be traced, among others, in the content of the corresponding guidelines/pathways.

Surprisingly, the content of the levels of PC integration in both cancer and CHF/COPD has been found to be statistically the same and moderate [20]. In turn, this suggests that the content of the guidelines/pathways is inasmuch a barrier for the integration of PC in

CHF/COPD as it is for cancer. The analysis of the results additionally reveals that both CHF/COPD and cancer guidelines/pathways suffer from the same weaknesses: lack of bereavement care recommendations, unclear specification of timing of holistic assessment and more importantly infrequent specification and no appreciable consensus on referral criteria.

Despite the appearance of referral criteria as a weakness in both CHF/COPD and cancer, in practice, for cancer this appears to be better handled, even though PC is still considered an EoL concept [21-22] This probably is attributed to the fact that the disease trajectory of cancer is more predictable than the one of CHF and COPD [23]. By contrast, in CHF/COPD this issue remains a fundamental obstacle [24].

An interesting question raised during this study is whether the level of PC integration was correlated to the year of the guideline/pathway publication and/or the quality of evidence that was employed for its development. Intuitively, we expected that newer guidelines/pathways utilizing higher quality evidence would correspond to higher levels of PC integration. Nonetheless, our analysis showed that these correlations do not exist. This finding could be attributed to two reasons: i) the existence of ongoing barriers like the lack of determination of referral criteria mentioned [25-26] above and ii) the lack of international consensus on the terminology “integrated PC” [24-28]. With respect to the latter, it is worth noting that the first consensus-based definition of integrated PC was only developed in 2016 in the framework of the InSup-C FP-7 Health-2012 European project [29].

PART II. Empirical part.

The theoretical part of this thesis has identified that even though integrated PC interventions can be effective, the guidelines/pathways suffer from weaknesses and conceptual ambiguities that act as barriers for advancing the integration of PC. For

CHF/COPD these theoretical barriers are not enough to explain the substantially limited access to PC services that such patients have. Understanding the roots of this limited access requires an examination of perceptions of CHF/COPD specialists and current practices on integrated PC. As perceptions of specialists can be affected by a country's culture, and given that even within the European Union there is no uniformity on integrated PC current practices, it pertains to investigate these topics locally in the level of countries. Therefore, for the empirical part of the thesis, we turn our focus to Belgium.

In Belgium, cardiologists and pulmonologists share in general a positive view for integrated PC and its potential benefits. An interesting finding is that some components of integrated PC, namely the holistic approach via multidisciplinary meetings, discussion of prognosis and therapeutic limitations, assessment of patient's goals, continuous goal adjustment, reduction of suffering and ACP, have been fully or partially implemented in Belgian hospitals. Strikingly, prognosis discussions have been found to be part of the treatment strategy for cancer patients; such discussions are quite unlikely to occur for CHF/COPD patients in general [30-31]. The determination of referral criteria seems to be a difficult issue and the participants voiced a variety of opinions. The analysis of the interviews revealed two conundrums. First, while some aspects of integrated PC are being utilized, PC specialists are not at all involved in this process for non-malignant diseases. Second, despite favoring an earlier integration PC, CHF/COPD specialists reported that in practice, PC is only initiated at the very EoL stage. The collective perceptions of specialists offer two explanations for these conundrums: i) misconceptions about PC and its role and ii) "bad name reputation" of PC.

As regards (i), the historical association of PC with cancer continues to influence the PC perceptions of cardiologists and pulmonologists [32]. At the same time, they still interpret PC as a "grim-reaper service" focusing exclusively on alleviation of pain and physical symptoms during the last days of life and not on all the other aspects (psychological, social and existential) of QoI and quality of care. These findings are in line

with previously published studies from different countries that suggest that there is i) a lack of communication between patients and caregivers concerning the overall role and benefits of PC in the quality of life of patients and family and ii) insufficient training and education of physicians in the fundamentals of PC [33-34]. As regards (ii), correctly or not, PC has become synonymous to death and dying [34]. Given that the public image of CHF and COPD is that of a chronic but "manageable" disease not ending to death, reference to PC leads to confrontation of patients and their family and renders prognosis discussions [30-31] more challenging for the specialists. It is therefore, not surprising that specialists are more reluctant to open such discussion early in the disease trajectory [33, 35].

Evaluating the integration of PC in guidelines/pathways of CHF/COPD, it is striking that bereavement care and recommendations were totally absent. This theoretical limitation was also empirically observed in both the perceptions and current practices of the specialists in CHF/COPD. Indeed, in Belgium, post-mortem conversations with family members are not available and psychological and spiritual support is seldom present. The availability of bereavement support has been investigated in other countries as well. Relevant studies from the UK and Australia demonstrate that it is indeed possible to provide bereavement support for the families, however, the efficacy of these services has yet to be evaluated [36-38].

With these perceptions of specialists and current practices of integrated PC in CHF/COPD, the next step is to practice the application of an early integrated PC intervention in the acute setting for CHF/COPD patients. For this reason, a feasibility prospective study with a threefold focus was designed: i) evaluate the QoL and quality of care of the existing standard treatment, ii) assess the effectiveness of an early PC intervention and iii) identify the practical barriers for the implementation of a PC intervention outside a PC ward and derive recommendations for their resolution.

Following the completion of the baseline phase, the QoL and quality of care was empirically examined based on the patients' and their informal caregivers' feedback. Two findings stand out from the analysis: i) both CHF/COPD patients and their informal caregivers share common beliefs concerning QoL and quality of care, as assessed by the CanHelp Lite [39] and the POS questionnaires [40] and ii) both CHF and COPD patients and their caregivers evaluate positively both the patient's QoL and quality of care.

The agreement between the perceptions of patients and their informal caregivers has been previously observed in both cancer and chronic disease [41-43]. As the patient's health deteriorates further, it is the informal caregiver that is often responsible for decision making [28]. In fact, this issue highlights the need for more transparent communication between healthcare providers and patients/informal caregivers; indeed a consensus of opinions between patients and informal caregivers is of little relevance if they are not well informed on the real stage of the patient's disease.

Given the severity of the included patients' disease, and since some of them died already during or shortly after the completion of the study, the positive evaluation of QoL and quality of care seems puzzling. This is not a new finding but rather a recurrent one [45-46]. A multitude of factors appears to contribute to these findings, but two more important ones can be distinguished.

The first factor concerns the public perception of CHF/COPD, which, as mentioned above, is that of a chronic disease that occasionally leads to exacerbations with subsequent hospitalizations but with no obvious link to death [47]. The patients develop various coping mechanisms and readjust them following subsequent exacerbations [42, 48]. With this mentality, the positive evaluation of QoL and quality of care by the patients can be a reflection of an acceptance of their condition and their hope to go home after being "cured" [47, 49]. However, despite the often prolonged periods of stability, the trajectories of CHF/COPD comprise a gradual deterioration of health accompanied by

more frequent and more life-threatening exacerbations. As the number of hospitalizations increases progressively, coping mechanisms start operating more as defense mechanisms against exposure to negative news, which signifies the denial or he difficulty of patients and their informal caregivers to accept the severity of the disease progression. In the meantime, and partially due to the limited PC education, health care providers are reluctant to engage to conversations on prognosis during the disease progression which further explains the insufficient knowledge that patients and informal caregivers have for the chronic disease [48]. Finally, one should not overlook the fact that for CHF/COPD death is still a taboo topic [50]. For the entire CHF/COPD population there is conflicting evidence on whether these patients want to know more about their disease [42, 51-52]. In response to this, healthcare providers are inclined towards non-disclosure of death-related info and postpone the initiation of PC until the last hours of life for these patients [50].

The second factor stems directly from our sample. A convenience sampling was used which resulted in the inclusion of a fraction of the overall eligible population that has specific characteristics. The included patients were below 80 years and, as is typically the case with studies similar to ours, they had a mild to moderate symptomatology. Older patients with presumably heavier symptomatology and more comorbidities were underrepresented, which limits the generalizability and implications of our results [51].

It becomes clear that a “one-size-fits-all” mentality is unlikely to succeed. The heterogeneity of this population and the diversity of their views on receiving clear medical information on the deteriorating condition, suggests that a more patient-oriented approach should be employed, where the patient is given the choice to decide whether (s)he want to know more about the disease.

The baseline phase was completed only after doubling of the planned overall duration (of the expected of 8 months to 16 months). Overcoming this challenge required a

sequence of readjustments in the study strategy. The retrospective feasibility assessment of the evolution of the baseline phase yielded a number of relevant lessons that can guide similar future studies

The first challenge of this study was the difficulty to recruit patients >80 years, although they clearly constitute a substantial proportion of the overall eligible population. The time estimation was developed based only on historical hospital admission rates, without differentiating between different age groups and accounting for recruitment difficulties due to the presence of the informal caregivers. The fact that older patients almost univocally declined to participate for practical reasons (physical emotional symptoms, impaired cognition and burdensome questionnaires) rendered those estimates inaccurate and created a selection bias in favour of younger patients physically more active and cognitively more intact. Our experience combined with existing literature suggests that this elderly population, which is usually frail and suffers from more severe symptoms, might be more amenable to qualitative research instead of quantitative measures [53-54].

The eligibility criteria employed in this study were clearly defined and easily detectable. According to the initial patient recruitment strategy, the identification of eligible patients was (after consensus) assigned to the personnel of the wards. This working model did not operate smoothly as the reported number of eligible patients was unrealistically low for an extended period. In response to these challenges, the main researcher assumed a more active participation in the identification of eligible patients by proactively checking electronic files and by participating in multidisciplinary ward meetings. The revised plan resulted in identification of more eligible patients, thereby confirming the sub-optimality of the initial one. Two factors contributed to the need of readjustment: i) the workload of the personnel and ii) the fact that the study was not performed in a PC ward, but in an acute ward, where PC specialists are not part of the multidisciplinary team. The heavy workload of the personnel inevitably leads to a prioritization of duties [55-57]. Our study

was an external one, thus adding to already heavy schedule of the personnel and additionally required dealing with a topic that is out of their comfort zone. One might argue that choosing for an autonomous strategy (without the involvement of the personnel of the wards) could have improved the efficiency of implementation. However, this was not planned to be an isolated study, but rather to be the first step in the gradual integration of PC in cardiology and pulmonology. With this in mind, it is important that all actors become involved so that knowledge, communication skills and trust can be built.

A last point of discussion for this chapter concerns the mentality of the involved personnel towards PC. Even though the baseline phase has been "minimally invasive", and not even the term "palliative care" was mentioned to participants, informal and qualitative discussions with the involved healthcare providers revealed some concerns on the compatibility of the study with the "curative" attitude of their wards. PC was understood as an end-of-life care as PC services were consulted mainly in the last days or last hours of patient's life. Although a direct extrapolation from findings of chapter 5 concerning specialists' misconceptions about PC and its role cannot be drawn, the emergence of the same mentality pattern hints that these misconceptions are shared by a larger number of healthcare providers. Literature points towards two directions: i) inadequate education and limited experience of the professional caregivers to start a dialogue on PC topics and ii) worries concerning the physical and mental frailty of these patients [58-59].

The methodological assessment of this study revealed both strengths and weaknesses. It has been proven impossible to use a representative sample for all the age spectrum of the eligible patients and we were only able to collect the desired number of participants by using a convenience sample. In turn, this lead to the prolongation of the inclusion phase since our initial estimates were based on historical data of eligible patients, independently of their age. Despite this core weakness, this study fulfilled almost all of

the methodological issues addressed in table 2 of chapter 9. Consequently, even if the initial design of the study has proven to be non-optimal, the methodological design of future studies could benefit from our recommendations.

The intervention phase

The intervention phase was based on the application of the MIJN WENSEN early integrated PC tool, which as mentioned in chapter 7, has been developed by the Palliative Support Team of the University Hospital Leuven and has already been applied in patients with malignant disease. Evaluating the completeness of the content of MIJN WENSEN with respect to the eleven IPC criteria presented in chapter 4, reveals that this intervention fullfils eight out of the eleven IPC criteria. More specifically, it leaves the timing of PC initiation and timing of the holistic assessment up to the physician in charge and does not provide particular focus on grief and bereavement care of the proxies of the patient.

Due to the prolongation of the baseline phase (from 8 to 16 months), the available time in the timeframe of this PhD thesis, for training of the personnel and the subsequent intervention phase decreased. In order to maximize the utilization of the available left/rest time, the training occurred concurrently with the intervention. For cardiology the overall duration of the intervention phase was 10 months (Oct 2017-July 2018). For pulmonology the overall duration of the intervention was shorter and lasted only 6 months (February 2017-July 2018) due to ward related organization issues (lack of personnel due to pregnancy and sickness leave). For cardiology the intervention was administered by one psychologist and one trainee, because the second psychologist had to take (an annual) a leave for health reasons. For pulmonology the intervention was eventually administered only by a ward nurse and the pastoral counsellor. In view of the outcome of the baseline phase, the identification of eligible patients and informal

caregivers was in this phase done mainly by the main researcher following the recommendations of chapter 7. Consequently, losses of eligible patients were minimized.

From the early stages of the intervention phase, we observed a dramatic decrease of inclusion rates for both CHF and COPD patients. For CHF, from a total of 107 eligible patients we included only four and for COPD from a total of 48, we included only two. The findings of the baseline phase were reconfirmed here. It proved impossible to recruit patients >80 years, but additionally, in this phase, we observed very high declining rates from younger patients as well. There were three categories of patients; those who immediately declined to participate, those who immediately agreed to participate and those who provided a positive answer but following consideration and discussion with their informal caregiver it became negative. In order to encourage the last category, we enhanced our strategy and agreed that the assistant physicians would visit these patients and encourage them to take part in the study. Retrospectively, we observed that this extra involvement did not yield noticeable improvements in the inclusion rates. Moreover, although attrition rates following signing the informed consent were very low, in order to promote patient-intervention team trust we also asked the assistants to participate more by providing the introductory flyer of the intervention. According to the responses of the eligible patients, the predominant reasons for declining to participate were the heavy symptomatology with percentages similar to the ones observed in the baseline phase. What differentiates the two phases is the fact that i) some eligible patients were discharged before having the time to decide for their participation and ii) some of them signed the informed consent, but were discharged before receiving the intervention. Indeed, the short hospitalization time (on average 2-4 days) proved to be a determining factor, because 9 CHF and 11 COPD patients signed the informed consent, but they were discharged before receiving the intervention. Dealing with short hospitalizations (which is an exogenous factor) requires agility and flexibility of the intervention team. Due to the eventual shortage of the involved personnel and their heavy workload, it was not always possible to act quickly. It is important to note that such

problems were absent in the baseline phase, because the intervention phase required more visits and more time investment from the people involved. These practical problems do not suggest a lack of cooperation between PC and non-PC involved actors, but rather one of the inherent difficulties implementing integrated PC within a short-time period.

Although it is difficult to quantify, our experience with eligible patients showed a dichotomy. CHF patients appeared to be not often fully aware of the severity of the illness. Some of the participant were genuinely surprised when approached and rebutted by claiming that they were not eligible. Most of the COPD patients did not question their eligibility, considering themselves as partially responsible for their condition due to chronic smoking. Even so, they declined to participate. Apparently, for both CHF and COPD patients advance care planning conversations over their wishes, needs and preferences for current and future care were inherently confronting and alluding to PC, whereas in the baseline phase such topics were absent. An interesting question is whether feeling confronted by such discussions stems from lack of “current condition awareness” or from denial or from avoidance due to the nature of this intervention.

In its essence, the intervention is an invitation to eligible patients to talk and learn more about their disease. In the end of chapter 6 we highlighted that in the short run, a viable solution for the implementation and integration of PC in CHF/COPD is to offer eligible patients the choice to engage in such discussions and services. The outcome of the intervention phase confirms this recommendation. It actually shows that patients might chose not to participate even if they are aware of the severity of their condition.

Despite the very limited number of participants, interactions with the healthcare providers that applied the intervention provided valuable feedback. Even though the intervention involved uncomfortable discussions for them as well, they did realize the merit of such a study and emphasized the need of specialized training and iterative

learning for future interventions. It appeared that a psychologist or a pastoral assistant were better trained/experienced to get involved in such discussions than nurses and physicians.

Last, we have to assess the feasibility of the intervention phase. Clearly conducting a prospective, before and after intervention study in acute wards for CHF and COPD proved to be non-feasible for the available time-period. However, the intervention phase constitutes a small laboratory where aspects of integrated PC were implemented in practice to patients that were given the choice to participate or not. Measuring the effectiveness of this intervention with all its constraints is probably feasible if the duration of the study is not a limitation and the involved team is agile enough to administer the intervention on time.

Lessons learned from the prospective before-after intervention study

Although the overall feasibility of the study (baseline and intervention phase) has been negative, a retrospective evaluation of the outcomes and the aggregate experience throughout the two phases provides fruitful conclusions for the road ahead. The lessons that we learned in the course of our study can be summarized as follows:

i) We have shown that operationally friendly referral criteria for CHF/COPD patients exist, however, the main obstacle has been to convince these patients on their eligibility. This shows that the debate for the referral criteria is actually a debate on when to communicate the true state of the patient.

ii) Patient related outcomes are clearly useful and provide a lot of insight for the QoL and quality of care, however, they are not well adapted to the most fragile part of the CHF/COPD population i.e. older patients with heavier symptomatology. A two-fold methodology comprising

both quantitative and qualitative instruments can help recruiting a more representative sample of the population

iii) Integrated PC requires both resources and their efficient coordination to be smoothly implemented. With PC specialists being identified as third parties PC implementation becomes more challenging.

iv) Hospitatlisation time of both CHF and COPD patients proved to be a decisive factorin the course of the intervention phase. Circumventing such strict timelines requires an extra agility from the involved team, which adds further to their workload.

v) The mentality of both patients and medical personnel is that acute wards in CHF and COPD are of curative nature, leaving little space for integrated PC. Nevertheless, the feedback of the medical personnel was encouraging and showed an acknowledgement of the potential benefits despite the existing fear concern of confronting the patients.

An alternative to implementing integrated PC in an acute setting would be to employ early PC in a homecare setting. As mentioned above, the short hospitalization of CHF/COPD patients renders the implementation of integrated PC intervention challenging and subject to very demanding organization between all the involved actors. Tranfering the intervention to the home setting, in theory, alleviates the time constraints and allows a qualitative approach to take place in an environment where patients would feel more confortable. This approach is advocated in a recently developed model for COPD patients that has to be yet empirically evaluated. It is interesting to observe that the developed protocol builds upon 5 pillars: (1) Training of the PHC team in care for end-stage COPD patients, (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 professional caregivers [60]. The theoretical requirements for the implementation of that protocol substantially overlap with our intervention. This is to be expected, because integrated PC cannot be applied in an isolated setting. By definition, integrated PC

requires the coordination of all involved actors for a prolonged period of time independently of the setting. Consequently, frequently mentioned barriers such as training of the involved personnel and misconceptions about PC will have to be faced. Moreover, even though the home setting constitutes a more comfortable environment for the patients and favors a more qualitative approach, it is not a priori clear that participation of patients will be higher that the one at an acute setting [51-52]. The attitude of these patients and their perceptions on death and dying have been shown to be rigid and not depending on the care setting.

Concluding remarks

Going back to the title of this PhD thesis, "Early integrated PC in CHF/COPD: a myth or a real benefit for patients and family?", our theoretical and empirical investigation allows us to conclude the following:

i) Existing models on integrated PC provide evidence of the benefits of PC integration in chronic disease. Less is known for CHF/COPD, but newer studies in the field show encouraging results.

ii) Existing guidelines/pathways on integrated PC in CHF/COPD show a growing awareness on the topic, however, their content is not optimal and acts as a barrier for the further integration of PC.

iii) Aspects of integrated PC are already part of standard treatment in CHF and COPD in Belgium. However, they are not considered to be related to PC. PC is still perceived as an end-of-life care and PC services are only consulted very late in the disease trajectory.

iv) Integrating PC in CHF/COPD, where physicians are reluctant to engage to uncomfortable conversations, patients' avoid to accept "bad-news" and the overall taboo of death vis-à-vis the public image of CHF and COPD prevail, cannot follow the "one-size-fits-all" model. This gradual and long term

process can start by offering to patients the choice to know more about their condition.

Overall, we can confirm that integrated PC in CHF and COPD is not a myth. However, the process of integrating PC early and alongside standard care treatment is far from ideal. In this hospital this journey has just begun.

Future research recommendations

With the underrepresentation of the older population in our research, an important and complementary study would be to qualitatively examine the QoL and quality of care of this population with unstructured or semi-structured interviews. The results of such a study when combined with the results of chapter 6 can provide a better understanding of the needs of the overall population of CHF/COPD patients and informal caregivers.

With the perceptions of cardiologists and pulmonologists at hand a natural next step is to assess the perceptions of the other members of the health care personnel e.g. nurses, social workers, psychologists, pastoral consultants etc. Even though cardiologists and pulmonologists shape the policy of the wards with respect to PC, the realization of this policy is team work by all the personnel.

Finally, since we were unable to assess the effectiveness of our intervention, a future replication of an intervention phase, but without time limitation, should be performed. The future design of such a study should take into account the short hospitalizations and focus on the agility and flexibility of the involved intervention team.

Future practical recommendations

An always recurring theme in PC is the misconceptions about PC consisting care for the dying patient. In practice, we cannot expect substantial improvements on the integration of PC without the resolution of this issue and further it is not realistic to assume that such misconceptions are going to be internally resolved by the non-PC specialists alone. A first step for the resolution of this issue is for PC-specialists to provide a detailed informational update on integrated PC and its role to the CHF/COPD healthcare providers. Integrated PC educational training focusing on practical aspects should be initiated only after current misconception have been resolved.

Experience with integrated PC shows that its successful implementation does not depend on "general, high-level recommendations" from various medical societies and healthcare organizations, but on the establishment of an inter-professional network between the PC team and the CHF/COPD health care providers. We therefore recommend that a PC representative joins the multidisciplinary meetings of the cardiology/pulmonology wards so as to gradually be perceived as a permanent member of the team.

Our last recommendation concerns the optimization of future guidelines and pathways with respect to the determination of the referral criteria. The eligibility criteria that we have used for our intervention study have been proven quite robust. These criteria can be used directly as referral criteria of the exact timing of the initiation of early integrated PC.

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Summary

Chronic heart failure (CHF) and Chronic Obstructive Pulmonary Disease (COPD) are two prominent chronic conditions with severe physical and psychological symptoms that are projected to become the first and the third leading causes of death worldwide by 2030. Patients with CHF/COPD are amenable to palliative care (PC) services, however and despite recommendations from health care organizations and health care societies, access to PC for these patients remains limited and confined only in the end-of-life stage. The focus of this thesis is the theoretical and empirical investigation of early-integrated PC in CHF/COPD in Europe and in Belgium.

Chapter 1 provides the general introduction of this PhD thesis and presents a historical overview of PC and the state-of-the-art of integrated PC in CHF and COPD.

In **chapter 2** we present the objectives of this PhD thesis. This PhD project theoretically and empirically investigates the early integrated PC in patients with advanced CHF and COPD in Europe and in Belgium.

In **chapter 3** is concerned with a qualitative systematic literature review of empirically-tested models on integrated PC in patients with malignant and non-malignant disease in Europe. Even though we have identified only one model for CHF and none for COPD, the results for all the included models show a strong agreement on the benefits of the involvement of a PC multidisciplinary team: better symptom control, less caregiver burden, improvement in continuity and coordination of care, fewer admissions, cost effectiveness and patients dying in their preferred place. Based on these findings, we have additionally been able to develop a generic framework that consist of the basis for the design of future models for integrated PC in Europe. This framework fosters integration of PC in the disease trajectory concurrently with treatment and identifies the importance

of employing a PC-trained multidisciplinary team with a threefold focus: treatment, consulting and training.

In **chapter 4** we systematically review the literature for guidelines/pathways of integrated PC in patients with advanced CHF or COPD in Europe. For the evaluation of the content of the included guidelines/pathways we use a set of 11 IPC criteria that was developed based on previous literature and through consensus between the InSup-C project members. Our findings show that these guidelines/pathways thoroughly discuss aspects like the alleviation of physical/psychological symptoms, the holistic approach, the enhanced communication and the involvement of a multi-disciplinary PC team. On the negative side, fundamental aspects like referral criteria, advanced care planning and bereavement care are inadequately addressed and associated with unclear recommendations.

In **chapter 5** we examine whether the content of the available guidelines/pathways concerning integration of PC practices is different in cancer and in CHF/COPD and to see whether it constitutes a barrier for the improvement of the level of PC integration. For this reason, we perform a quantitative evaluation between integrated PC in published guidelines for cancer and CHF/COPD in Europe. The content of integrated PC in guidelines/pathways has been measured with a set of 11 PC criteria. The levels of integration between CHF/COPD and cancer guidelines/pathways have been shown to be statistically the same and moderate. Moreover, the quality of evidence utilized and the date of development of the guidelines/pathways appear not to impact upon the PC integration in the guidelines. Therefore, the content of the guidelines/pathways is inasmuch a barrier for the integration of PC in CHF/COPD as it is for cancer in Europe. Our findings also reveal that both CHF/COPD and cancer guidelines/pathways suffer from the same weaknesses: lack of bereavement care recommendations, unclear specification of timing of holistic assessment and more importantly infrequent specification and no appreciable consensus on referral criteria. Given the similarities detected between cancer

and CHF/COPD, other barriers appear to play a more prominent role for the further integration of PC.

In **chapter 6** we carry out a qualitative study h with the aim to explore perceptions of cardiologists (experts in CHF) and pulmonologists (experts in COPD) and current practices of integrated PC in patients with advanced CHF/COPD in Belgium. The participants of this study (cardiologists and pulmonologists, working in public hospitals in Belgium), have participated in semi-structured interviews based on integrated PC indicators. A total number of 22 CHF/COPD specialists have participated in the study. Our findings reveal that integrated PC and its potential benefits are viewed positively by the participants. However, even though a number of integrated PC components like the holistic approach via multidisciplinary teams, prognosis discussion and illness limitations, patient goals assessment, continuous goal adjustment, reduction of suffering and advanced care planning are partially implemented in several health centers, PC specialists are absent from such implementations and PC is still an end-of-life care. Misconceptions about PC and its association to death and end-of-life have been found to be decisive factors for the exclusion of PC specialists and the late initiation of PC itself. Improved education and enhanced communication is expected to alleviate existing challenges and thus improve the quality of life for the patients.

C**hapter 7** reports on the protocol of a feasibility prospective study in cardiology and pulmonology wards of UZ Leuven. The aim of this study is to explore whether an "Early Integrated PC" intervention can be performed in an acute setting and if it will have an effect on: i)the satisfaction of care and ii) the quality of life and the level of symptom control of CHF/COPD patients and their informal caregivers.

In **chapter 8** we explore i) the quality of life (QoL) and symptom control, ii) and the quality of care in CHF/COPD patients in an acute hospital setting. For this reason, eligible patients and their most significant informal caregiver filled in i) POS questionnaire that assesses

the QoL and the symptom control, ii) the CanHelp questionnaire that assesses quality of care and iii) a self-developed ad-hoc questionnaire that assesses quality of care and elements of advance care planning. These questionnaires have been completed at inclusion in the study and after a three-month follow-up. The majority of the CHF/COPD participants have been between 60 to 79 years old with mild to moderate symptomatology. Both patients and their informal caregivers share common and overall positive beliefs concerning patient's QoL and quality of care. Beliefs of both groups remain unchanged at both evaluation moments in the study. The severity of the healthcare condition of the included patients appears to be at odds with their positive evaluation of QoL and quality of care. Possible factors contributing to this finding might be the reluctance of physicians to engage to uncomfortable conversations, the patients' denial of "bad-news" and the overall taboo of communication about death. Resolving all these issues is a long-term process and the first step is to be proactive and to inform patients and family that they have the choice and the right to know more about their diagnosis and prognosis.

In **chapter 9** we assess the feasibility of the baseline phase and describe the challenges that emerged during the study and the lessons learned from conducting it. The feasibility assessment has been overall positive. The required sample size has been collected but older patients have been underrepresented. The majority of the participants are younger and with milder symptomatology. Despite the well-designed eligibility criteria, it has been necessary to readjust the recruitment process and directly involve the main researcher in the identification of eligible patients.

In **chapter 10** we provide the general discussion of this PhD thesis and an overview of future prospects based on this project.

Curriculum Vitae



EDUCATION AND TRAINING

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CONFERENCE POSTER PRESENTATIONS

Johan Menten, Karen Van Beek, Naouma Siouta (on behalf of InSup-C team). Patient-centered Integrated Palliative Care Pathways in Advanced Cancer and Chronic Disease: A Systematic Review. EAPC Congress, June 2014, Lleida. Spain.

Van Beek Karen, Siouta Naouma, Hughes Sean, Preston Nancy, van der Eerden Marlieke, Groot Marieke, Garralda Eduardo, Hodiamont Farina, Dybek Eva, Busa Csilla, Kiss Zsuzsanna, Payne Sheila, Ildiko Radvanyi, Hasselaar Jeroen, Centeno Carlos, Radbruch Lukas, Csikoska Agnes, Menten Johan. Integration of Palliative Care in Patients with Cancer in Europe. Where Do we Stand and what are the Challenges? EAPC Congress, May 2015, Copenhagen, Denmark.

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